CGRP AND ADRENOMEDULLIN MODULATE SYNAPTIC TRANSMISSION IN PURKINJE CELLS

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Binding studies have demonstrated the presence of calcitonin gene-related peptide (CGRP) receptors in the cerebellum. There has been little work on the electrophysiology and pharmacology of CGRP in the cerebellum. We have assessed the effect of CGRP, adrenomedullin, and the antagonist CGRP₈₋₃₇ on synaptic transmission between parallel fibres (PFs) and Purkinje cells (PCs) and on spontaneous synaptic events (mEPSCs).

Sagittal cerebellar slices (200- μ m thick) were obtained from rats and whole-cell patch clamp recordings were made from PCs whilst stimulating PFs. The 10-min application of 50 and 10 nM CGRP significantly decreased EPSC amplitude (50 nM $76.95 \pm 7.11\%$, $n = 10$; 10 nM $77.38 \pm 7.11\%$, $n = 8$; $p < 0.01$). The effect of 10 nM CGRP was inhibited with 5-min preapplication of 1 μ M CGRP₈₋₃₇ ($106.03 \pm 9.29\%$, $n = 6$, $p < 0.01$) but not with 100 nM CGRP₈₋₃₇ ($79.91 \pm 5.61\%$, $n = 7$). However, 10 nM CGRP₈₋₃₇ alone significantly decreased EPSC amplitude similar to CGRP ($48.34 \pm 6.55\%$, $n = 5$, $p < 0.01$). In contrast, 50 nM adrenomedullin significantly increased EPSC amplitude ($143.58 \pm 24.5\%$, $n = 7$, $p < 0.01$).

10 nM CGRP increased the paired pulse ratio ($105.43 \pm 4.95\%$, $n = 6$) indicating the effect could be presynaptic. 50 nM CGRP significantly decreased the frequency of spontaneously evoked mEPSCs ($62.4 \pm 7.4\%$, $n = 5$, $p < 0.01$) but did not affect the amplitude.

This demonstrates that CGRP modulates EPSC responses following PF stimulation of PCs and can be blocked by CGRP₈₋₃₇. This effect is probably through CGRP receptors rather than through adrenomedullin receptors and is likely to be presynaptic