Current Drug Metabolism 2007 vol.8 N2, pages 177-185

Modulation of neurotransmitter release by carbon monoxide at the frog neuro-muscular junction

Sitdikova G., Islamov R., Mukhamedyarov M., Permyakova V., Zefirov A., Palotás A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

Carbon monoxide (CO) is an endogenous gaseous messenger, which regulates numerous physiological functions in a wide variety of tissues. Using extracellular microelectrode recording from frog neuro-muscular preparation the mechanisms of exogenous and endogenous CO action on evoked quantal acetyl-choline (Ach) release were studied. It was shown that CO application increases Ach-release in dose-dependent manner without changes in pre-synaptic Na+ and K+ currents. The effect of exogenous CO on Ach-release was decreased by prior application of guanylate cyclase inhibitor ODQ and prevented by application of a cyclic guanylate monophospate (cGMP) analog 8Br-cGMP. Pre-treatment of the preparation with adenylate cyclase inhibitor MDL-12330A has completely abolished the effect of CO, whereas elevation of intracellular level of cyclic adenosine monophospate (cAMP) mimicked and eliminated CO action. Application of cGMP-activated phosphodiestherase-2 inhibitor EHNA did not prevent CO action, whereas inhibition of cGMP-inhibited phosphodiestherase-3 by quazinone has partially blocked the effect of CO. Utilizing immuno-histochemical methods CO-producing enzyme heme-oxygenase-2 (HO-2) was shown to be expressed in skeletal muscle fibers, mostly in subsarcolemmal region, karyolemma and sarcoplasmic reticulum. Zn-protoporphirin-IX, the selective HO-2 blocker, has depressed Ach-release, suggesting the tonic activating effect of endogenous CO on pre-synaptic function. These results suggest that facilitatory effect of CO on Ach-release is mediated by elevation of intracellular cAMP level due to activation of adenylate cyclase and decrease of cAMP breakdown. As such, endogenous skeletal muscle-derived CO mediates tonic retrograde up-regulation of neuro-transmitter release at the frog neuro-muscular junction. © 2007 Bentham Science Publishers Ltd.

http://dx.doi.org/10.2174/138920007779815940

Keywords

Acetyl-choline, cAMP, Carbon monoxide, Evoked acetyl-choline release, Heme-oxygenase 2, Neuro-muscular junction