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PREVENTION OF EATING BEHAVIOR DISORDERS BY INDIRECT BALANCING OF ACTIVATING AND REWARD SYSTEMS

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The aim is to experimentally test the practical approach for optimizing eating behavior and preventing obesity and metabolic disorders by indirect balancing of activating and reward systems. We applied video surveillance of the eating behavior of male laboratory animals (rats) (n = 20) with a body mass between 250–280 g raised and maintained in the standard conditions of alimentation ration with *ad libitum* access to food and water. Activating and reward systems relationships were indirectly evaluated by neuropsychological assessment based on emotion profile measurements according to the guide (Rat Grimace Scale (RGS): The manual). Multi sensory stimulation in the enriched environment associated with hedonic eating initiated a significant increased indices of physical activity, acts of eating and searching behavior, action units of (AU) that express positive emotional status through psychomotor reactions and acts of grooming and relaxation. The arrangement of the environment naturally (area of land along forest river or lake), the promotion of individualized activities based on the consolidation of sensorimotor integration that produces a hedonic action, generates the balancing of the energy metabolism on the background of the formation of the alternative addiction. Neuroplasticity in the neural circuit of the activation and the reward systems determines the motivated behavior under centripetal and centrifugal influences.

Keywords: eating behavior, activating reward systems.

INTRODUCTION

Since the seventeenth century it has been suggested that emotional stress plays a role in the etiology of type 2 diabetes, and depression is a risk factor for the development of diabetes mellitus. Not only depression but also general emotional stress with anxiety, sleep problems, anger, and hostility are associated with an increased risk for the genesis of metabolic disorders and type 2 diabetes. The neuropsychological etiology of eating behavior disorders is complex, persistent, and difficult to treat. Problems associated with metabolic imbalance, non-optimized body weight and body composition are mainly solved pharmaceutically and taking into account nutritional factors, whereas the cognitive and psycho-emotional profile of the individual is a superstructural determinant and the most difficult to correct factor. The epidemiology of bulimia and anorexia nervosa proves the close dependence of eating behavior on the personal psycho-emotional status. Fine adjustment of the activity of the neuronal circuit system including the orexinergic lateral area of the hypothalamus (LH), the dopaminergic center in the ventral tegmental area (VTA), its axonal projections to the nucleus accumbens (NAc), and GABAergic negative feedback from NAc to LH is urgently needed for coordinating eating behavior, expression of emotions, motivation, digestion and nutrient absorption. The initiation and maintenance of the activity of these activating and reward systems is determined by the perception and recognition of multi sensory signals from the external environment and neurohumoral signals from the internal environment during feeding. The orexinergic activating system that ensures the regulation of the motivated behavior, the mesolimbic and mesocortical reward systems that modulate the activity of the upper cerebral formations are chemosensitive to the fluctuations of the glucose concentration in the blood circulation. It is important that eating high-

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carbohydrate foods and drug abuse act similarly and cause addictive behavior[1]. The energy balance centripetally coordinates the LH-VTA-NAc-LH neural circuit through leptin[2] and ghrelin[3,4,5,6]. The sensitivity of this neural circuit is reduced in the case of food excess and obesity. The sensitivity threshold of the reward system increases as a result of consuming foods with a hedonic character, which facilitates the genesis of overeating and addictions[1]. Thus, peripheral signals come from metabolic and hormonal stimuli (glucose, leptin, ghrelin)[7]. The trigger of the activity of the orexinergic activating system is hunger on the background of a reduced concentration of glucose in the blood inflow to the hypothalamus, whereas the launch of the reward system in the search for and consumption of food is provided by a complex of reflector sensory signals that characterize the hedonic (palatable) properties of the food consumed (pleasant appearance, aroma and taste)[8]. Proportional relationships were found between the concentration of sucrose in the food consumed and the intensity of dopamine release in the terminals of DA-ergic neurons projecting from VTA to NAc. It was found that food rich in fats also activates DA-ergic neurons of the mesolimbic reward system. Shifts in the activity of the mesolimbic reward system are also manifested at the level of dopamine receptors as an increase in the binding capacity of D1 receptors on NAc neurons both in the core and in the membrane of this nucleus when eating tasty appetizing food[9]. It is for interest that other forms of behavior (sexual behavior, exercise, social play) also trigger the mechanisms of action of the reward systems: mesolimbic and mesocortical[8]. These forms of behavior and eating behavior induce neural interactions that close the activating system of the lateral hypothalamus and the mesolimbic reward system into a single coordinating mechanism. Insufficient activity of the mechanisms of interaction between the activating system and the reward system can lead to the development of anhedonia. In the case of anhedonia the predominance of motivated behavioral activity causing a feeling of pleasure, satisfaction and delight is reduced. As it is known, orexinergic LHA neurons project their axons directly to VTA dopaminergic neurons and receive collaterals of GABAergic inhibitory needle neurons NAc. However, axons of glutamatergic neurons are also projected from the LHA to the VTA[10,11,12,13]. The aim is to experimentally test the practical approach for optimizing eating behavior and preventing obesity and metabolic disorders by indirect balancing of activating and reward systems.

