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Neuropeptide FF diminishes the number of apnoeas and cardiovascular effects produced with systemic administration of endomorphin-1

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Neuropeptide FF (NPFF) behaves as an endogenous opioid-modulation peptide that seems to be involved in opiate-induced tolerance and dependence and is thought to present strong inhibitory interaction with opioids. Although pharmacological properties of NPFF on pain perception and opioid-induced tolerance seem to be well documented, its effect on breathing pattern and respiratory depression induced by opioids remains unclear. The aim of the present study was to examine an impact of intravenous NPFF injection on respiration and its potency in elimination post-opioid apnoea. Experiments were performed on urethane-chloralose anaesthetized male Wistar rats breathing spontaneously room air. Respiratory parameters, arterial blood pressure and heart rate were measured. Rats were treated with an intravenous injection of NPFF in four doses: 0.1; 0.3; 0.6 and 1.2 mg/kg. Two minutes later, a dose of endomorphine-1 (EM-1) (50 μg/kg) was administered. Systemic injection of NPFF in doses: 0.1–0.6 mg/kg evoked only dose dependent hypertensive effect. The highest dose caused also a short-lived reduction in tidal volume, which affected minute ventilation immediately after the challenge and evoked a single episode of apnoea in one rat lasting 3.7 s. Bolus injection of 50 μg/kg of endomorphin-1 was administered into the femoral vein of control animals without NPFF pre-treatment evoked apnoea in 5 of 6 rats of mean duration of 11.2±1.2 s, short-lived hypotension and a slow down in the heart rate. Pre-treatment with NPFF diminished the number of post-endomorphin-1 apnoeas, to 2 in 5 rats at a dose of 0.1–0.3 mg/kg and to 1 in 5 animals at a dose of 0.6 mg/kg. EM-1 induced hypotensive effects and decrease in the heart rate were also reduced at all tested doses of NPFF. Our experiments showed that stimulation of neuropeptide FF receptors in the periphery diminishes the number of EM-1-induced arrests of breathing, as well as its hypotensive effect.

Recent Publications

1. Li N, Han Z L, Wang Z L, Xing Y H, Sun Y L, et al. (2016) BN-9, a chimeric peptide with mixed opioid and neuropeptide FF receptor agonistic properties, produces nontolerance-forming antinociception in mice. Br J Pharmacol. 173(11):1864–80.
2. Lin Y T, Kao S C, Day Y J, Chang C C and Chen J C (2016) Altered nociception and morphine tolerance in neuropeptide FF receptor type 2 over-expressing mice. Eur J Pain. 20(6):895–906.
3. Ayachi S and Simonin F (2014) Involvement of mammalian RF-amide peptides and their receptors in the modulation of nociception in rodents. Front Endocrinol (Lausanne) 5:158.
4. Moulédous L, Mollereau C and Zajac J M (2010) Opioid-modulating properties of the neuropeptide FF system. Biofactors 36(6):423–9.

Biography

Piotr Wojciechowski is an Assistant in the Department of Respiration Physiology, Mossakowski Medical Research Centre, Warsaw, Poland. His interests scope within the crosstalk and interaction between neuropeptide and opioid systems and their effects on cardio-respiratory pattern.

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