4th International Meeting on Calcitonin Gene-Related Peptide (CGRP)
TheScientificWorld (2001) 1(S1), 22
ISSN 1532-2246; DOI 10.1100/tsw.2001.439

ALTERED NEUROADAPTATION IN OPIATE DEPENDENCE AND NEUROGENIC INFLAMMATORY NOCICEPTION IN αCGRP DEFICIENT MICE

A.-M. Salmon, I.M. Damaj, L.M.Marubio, M.P. Epping-Jordan, E. Merlo Pich, and J.-P. Changeux
Institut Pasteur, Neurobiologie Moleculaire-Biotechnologie, 25 Rue du Dr. Roux, 75015 Paris, France

αCGRP is expressed in a variety of cell types in both central and peripheral nervous system[1]. Among its various functions, it is involved in the complex process of pain signaling[2,3]. Yet, the precise contribution of αCGRP is still unclear.

Using αCGRP deficient mice (-/-), we show that the lack of αCGRP underlies an attenuated response to chemical pain and inflammation[4]. In other words, αCGRP is critical for the production and, possibly, the transmission of pain signals associated with neurogenic inflammation. Furthermore, αCGRP -/- mice present a reduction in the antinociceptive response to morphine, indicating a modulatory role (agonist) of αCGRP in opioid pathways[5]. In contrast, the antinociceptive response to nicotine is potentiated, showing a negative modulation of nAChR function by this neuropeptide[4]. Thus, αCGRP has a complex role in the modulation of analgesic drug pathways.

Moreover, αCGRP -/- mice do not show changes in morphine self-administration and tolerance, but display a marked decrease in morphine withdrawal signs[4]. We suggest that αCGRP may influence the contribution of peripheral signals to the aversive emotional state occurring in the opiate dependence syndrome.

Taken together, these results show that αCGRP plays a critical role in mediating both chemical inflammatory pain and sensitivity to morphine withdrawal. Antagonists of αCGRP may thus offer novel therapeutics for the treatment of pain and drug addiction.

REFERENCES

1. Rosenfeld, M.G., Amara, S.G., and Evans, R.M. (1984) Science 225, 1315–1320.
2. Hughes, S.R. and Brain, S.D. (1991) J. Pharmacol. 104, 738–742.
3. Gibbins, I.L., Furness, J.B., and Costa, M. (1987) Cell Tissue Res. 248, 417–437.
4. Salmon, A.M. et al. (2001) Nature Neurosci. 4, 357–358.
5. Salmon, A.M. et al. (1999) NeuroReport 10, 849–854.