Oleoylethanolamide (OEA) restores skeletal muscle insulin signaling and mitochondrial energetics in rats fed on a high-fat diet

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Skeletal muscle plays a fundamental role in glucose homeostasis by internalizing large quantities of ingested glucose, under the action of insulin. High-fat diets (HFDs) can increase muscle lipid content and deregulate glucose homeostasis. Oleoylethanolamide (OEA), an endocannabinoid-like compound, has been shown to have several beneficial effects against HFD-induced metabolic imbalances. We investigate the effect of OEA on HFD-induced rat muscle dysmetabolism. Male Wistar rats were divided into four groups: fed a low-fat diet (control); fed the control diet and received intraperitoneal (i.p) injection of OEA (LO) for 2 weeks; fed a high-fat diet (HFD) (HV); and fed the HFD and received i.p injection of OEA for 2 weeks (HO). Muscle lipid content, Western blot analysis, and energy parameters were analyzed in all experimental groups. We found that HV had triacylglycerol accumulation compared to both the LV and LO groups. Furthermore, a greater expression, in HV compared to LV and LO, of the phosphorylated form of proteins involved in insulin pathways, was measured. Administration of OEA to HFD-fed rats reduced lipids and restored insulin signaling. HV rats had increased expression of complexes II, III, and IV of the respiratory chain, but no change in the expression of complexes I and V. Furthermore, carnitine palmitoyltransferase-1 activity and expression were increased in HV compared to both LV and LO rats. The OEA reported the expression of all analyzed proteins to control values. OEA improves muscle insulin signaling by reducing lipid accumulation and restoring mitochondrial functions.