

Olive oil-derived endocannabinoid-like mediators inhibit palatable food-induced reward and obesity

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Background:

The highly palatable and caloric foods (HPF) typical of the “Western diet”, affect brain synaptic homeostasis to promote appetite and HPF-dependent addictive behaviour. Here, we aimed at assessing if the lipoaminoacids, OIGly and OIAla, endogenously produced from the oleic acid abundantly present in the Mediterranean diet⁷, are capable of interfering with HPF-induced obesity, possibly via a gut-brain mechanism involving the microbiome

Methods and Results:

Behavioural (CPP:Conditioned-Place-Preference test), pharmacological, electrophysiological and profiling (targeted lipidomics and metagenomics) techniques were applied to adult mice fed with chow or with isocaloric 7-week diets with high content of fat from olive oil (HFD-O) or lard (HFD-L). OIGly or OIAla prevented addictive behaviours and dopamine neuron firing, and, like HFD-O, reduced body weight gain and food intake in mice under a HFD-L. They produced taxonomic shifts in both the small and large intestinal microbiota, with increase or decrease, respectively, of three taxa that are known to be negatively (*Akkermansia*), or positively (*Streptococcus* and *Lachnospiraceae*) associated with food addiction. OIGly or OIAla also produced potentially beneficial changes (i.e. an increase of *Parasutterella* or *Faecalibaculum*) that were also seen following HFD-O.

Conclusions:

The results of this study warrant further investigation on the capability of olive oil-rich diets, such as the Mediterranean diet, to produce beneficial effects via actions on food reward of oleic acid-derived lipid mediators.

Keywords:

Lipoamminoacids, high-fat diet, *Akkermansia*, *Streptococcus*, *Lachnospiraceae*

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Thematic Area:

- Microbiome: from Research to Clinics

Infrastructures:

N.A.