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COMPARATIVE ANALYSIS OF THE EFFECTS OF GHRELIN ANTAGONISTS ON THE EATING BEHAVIOR OF RATS IN A MODEL OF COMPULSIVE OVEREATING UNDER STRESS

Netesa M.A. (Institute of experimental medicine),
Afolabi S.O. (ITMO University)
Scientific Supervisor: Prof. Dr. Shityakov S.V. (ITMO University)
Prof. Dr. Lebedev A.A. (Institute of experimental medicine)

Introduction

Addictions are becoming an increasingly common problem today; at the same time, they pose a serious threat to life and health. Stress is an integral part of everyday life, stimulating the production of various neuropeptides, including ghrelin, and contributing to the formation of addictions [1]. The peptide hormone ghrelin is involved in the regulation of a wide variety of processes, including the processing of food reward signals and the formation of food addiction [2].

Main part

The aim of the study was to conduct a comparative analysis of the impacts of ghrelin receptor antagonists by assessing their effect on the feeding behavior of rats with food addiction during stress and calculating their binding energy to the ghrelin receptor in silico. As an eating behavior model the compulsive overeating of high-calorie foods submitted by a mixture of Nutella chocolate paste (Ferrero, Alba, Turin, and Italy), ground rat pellet food (4RF18 ;Mucedola; Settimo Milanese), and water in 0.52:0.33:0.15 proportion was chosen [3]. 15 minutes before feeding the mixture, rats receive an olfactory stimulus of a treat, which is then consumed within 1 hour. The mixture is given every second day and the formation of addictive behavior takes 25 days. For stress developing an electrical stimulation of limbs [4] was employed. The electrical stimulation was given with a current of 0.6 mA for 1 minute in an hour before the feeding with a treat once a week. After 30 minutes post stress rats was intranasal administered with D-Lys3-GHRP-6 (Tocris, England), YIL 781 (Tocris, England) and agrelax (Institute of Experimental Medicine, Russia) in concentrations of 10 mg in 10 ml (10 ml in each nostril). For receptor structure prediction the web-site https://robetta.bakerlab.org/ [5] and for binding site calculation the http://sts.bioe.uic.edu/castp/ [6] were used. AutoDock 4 was employed to prepare the molecular docking [7].

The amount of Nutella chocolate paste mixture eaten was: 15.8±0.5 g without and 18.6±0.9 g after stress, as well as 16.2±0.9, 13.2±0.9 and 13.0±0.9 after the administration of D-Lys3-GHRP-6, YIL 781 and agrelax, respectively. The binding energy was -4.29 kcal/mol for D-Lys3-GHRP-6, -7.88 for YIL 781 and -7.75 for agrelax.

Conclusion

Agrelax and YIL 781 had a greater effect on the eating behavior of rats in the model of compulsive overeating of high-calorie foods relative to D-Lys3-GHRP-6, while the results in vivo and in silico correlated well.

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