

EFFECT OF NOVEL NOCICEPTIN/ORPHANIN FQ–NOP RECEPTOR LIGANDS ON FOOD INTAKE IN WISTAR RATS

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Activation of the NOP receptor by the endogenous ligand nociceptin/orphanin FQ (N/OFQ) stimulates feeding in freely feeding rats (2). The present study evaluated the effect of two newly synthesized peptidergic NOP receptor agonists and one NOP receptor antagonist on food intake.

[(pF)Phe⁴Aib⁷Arg¹⁴Lys¹⁵]N/OFQ-NH₂ (UFP-112) has been designed as a novel peptide ligand for the N/OFQ peptide receptor (NOP) (Calò, personal communication) by combining into the same peptide sequence several different chemical modifications previously reported to increase N/OFQ potency. In vitro data obtained in the electrically stimulated mouse vas deferens demonstrated that UFP-112 behaved as a full agonist at the NOP receptor displaying very high potency (pEC₅₀ 9.43). UFP-113 ([F/G(pF)Phe⁴Aib⁷Arg¹⁴Lys¹⁵]N/OFQ-NH₂) has been designed as a partial agonist at the NOP receptor (Calò, personal communication).

Freely feeding Wistar rats were injected into the brain lateral ventricle with the NOP receptor agonists UFP-112 (0.01, 0.03, 0.05 and 0.1 nmol/μl), UFP-113 (0.03, 0.05, 0.2, and 0.4 nmol/μl) alone or with the pre-treatment with NOP receptor antagonist UFP-101 ([Nphe¹,Arg¹⁴,Lys¹⁵]N/OFQ NH₂) (7.4, 10 and 20 nmol/μl).

Results showed that UFP-112 produced, starting from the dose of 0.03 nmol/μl, a potent and far more pronounced hyperphagic effect than that of N/OFQ 4.2 nmol/μl. The partial agonist UFP-113 produced a significant increase in food intake starting from the dose of 0.05 nmol/μl. As already known the NOP receptor antagonist UFP-101 did not modify feeding in freely feeding rats (1). Tested at the dose of 20 nmol/μl, against UFP-112 (0.05 nmol/μl), it significantly reduced its hyperphagic effect, while it significantly reduced, at the dose of 10 nmol/μl the hyperphagic effect of UFP-113 (0.2 nmol/μl). The present findings indicate that UFP-112, UFP-113 may act as potent and long-lasting NOP receptor agonists. Overall, the results indicate that these compounds may represent valuable pharmacological tools to investigate the functional role of the brain N/OFQ system.

[1] Economidou D, Policani F, Angellotti T, Massi M, Terada T, Ciccocioppo R.. Peptides. 2006; 27:775-783

[2] Pomonis JD, Billington CJ, Levine AS. Neuroreport. 1996; 8:369-371.