

Opioids, Substance P and Some Other Delicate Neurochemical Regulators of Body Weight and Appetite

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Mini Review

Obesity is one of the biggest challenges in the modern world. It is an established risk factor in the development of a variety of metabolic conditions such as metabolic syndrome, diabetes mellitus, cardiovascular diseases and others. By its nature obesity is heterogeneous condition and a wide range of factors are included in its etiology. It has specific neurobiological base in which the system of rewards has an important biological role. In recent years growing body of literature demonstrated neurobiological and behavioral relationships between food intake, drug addiction and withdrawal syndrome [1-3].

Directly involved in the sense of pleasure, opioid receptors and endogenous opioid peptides are main "players" in functioning of reward and pleasure system. The results of numerous studies provided evidence of interaction between different subtypes of opioid receptors and systems that regulate energy balance. According to the results of recent studies, obesity is closely related to aberrations in opioidergic neurotransmission, thus, correlating with the changes in the number of opioid receptors in the brain. Recent data provided convincing evidence on participation of opioidergic neurotransmission in feeding behavior. In this regard, it is necessary to note that the number of opioid receptors in corpus striatum and thalamus and body mass index (BMI) are inversely related. In patients suffering from obesity elevated plasma concentrations of β -endorphin have been demonstrated. Moreover, opiate receptor antagonists prevented development of obesity in genetically obese experimental animals [4,5].

Presumably, the failure of opioid receptors is the main reason of overeating as an attempt to compensate the lack of positive emotions. In this regard there is enough evidence, indicating the involvement of opioidergic neurotransmission in the regulation of nutritional practices and obesity. Whether abnormalities in the endogenous opioid system play a primary role in overfeeding and weight gain or represent one of the numerous biochemical consequences of this metabolic state is still unclear. Understanding the role of opioids mediating food reward and promoting the overconsumption of appetising food may provide insights into new approaches to prevent obesity.

Dopaminergic receptor system has been given a leading role in regulation of reward and motivation system associated processes. Moreover, its functioning is closely interrelated with cognitive functions. Substantial data obtained recently argue in favor of participation of dopaminergic neurotransmission in nutritional practices [6]. Interestingly, it has been demonstrated, that the main regulators of hunger and satiety, such as ghrelin, leptin and insulin, which participate in development of feeding behavior development, affected the dopaminergic system [7]. Moreover, it is quite remarkable that proopiomelanocortin (POMC), the anorexigenic hypothalamic regulator of food uptake, simultaneously is the precursor of some endogenous opioid peptides. Substance P (SP), a member of tachykinin peptide family, is expressed in the central nervous system, as well as in peripheral tissues, including the gastrointestinal tract, blood vessels and immune system. SP interacts with G-protein coupled neurokinin (NK) receptors, particularly, with NK-1R, which was found to have the highest affinity to it. NK-1 is involved in different neurophysiological processes, and a role for pharmacological antagonists of NK-1R has been proposed in treating some stress conditions and emotional disorders, such as depression and anxiety.

The fact of the presence of substance P in certain sections of the digestive tract and in the areas of the hypothalamus, responsible for regulation of feeding behavior, such as arcuate nucleus and nucleus ventricularis, in conjunction with the presence of NK receptors in corresponding areas of the hypothalamus, provide an additional evidence of the involvement of this compound in the regulation of nutrition [8]. Substance P have been shown to play an important role in the regulation of eating behavior and motivation. Orexigenic effect of SP has been proposed by some investigators, moreover, a significant decrease in body weight and increase in glucose utilization and sensitivity to insulin effect mediated by NK-1 receptors antagonist action has been demonstrated, which suggests that substance P and NK-1 receptor could be considered as effective targets for counteracting obesity.

Polymorphism of the genes, underlying the functioning of the above-mentioned receptor systems, obviously is of great interest in terms of the predisposition to obesity among subjects

belonging to different gene populations. It seems particularly promising in the context of the interconnection between childhood food addiction syndrome and parental feeding practice [9,10].

Further development of research in the field of neurochemistry of obesity will allow scientists to approach a qualitatively new interpretation of the social-behavioral aspects of obesity from the point of view of cause-effect relationships. This has a potential to contribute to the development of effective novel pharmacological strategy to control the obesity epidemics.

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