Study of inflammation mediated by lipids in a Microglia Cell Model to deepen into brain dysregulation by obesity

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Obesity although preventable, has currently reached a worldwide pandemic level, being responsible for the development of non-communicable diseases. Over the last years, several investigations suggested that brain plays a major role in obesity development: saturated fatty acids bind to toll-like receptors 2 and 4 in the hypothalamus, triggering inflammatory processes resulting in overconsumption and food addiction. Some concerns arise since the current western diet, associated with high-fat and -fructose consumption, often provides considerable amounts of saturated fatty acids. As there are also brain receptors for long chain unsaturated fatty acids, omega 3 from fish oils have been demonstrated to revert hypothalamic inflammation. Their anti-inflammatory effects have been associated to activation of PPARs, which regulate inflammatory genes expression and the activation of NFkB. Microglia is the main cellular component of the brain innate immune system and a key player in both regulation and protection of the CNS homeostasis. Excessive activation of microglia and inflammation-mediated neurotoxicity are implicated in the progression of several neurological disorders. Consequently, to analyse microglia cells activation by a solution (palmitic acid (C16:0)/fructose) mimicking the western pattern diet, human microglia cells (HMC3) cells were co-transfected with pDisplay FLIPE-600n^{surface}biosensor, detecting the specific release of glutamate; by the genetically encoded red fluorescence sensor for hydrogen peroxide detection, HyPerRed; and by the miRFP703-IkBa, a sensor for canonical activation of NFkB, used to assess the inflammatory response. HMC3 cells were exposed to the stimuli solution, which induced a specific release of glutamate, a neurotoxicity indicator, from living microglia. As previously reported in rats fed a high fat diet, oxidative stress, through the production of reactive oxygen species was detected. The discussed inflammatory action was detected by an increase in NFkB expression.

Furthermore, solutions of omega 3 EPA and DHA (1:1), CLA isomers [rumenic acid - C18:2 *c*9*t*11 and C18:2 *t*10*c*12 (1:1)] and the CLNA isomer punicic acid (PUA) C18:3 *c*9t11*c*13, were added to the cells prior to the stimuli. Omega 3 fatty acids are expected to present beneficial effects on preventing the oxidative stress and in the inflammatory and neurotoxic action in the hypothalamus. CLA and CLNA are agonist of all PPAR isoforms and were shown to exert anti-inflammatory effects. Thus, they are expected to exert the same beneficial effects as omega 3.