Imbalanced dietary omega-3 content from pregnancy affects adult offspring's behavior through dysregulation of the endocannabinoid system

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Dietary fatty acids seem to play a pivotal role in normal fetal brain development and their imbalance during early developmental phases may be responsible for a major vulnerability to develop psychiatric conditions later in life.
More importantly, endocannabinoids are arachidonic acid derivatives whose levels are regulated by the activity of metabolic enzymes, as well as by arachidonic acid availability.
Since the only sources of arachidonic acid in mammals are diet and the enzymatic production in the liver from shorter-chain essential fatty acids, we hypothesize that imbalances in fatty acid composition of food might alter the endocannabinoid system, possibly increasing the risk of developing psychiatric-like behaviors.
In the present study, we investigated (1)whetheromega-3 fatty acid intake from pregnancy could lead to the development of psychiatric-likesymptoms in the adult male offspring and (2) the impact of lifelong dietary omega-3 imbalances on the endocannabinoid system in the prefrontal cortex and hippocampus of these animals.
To this aim, pregnant Sprague-Dawley rats were fed with three diets, differing in omega-3 content: a standard (omega-3: omega-6= 1: 8.6), a poor (omega-3: omega-6=1: 4.5) or a rich diet (omega-3: omega-6=1: 23.9) from gestation throughout lactation. After weaning, the offspring was submitted to the same dietary regimen of the corresponding dam. Adult male rats were tested for behavior and biochemical analyses were carried out in order to evaluate CB1 receptor density and functionality, endocannabinoid levels as well as the expression of their synthetic and degradative enzymes in the prefrontal cortex and hippocampus.
Administration of poor and rich diets is associated with significant cognitive deficits in the classic and spatial variants of the novel object recognition test compared to rats fed with a standard diet. More interestingly, only adult male rats fed with rich diets show significant alterations in the emotional sphere, as demonstrated by an increased immobility time in the forced swim test and a reduction of the time spent in social exploration in the social interaction test.
This behavioral phenotype is associated with significant alterations in the endocannabinoid system both in the prefrontal cortex and hippocampus. In particular, in the prefrontal cortex, both diets induce a reduction in the endocannabinoid, 2-AG, whereas only the rich diet also reduces AEA levels. These changes are associated with increases in the levels of the degradative enzymes, MAG lipase and FAAH. In contrast, in the hippocampus, no changes are present after administration of poor diets whereas diets enriched in omega-3 result in a reduction of AEA synthesis and increased 2-AG degradation.
As a whole, these data suggest that imbalances in dietary omega-3 fatty acid content from pregnancy increase the risk of developing psychiatric-like symptoms in the adult male offspring and that this effect might rely on dysregulations of the endocannabinoid system in specific brain regions.
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