Modulation of synaptic transmission by omega-conotoxins CVID and CVIB in spinal superficial dorsal horn

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The selective blocker of N-type voltage-gated Ca2+ channels (VGCCs) CVID (Lewis *et al.*, 2000) and non-selective N- and P/Q- types antagonist, CVIB, are likely to be of interest as both research tools and potential anti-nociceptive agents. In the present study, the effects of these omega-conotoxins on synaptic transmission between primary Aδ and C primary afferents and dorsal horn superficial laminae neurons of rat spinal cord were tested by comparison of evoked excitatory postsynaptic currents (EPSCs) amplitude distributions in the absence and the presence of toxin. CVID (200 nM) completely inhibited both poly- and mono-synaptic EPSCs. CVIB (235 nM) reduced the mean of monosynaptic EPSCs amplitude distribution on average to 48 ± 8% ($n=5$, $p<0.02$) of control, without affecting the area of the distributions. In contrast, for polysynaptic transmission the area in the presence of CVIB was on average 55 ± 15% ($n=7$, $p<0.05$) of control. Given that N-type VGCCs are localised both pre- and post-synaptically and P/Q- VGCCs presynaptically (Murakami *et al.*, 2004), it can be hypothesised that: (i) CVID has higher affinity to postsynaptic N-type VGCCs in interneurons receiving nociceptive information than CVIB; (ii) CVIB predominantly blocks presynaptic P/Q-type VGCCs reducing the probability of transmitter release from interneurons; and (iii) synaptic transmission between primary afferents and superficial laminae neurons is mainly mediated by N-type VGCCs. Further investigation on the modulation of synaptic transmission in interneurons by omega-conotoxins is likely to reveal new information on mechanisms of propagation of nociception in superficial dorsal horn.

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