Preclinical effects of oleoylethanolamide on normal food intake and on frustration stress-induced binge-like palatable food consumption: possible implications for eating disorders

S. Gaetani

Dip. di Fisiologia e Farmacologia "V. Erspamer",Sapienza Università di Roma,P.le Aldo Moro, 5 - 00185 Roma

Eating disorders and obesity are disorders of complex, unknown etiology with a high morbidity, a wide and complicated range of causes and manifestations and a high mortality. Recently, a growing body of evidence have witnessed that neurobiological vulnerabilities make a substantial contribution to the pathogenesis of these disorders.
Many studies have analyzed how and why voluntary behaviors, such as eating larger amounts of food than usual, at some point move beyond control in some people and develop into an eating disorder. Of course, unhealthy eating habits are the necessary precondition for disease development, however alterations of the endogenous mechanisms that modulate food intake and energy balance play a dramatic role in controlling individual vulnerability.
Current treatments for obesity and eating disorders lack sufficient efficacy and are complicated by high relapse rates and a wide range of side effects, thus highlighting the need to identify novel pharmacological targets that could lead to the development of more effective and safer therapies. Research efforts have produced a large body of evidence on the role played by pathways and mechanisms underlying the nutrient-induced regulation of energy intake, as well as the changes, both peripherally and in the central nervous system, brought about by the consumption of high-fat, energy-dense diets.
Among these mechanisms, we have been focusing on the role played by the lipid signal oleoylethanolamide (OEA). OEA acts as a satiety signal, which is generated in the intestine, upon the ingestion of fat, and ends in the central nervous system. In the intestine OEA activates peroxisome proliferator-activated receptor-alpha (PPAR-alpha) that plays an important role for the absorption, storage, and use of dietary fat. At the brain level different neuronal pathways, including oxytocinergic, noradrenergic, and histaminergic neurons, seem to mediate OEA hypophagic action. Whether OEA's signal can directly or indirectly activate these neurons remains to be fully elucidated.
We demonstrated that exogenously administered OEA is able to modulate feeding behaviour in rats and mice by stimulating across-meal satiety and it is effective in reducing food intake and body weight gain in animals ad libitum exposed to a fat-enriched diet. At the same time the brain mechanisms activated by OEA treatment seems to be influenced by the fat content of the diet, thus suggesting that OEA might be part of those mechanisms that become deregulated by the exposure to an obesogenic condition.
We recently explored the effects of OEA in an animal model of binge-eating, in which female rats with a history of intermittent food restriction show binge-like palatable food consumption after 15 min exposure to the sight of the palatable food (frustration stress). Our preliminary findings demonstrated a positive effects of OEA in restoring a normal feeding behavior in this model.
Overall, these preclinical findings support the hypothesis that OEA might represent a novel potential pharmacological target for the treatment of obesity and eating disorders.