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Effects of central RVD-Hemopressin (α) adminitrationon anxiety, feeding behavior and hypothalamic neuromodulators in the rat

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The endocannabinoid (eCB) system plays an important role in mood disorders, as such anxiety and depression. In addition, the eCB system is involved in the regulation of food intake, metabolism and calorie storage. However, it is well known that the first generation of CB1 blockers designed to reduce food intake and body weight, such as Rimonabant, was discontinued due to psychiatric disorders, such as anxiety and depression. The discovery of RVD-hemopressin(α) [RVD-hp(α)], an hemoglobin α chain-derived peptide, revealed a promising research field for the pharmacotherapy of obesity. RVD-hp(α) was found to bind CB1 receptors, as negative allosteric modulator and as a positive allosteric modulator of CB2 receptor. In addition, pharmacological evidences reported a possible link between brain hypocretin/orexin, monoamine and eCB systems, as regards appetite and emotional behavior control. Considering this, the aim of our work was to investigated the effects of RVD-hp(α) on anxiety like behavior and food intake after central administration and related it to monoamine levels, proopiomelanocortin (POMC) and orexin-A gene expression, in the hypothalamus. We have studied the effects of central RVD-hp(α) (10 nmol) injection on anxiety-like behavior and feeding using different behavioral tests. Hypothalamic levels of norepinephrine (NE), dopamine (DA) and serotonin (5--HT) and gene expression of orexin-A and POMC were measured by high performance liquid chromatography (HPLC) and real-time reverse transcription polymerase chain reaction (RT-PCR) analysis, respectively. Central RVD-hp(α) administration decreased locomotion activity and stereotypies. Moreover, RVD-hp(α) treatment inhibited anxiogenic-like behavior and food intake, NE levels and orexin-A gene expression, in the hypothalamus. Concluding, in the present study we demonstrated that central RVD-hp(α) induced anxiolytic and anorexigenic effects possibly related to reduced NE and orexin-A and POMC signaling, in the hypothalamus. These findings further support the central role of the peptide in rat brain thus representing an innovative pharmacological approach for designing new anorexigenic drugs targeting eCB system.

Recent Publications

1. Leone S, Recinella L, Chiavaroli A, Martinotti S, Ferrante C, Mollica A, et al. (2017) Emotional disorders induced by Hemopressin and RVD-hemopressin(α) administration in rats. Pharmacol Rep.69:1247–1253.
2. Ferrante C, Recinella L, Leone S, Chiavaroli A, Di Nisio C, Martinotti S, et al. (2017) Anorexigenic effects induced by RVD-hemopressin(α) administration. Pharmacol Rep. 69:1402–1407.
3. Rubino T, Zamberletti E, Parolaro D (2015) Endocannabinoids and Mental Disorders. Handb Exp Pharmacol. 231:261–83.
4. Gatta-Cherifi B, Cota D (2016) New insights on the role of the endocannabinoid system in the regulation of energy balance. Int J Obes (Lond). 40:210–9.
5. Dodd GT, Mancini G, Lutz B, Luckman SM. (2010) The peptide hemopressin acts through CB1 cannabinoid receptors to reduce food intake in rats and mice. J Neurosci 30:7369–76.

Biography

Sheila Leone had completed Medicine & Surgery degree and Post-graduated in Clinical Pharmacology from University of Modena and Reggio Emilia (Modena, Italy) She worked as assistant professor of Pharmacology (BIO/14), Department of Pharmacy from University of Chieti "G. D'Annunzio" (Chieti, Italy). The research activity is mainly focus on neuropharmacology, cardiopharmacology, endocrinology and behavior of synthetic and vegetal drugs. Department of Pharmacy, University "G.d'Annunzio" Chieti-Pescara (Chieti, Italy). Author of papers (for the most part in international journals) and communications at National and International Congresses.

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