MATERIALS AND METHODS

An experimental model in laboratory animals (rat) was applied for indirect testing of activating and reward central systems relationships during eating behavior by means of facial psychomotor reaction evaluation. We utilized video surveillance of the eating behavior of male laboratory rats (n = 20) with a body mass between 250–280 g raised and maintained in the standard conditions of alimentation ration with *ad libitum* access to food and water with lighting from 8:00 a.m. to 06:00 p.m. At least 3 days before the start of the experiment, for the purpose of adaptation, the experimental (n = 10) and control (n = 10) animals were placed in cages equipped with a dosed feeder and drinker. Control and experimental animals were subjected to food deprivation for 24 hours before the start of the experiment to initiate motivation. During the experiment, the control group was kept on a standard diet, and the animals of the experimental group alternated the use of various foods they preferred: meat, fish, cottage cheese, eggs, dried sunflower and pumpkin seeds, wheat grains, oatmeal, beets, carrots, apples. The condition was met: the daily diet for experimental animals for 5 days should never be repeated, providing the effect of novelty and attractiveness. The set of products met the requirements highlighted in international publications[14,15]. Neuropsychological assessment was based on mood and emotion profile measurements: the duration and frequency of grooming acts, the duration of the relaxed position and the action units (AU) characteristic for certain emotional expressions according to the guide (Rat Grimace Scale (RGS): The manual)[16]. To estimate by morphometric analysis of the expression of emotions in laboratory animals, the following criteria were used: opening and bulging of the eyes; raising and movement of vibrissae; flattening of the nose and cheeks; the location of the auricles relative to the head; wrinkling and color of the inner surface of the auricles; as well as arching the back; lifting of hair and tension of the fingers. Quantitative measurements of the expression of emotions in the head area of the animal included the determination of: 1 – the ratio of the height and length of the eyeball; 2 – the ratio of the height and length of the eyebrows; 3 – the angle of inclination of the eyebrows; 4 – the angle of the auricles relative to the head (Fig. 1).

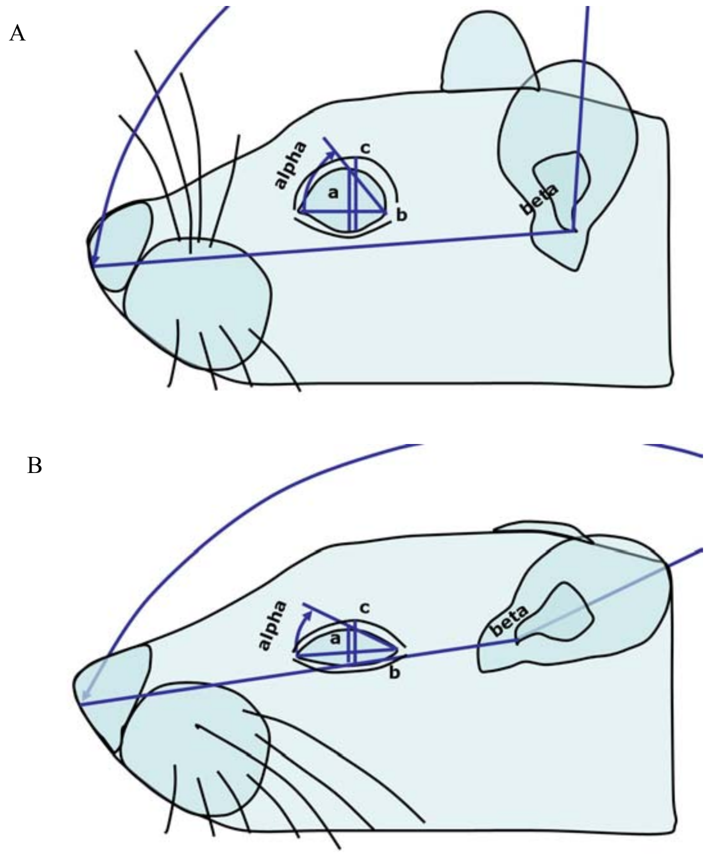

Figure 1. Morphometric indices used to quantify the expression of emotions in laboratory animal (rat): A – the manifestation of relaxation and pleasure; B – manifestation of tension and pain; a – eye height; b – the width of the eye; c – eyebrow height; alpha – the angle of inclination of the eyebrows; beta – the angle of inclination of the auricle.

