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Inactivation of N-Type Calcium Current in Rat Sympathetic Neurons

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Inactivation of N-type calcium current has been reported to be voltage dependent(Jones & Marks, 1989) and Ca^{2+} dependent(Cox & Dunlap, 1994). We examined inactivation by recording currents from the same cell both in $[Ba^{2+}]_o$ and $[Ca^{2+}]_o$ in rat sympathetic neurons. With 11 mM internal EGTA, fractional inactivation[1- (current amplitude at the end of 5 sec pulse/peak current amplitude)] was larger in Ca^{2+}(0.80 $\pm$ 0.07) than in Ba^{2+}(0.69 $\pm$ 0.10)(n=31, $p<0.001$), but the current traces were nicely fitted with two exponential components both in Ba^{2+} and Ca^{2+}. The presence of EGTA argues against a classic Ca^{2+} dependent mechanism for this enhancement. However, there are potential problems with the use of EGTA. First, the release of H^+ by EGTA during Ca^{2+} chelation could acidify the cell. Second, EGTA is relatively slow Ca^{2+} buffer, so $[Ca^{2+}]$ near the channel could increase during Ca^{2+} influx. To determine if these problems influenced our results, we repeated our experiments using 20 mM internal BAPTA. There were no statistical differences in inactivation between cells containing EGTA or BAPTA. With internal BAPTA, the current traces were also nicely fitted with two exponential components and fractional inactivation was also larger in Ca^{2+}(0.84 $\pm$ 0.04) than in Ba^{2+}(0.71 $\pm$ 0.04)(n=8, $p<0.001$). Our findings are not compatible with classic Ca^{2+} dependent inactivation mechanism with following reasons. First, it does not show strong Ca^{2+} selectivity. Not only in Ca^{2+} but also in Ba^{2+}, inactivation has two components even with 20 mM internal BAPTA. Second, the peak of inactivation was shifted by 10 mV to the left relative to the I-V peak for both in Ca^{2+} and Ba^{2+}. Our hypothesis is that Ca^{2+} exerts its effect by altering voltage dependent pathways to inactivation.

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