Cannabinoids have been used for the treatment of chronic pain for millennia with documented results of numerous clinical trials in non-pregnant patients. Exogenous cannabinoids act through the mechanism of “kick-starting” the components of the endogenous cannabinoid system (endocannabinoid [eCB] system). ECS serves as a pharmacological target for the treatment of obesity, inflammation, cardiovascular and neurodegenerative diseases, and pain. The clinical syndrome of endocannabinoid deficiency (ECD) is linked to numerous pain-related conditions in adults. Described by Russo in 2004, the concept of ECD has been developed and applied to such conditions as irritable bowel syndrome, fibromyalgia, migraine, and autism [9]. The clinical definition of the syndrome is important, since it leads to the therapeutic application of the cannabis derivatives to its treatment.

The “developmental programming” hypothesis opens the opportunity for understanding the origin of adult diseases and their prevention at the most adaptable stage of individual’s life - in the womb.

Maternal obesity (MO), affects 44% of all pregnant and has increased in a linear fashion between 2005 and 2014, and is associated with significant health risks for mothers and their offspring. However, the results of numerous maternal lifestyle changing trials (i.e. UPBEAT, LIMIT) and surgical interventions for weight reduction remain controversial and unable to demonstrate the benefits of such for fetal and maternal health. Therefore, there is a clear need to identify novel mechanisms and pharmacological targets underlying gene-environment interactions in MO. Remarkably, there is experimental and epidemiological evidence that the spectrum of the diseases which are included in the definition of ECD are “programmed in uterus” by MO. However, there are no reports available connecting MO and ECD.

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We hypothesize that MO programs offspring health at least in part through the mechanism of the Fetal Syndrome of Endocannabinoid Deficiency (FSECD).

This hypothesis differs from the present explanation of the phenomenon of fetal programming and brings all present theories under the umbrella of one syndrome. FSECD hypothesis is evident from the perspective of 1) the involvement of ECS in obesity, 2) experimentally-proven shared phenotypes of ECS disbalance in MO, and 3) evidence from human and non-human primate studies regarding fetal and placental ECS disbalance in MO.

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**Evaluation of the hypothesis**

**Clinical syndrome of endocannabinoid deficiency**

**Introduction**

Maternal obesity (MO) affects 64% of all pregnant and has increased in a linear fashion between 2005 and 2014, and is associated with significant health risks for mothers and their offspring. However, the results of numerous maternal lifestyle changing trials (i.e. UPBEAT, LIMIT) and surgical interventions for weight reduction remain controversial and unable to demonstrate the benefits of such for fetal and maternal health. Therefore, there is a clear need to identify novel mechanisms and pharmacological targets underlying gene-environment interactions in MO. Remarkably, there is experimental and epidemiological evidence that the spectrum of the diseases which are included in the definition of ECD are “programmed in uterus” by MO. However, there are no reports available connecting MO and ECD.

**Materials and Methods**

Animals were housed in a non-pregnant canine model and in lean and obese subjects, HFD did not affect AEA, but decreased 2-AG concentrations. In opposite to this, in human and non-human primate models, 2-AG levels in systemic circulation in HFD dams agrees with these data. However, the effect of HFD on AEA/2-AG levels in systemic circulation is controversial: in pregnant patients. Exogenous cannabinoids act through the mechanism of “kick-starting” the components of the endogenous cannabinoid system (endocannabinoid [eCB] system). ECS serves as a pharmacological target for the treatment of obesity, inflammation, cardiovascular and neurodegenerative diseases, and pain. The clinical syndrome of endocannabinoid deficiency (ECD) is linked to numerous pain-related conditions in adults. Described by Russo in 2004, the concept of ECD has been developed and applied to such conditions as irritable bowel syndrome, fibromyalgia, migraine, and autism [9]. The clinical definition of the syndrome is important, since it leads to the therapeutic application of the cannabis derivatives to its treatment.

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