The ugly the bad and the good": how oleoylethanolamide can ameliorate neurochemical and behavioral aspects of eating disorders”

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Binge eating is a prototypical eating-related maladaptive behavior that may determine fluctuations in body weight and in some instance may cause obesity. It also represents a central feature of bulimia nervosa (BN) and binge eating disorders (BED). It is a condition in which the subject consumes an amount of food that is definitely larger than what most individuals would eat in a similar period and it is characterized by a subjective sense of loss of control over food consumption. In recent years, it has been recognized that BN and BED share important commonalities with substance abuse.

Current treatments for 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, Romano et al., 2015). OEA acts as a satiety signal, which is generated in the intestine, upon the ingestion of fat and ends in the central nervous system, where it modulates the neuronal activity of key hypothalamic and brainstem areas involved in the control of energy balance.

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.

As a further step in our research we hypothesized that OEA might be able to restore a normal feeding behavior in a model of aberrant eating pattern. We tested this hypothesis by exploring 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; Cifani et al., 2009). In the same model, we also evaluated whether OEA is able to affect dopaminergic transmission in key brain structures. The rationale for these latter experiments stems from previous observations that intestinal OEA

generated upon the ingestion of fat food stimulates central dopaminergic activity in mice fed with a high fat diet, thus regulating the reward value of fat (Tellez et al., 2013).

In our study OEA was administered at three different doses (2.5, 5, 10 mg/kg intraperitoneally) to binge-eating rats subjected to a microdialysis analysis performed within the shell of the nucleus accumbens (AcbSh). The feeding behavior of these rats was evaluated by measuring the amount of palatable food consumed 2 h after OEA administration, which preceded the exposure to the frustration stress. At the same time dialysates were collected and the dialysate levels of dopamine were evaluated by HPLC coupled to an electrochemical detector.

Our results demonstrated that OEA was able to prevent binge-eating in this rat model, thus restoring a “normal” feeding behavior, and was also able to decrease the dopamine efflux in the AcbSh that is induced by the exposure to the frustration stress procedure.

These results suggest that OEA is able to modulate feeding behavior acting not only within the caloric-homeostatic control system but also within the hedonic-homeostatic circuits, supporting the hypothesis that OEA might represent a novel potential pharmacological target for the treatment of obesity and eating disorders.

Cifani et al., (2009), Psychopharmacology, 204, 113–125

Romano et al. (2015) Front Pharmacol, 6:137

Tellez et al., (2013) Science, 6147, 800-802