In combination with experimental research in laboratory animals we performed the measurements of certain movements in areas of the face (facial psychomotor reactions) in voluntary healthy human beings, placing the serial face images in a coordinate system and plotting points on the key most mobile areas. Considering the anatomy of facial muscles when identifying each point on the face we applied Facial Action Coding System (FACS). FACS is a methodology that allows classification, qualitative and quantitative evaluation of the mimic psychomotor reaction of a person when his emotion profile is changed[17,18]. Personal eating behavior was assessed by the application of the questionnaire (Adult Eating Behavior Questionnaire, AEBQ) in humans[19].

The experimental model of the prophylaxis practical approach consists of placing the animals in cages with the multi sensory enriched environment (Environmental Enrichment, EE) and feeding them with hedonic foods on the background of nutritional deprivation. Alternatively, in healthy humans this practical approach for prevention of obesity and metabolic disorders can be health promoting and realized at the recreation and training summer camp under natural forest river environment conditions.

The statistical analysis was performed with the application of the ANOVA test and by the use of the Student criterion and the non-parametric Wilkoson criterion.

RESULTS AND DISCUSSION

Multi sensory stimulation in the enriched environment associated with hedonic eating in limited quantities initiated a significant increase in the frequency and duration of physical activity, acts of eating and searching behavior, action units of (AU) that express positive emotional status through psychomotor reactions and acts of grooming and relaxation.

Our quantitative morphometric measurements of the expression of emotions in the head region of the animal also confirm the presence of significant changes in motivated eating behavior based on the consumption of hedonic food. The ratio of the height and length of the eyeball undergoes a shift in the direction of its increase (from 0.832 to 0.955; 0.960 and 0.947, P <0.05, on the 1st, 3rd and 5th day of the hedonic diet, respectively). The ratio of eyebrow height and length increases associated with a similar ratio for the eyes (from 1.187 to 1.235; 1.245 and 1.252, P <0.05, on the 1st, 3rd and 5th day of the hedonic diet, respectively). Shifts in the angle of inclination of the eyebrows are very indicative for the expression of positive and negative emotions; under these experimental conditions in the course of eating behavior, the angle changed from 41.2° to 46.3°; 46.8° and 47.3°, P <0.05, on the 1st, 3rd and 5th day of the hedonic diet consumption, respectively). The angle of the auricles relative to the head also significantly changed with pronounced dynamics from 110.2° to 136.0°; 133.0° and 131.8°, P <0.05, on the 1st, 3rd and 5th days, respectively.

An unexpected transition to a diet based on the pronounced hedonic properties of the food consumed immediately affects the emotional profile of the experimental animal. This psychomotor reaction manifested central reward system triggering. Unfortunately, most of the works devoted to the recognition of emotions in laboratory animals describe the response to pain associated with the activation of the nocicetive systems of the body, while the expression of positive emotions, reflecting the induction of the activity of the reward system, is little represented in the literature[16].

The comparison of the indices of eating behavior in students of the Faculty of Physical Education and Sports during the summer camp recreation and training program and in those of the Faculty of Natural Sciences non-trained persons manifested an improvement of nutrition and neuropsychological indices in athletes. Indices of the aerobic abilities of the body are authentically increased in individuals who have undergone summer camp in comparison with non-trained persons. Pulse oximetry obtained results revealed a shift in blood oxygen saturation in the dynamics of aerobic effort after camp training program on the forest river bank. In combination with favorable adaptive changes in the gas exchange system psychomotor mimic reactions of individuals demonstrates the predominance of facial movements in the area of muscles localization: *m. zigomaticus major* and *m. buccinator* (Action Unit, AU12 – pleasure expression), proving the maintenance of a positive emotional state. Moreover, in response to imitation of a threatening environment (disaster video presentation) the manifestation of facial movements in the muscles area: *m. corrugator supercilii* and *m. orbicularis oculi* (AU4 – fear expression) is significantly reduced.

CONCLUSION

Thus, the arrangement of the environment naturally (area of landscape along forest river-lake bank or environmental enrichment for laboratory animals), the promotion of individualized locomotor activities based on the consolidation of sensorimotor integration could produce an essential hedonic action. This hedonic effect of novel changed life style indirectly generates a balance of central activating and reward systems activity. As a result, optimized eating behavior is stabilized on the background of the formation of alternative addiction.

Neuroplasticity in the neural circuit of the activating and the reward systems determines the motivated attention focused behavior under centripetal and centrifugal influences.

