Subpopulations of CART immunoreactive fibres in the superficial laminae of the rat spinal cord

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Cocaine and amphetamine regulated transcript (CART) peptides are widely distributed in the central nervous system and have been implicated in the regulation of several physiological functions including pain modulation. The anatomical relationship of the CART-containing neuronal elements and the spinal sensory system, however, is unknown yet. We used immunohistochemistry with antibody against CART(55-102) together with markers for various populations of primary afferents, local interneurons and descending axons to study the distribution and origin of CART-containing fibres in the rat spinal cord.

Dense plexus of CART positive axons were located in lamina I and the lateral spinal nucleus. A few weakly stained cells and scattered terminals were also found in lamina II. CART cells and fibres also appeared around the central canal and in the lateral horn of the upper thoracic cord. This distribution could be followed from the cervical to the sacral segments. The majority of CART-erg axons contained both SP and CGRP in lamina I, which are characteristics for nociceptive primary afferents. Many of them were also labeled with galanin. In the dorsal root ganglions about 15% of small cells expressed CART. Many of them also contained both SP and CGRP. These results suggest that the majority of CART positive axons in the superficial laminae has primary afferent origin.

We also investigated the postsynaptic targets of CART positive axons in the superficial laminae. Projection cells in lamina I convey nociceptive and non-nociceptive information from the periphery to higher brain centres and most of them express NK1 receptor on which SP acts. Many CART terminals showed synaptophysin positivity and formed close apposition with NK1 immunoreactive dendrites. Projection neurons in lamina I have been identified by injection of retrograde tracer Cholera toxin β subunit into the lateral parabrachial nucleus where the majority of them terminate. Many cells received contacts from CART positive terminals that also contained SP.

The present results provide morphological evidence for the involvement of CART peptide in pain processing at the spinal level.