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Inactivation of N-Type Calcium Current in Rat Sympathetic Neurons

Mi Sun Lee and Yong Sook Goo*

Dept. of Physiology, Chungbuk National Univ. Med. School, Cheongju, 361-763, Korea

Inactivation of N-type calcium current has been reported to be both voltage dependent and Ca^{2+} dependent. We have investigated the effects of Ba^{2+} and Ca^{2+} on N-channel inactivation in rat superior cervical ganglion neurons using the whole cell confuguration of patch clamp technique. Inactivation was larger in Ca^{2+} than in Ba^{2+} even with 20 mM BAPTA. which argues against a classic Ca^{2+} dependent inactivation mechanism. The inactivation vs voltage relationship was U-shaped in both divalent cations. This U-shape superficially appeared to mirror the amplitude of inward current. However, superimposing the inactivation-voltage and the current-voltage relationships shows that the inactivation curve is much broader and the peak of inactivation is shifted by 10 mV to the left of peak current in both Ba^{2+} and Ca^{2+}. In both Ba^{2+} and Ca^{2+}, substantial inactivation occurs at voltages generating little or no inward current. It has been shown that a purely voltage dependent mechanism can account for this U-shaped inactivation (Patil et al., 1998). The magnitude of Ca^{2+} effect on inactivation was inversely related with the magnitude of inactivation in Ba^{2+} as if the mechanisms of inactivation were the same in both Ba^{2+} and Ca^{2+}. In support of this idea, we could separate a fast ($\tau \sim 200$ ms) and a slow ($\tau \sim 2000$ ms) component of inactivation in both Ba^{2+} and Ca^{2+} using 5 sec pulses. To answer the existence of the divalent cation dependent inactivation, the effects of monovalent cation vs divalent cation on inactivation were investigated. For the experiment of monovalent cation, we used methylammonium (MA^+) chloride as charge carrier. With MA^+ external, the fractional inactivation at the end of 5 sec decreased significantly (0.34 ± 0.10 vs 0.66 ± 0.11 in 5 Ba^{2+}, $p<0.001$, $n=5$) and there was only single slow ($\tau > 2000$ ms) component of inactivation. These results suggest that the fast component of inactivation might be divalent cation dependent.