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REFERENCES

1. Kenny, P.J. Reward Mechanisms in Obesity: New Insights and Future Directions. *Neuron*. 2011, **69**(4), 664–679.
2. Leshan, R.L., Opland, D.M., Louis, G.W., Leinninger, G.M., Patterson, C.M., Rhodes, C.J., Münzberg, H., Myers, M.G.Jr. Ventral tegmental area leptin receptor neurons specifically project to and regulate cocaine-and amphetamine-regulated transcript neurons of the extended central amygdala. *J Neurosci*. 2010, **30**, 5713–5723.
3. Abizaid, A., Liu, Z.W., Andrews, Z.B., Shanabrough, M., Borok, E., Elsworth, J.D., Roth, R.H., Sleeman, M.W., Picciotto, M.R., Tschöp, M.H., et al. Ghrelin modulates the activity and synaptic input organization of midbrain dopamine neurons while promoting appetite. *J Clin Invest*. 2006b, **116**, 3229–3239.
4. Jerlhag, E., Egecioglu, E., Dickson, S.L., Andersson, M., Svensson, L., Engel, J.A. Ghrelin stimulates locomotor activity and accumbal dopamine-overflow via central cholinergic systems in mice: Implications for its involvement in brain reward. *Addict Biol*. 2006, **11**, 45–54.
5. Jerlhag, E., Egecioglu, E., Dickson, S.L., Douhan, A., Svensson, L., Engel, J.A. Ghrelin administration into tegmental areas stimulates locomotor activity and increases extracellular concentration of dopamine in the nucleus accumbens. *Addict Biol*. 2007, **12**, 6–16.

6. Perello, M., Sakata, I., Birnbaum, S., Chuang, J.C., Osborne-Lawrence, S., Rovinsky, S.A., Woloszyn, J., Yanagisawa, M., Lutter, M., Zigman, J.M. Ghrelin increases the rewarding value of high-fat diet in an orexin-dependent manner. *Biol Psychiatry*. 2010, **67**, 880–886.
7. DiLeone, R.J., Narayanan, N.S., Guarnieri, D.J. Feeding as a Reward Mechanism. *Sleep Loss and Obesity*. 2012, 47-60.
8. Harb, M.R., Sousa, N., Zihl, J., and Osborne, A.F.X. Reward components of feeding behavior are preserved during mouse aging. *Front. Aging Neurosci*. 2014, **6**, p. 242.
9. Watson, R.R., Preedy, V.R., Zibadi, S. Chocolate in Health and Nutrition. New York: Humana Press. Springer, London: Heidelberg Dordrecht. 2013, 552 p.
10. Russo, S.J. and Nestler, E.J. The Brain Reward Circuitry in Mood Disorders. *Nature Reviews Neuroscience*. 2013, **14**(9), 609-625.
11. Dallman, M.F., Pecoraro, N., Akana, S.F., La Fleur, S.E., Gomez, F., Houshyar, H., Bell, M.E., Bhatnagar, S., Laugero, K.D., Manalo, S. Chronic stress and obesity: A new view of "comfort food". *Proc Natl Acad Sci USA*. 2003, **100**, 11696–11701.
12. Macht, M., Mueller, J. Immediate effects of chocolate on experimentally induced mood states. *Appetite*. 2007, **49**, 667–674.
13. Imaizumi, M., Takeda, M., Suzuki, A., Sawano, S., Fushiki, T. Preference for high-fat food in mice: Fried potatoes compared with boiled potatoes. *Appetite*. 2001, **36**, 237–238.
14. Guide for the care and use of laboratory animals. National Research Council. Eighth Edition. Washington (D.C.): The National Academies Press (USA), 2011, 220 p.
15. Nutrient Requirements of Laboratory Animals. National Research Council. Fourth Revised Edition. Washington (DC): The National Academies Press (USA), 1995, 192 p.
16. Sotocinal, S.G. et al. The rat grimace scale: a partially automated method for quantifying pain in the laboratory rat via facial expressions. *Mol. Pain*. 2011, **7**, p. 55.
17. Ekman, P. and Friesen, W. Facial Action Coding System: A Technique for the Measurement of Facial Movement. Consulting Psychologists Press, Palo Alto, 1978.
18. Friesen, W., Ekman, P. EMFACS-7: Emotional Facial Action Coding System. Unpublished manual, University of California, California, 1983.
19. Hunot, C., Fildes, A., Croker, H., Llewellyn, C.H., Wardle, J., Beeken, R.J. Appetitive traits and relationships with BMI in adults: development of the adult Eating Behaviour Questionnaire. *Appetite*. 2016, **105**, 356-363.