



Endocannabinoid System and Reproductive Functions”

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Editorial

Δ^9 -tetrahydrocannabinol (Δ^9 -THC), the main biologically active component of marijuana plant, *Cannabis sativa* [1], mimics some biological activities of endogenous natural lipids called endocannabinoids (eCBs). They activate specific signaling pathways that involve the central type 1- and peripheral type 2- cannabinoid receptors (CB1 and CB2 respectively) and also type 1 vanilloid receptor (TRPV1). The main eCBs in biological systems are anandamide (AEA) and 2- arachidonoylglycerol (2-AG). Their physiological action at both central and peripheral level depends on their rate of synthesis, transport and degradation. The main enzymes involved in eCBs biosynthesis are N-arachidonoyl-phosphatidylethanolamine phospholipase D (Nape-PLD) for AEA and diacylglycerol lipases (DAGL α and DAGL β) for 2-AG. The fatty acid amide hydrolase (FAAH) drives the degradation of AEA and to a lesser extent of 2-AG whereas the monoacylglycerol lipase (MAGL) is the main metabolizing enzyme for 2-AG [2]. The activity of eCBs, in parallel to their biosynthesis and degradation, has been largely reported in the central nervous system (CNS) and in peripheral tissues of both vertebrates and invertebrates [3]. As a consequence, an evolutionarily conserved “endocannabinoid system” (ECS) is widespread involved in the control of many biological functions in brain, testis, ovary, placenta, blood, adipose tissues, epithelial cells, and so on with outcomes on cell proliferation, survival, differentiation and death [4].

ECS and Reproduction

A part from involvement in the control of pain and visceral functions [5], ECS is critical for the central and local control of reproductive functions in both sexes [6,7]. Centrally it modulates the release of Gonadotropin Releasing Hormone (GnRH) which in turn affects gonadotropin release and sex steroid biosynthesis. Impact on sexual behavior has also been reported [7]. Locally ECS has a role in gametogenesis, sperm maturation, fertilization, implantation, embryo development, labor and delivery [7].

Reproduction strongly depends on diet and energy homeostasis, with increased infertility rate in parallel to the increase of metabolic disorders. The involvement of ECS in the central pathways integrating environmental cues and reproduction has been widely reported. It occurs through the regulation of neuronal pathways involved in the

modulation of food intake, appetite and also stress. In facts, eCBs cooperate with hypothalamic peptides in the regulation of energy homeostasis, stimulate food intake and promote the accumulation of body fat, thus working as orexigenic factors [8].

The activity of eCBs strongly depends on eCBs tone that is modulated by FAAH activity. The detection of low FAAH activity and high levels of eCBs in obese subjects strongly sustains ECS involvement in the control of body weight. Nevertheless, the main eCBs, AEA and 2-AG, are derivatives of arachidonic acid which is a n-6 long chain polyunsaturated fatty acid (n-6 PUFA) provided from diet and thereafter absorbed and incorporated into tissue membranes [9].

Summary

Thus, ECS is a key signalling system in reproduction and links neuroendocrine and reproductive functions; possible diet-dependent contribute to the tone of eCBs and intervention to preserve the activity of ECS in health and disease may be suggested.

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