Nutritional n-3 PUFAs deficiency during perinatal period alters brain immune system and neuronal plasticity

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Low dietary intake of the n-3 polyunsaturated fatty acids (PUFAs) is a causative factor of neurodevelopmental disorders. However the mechanisms linking n-3 PUFAs low dietary intake and neurodevelopmental disorders are poorly understood. Microglia, known mainly for their immune function in the injured or infected brain, have recently been demonstrated to play a pivotal role in regulating maturation of neuronal circuits during normal brain development. Disruption of this role during the perinatal period therefore could significantly contribute to psychopathologies with a neurodevelopmental neurodevelopmental component. N-3 PUFAs, essential lipids and key structural components of neuronal membrane phospholipids, are highly incorporated in cell membranes during the gestation and lactation phase. We previously showed that in a context of perinatal n-3 PUFAs deficiency, accretion of these latter is decreased and this is correlated to an alteration of endotoxin-induced inflammatory response. We thus postulated that dietary n-3 PUFAs imbalance alters the activity of microglia in the developing brain, leading to abnormal formation of neuronal networks. We first confirmed that mice fed with a n-3 PUFAs deficient diet displayed decreased n-3 PUFAs levels in the brain at post-natal days (PND)0 and PND21.We then demonstrated that n-3 PUFAs deficiency altered microglia phenotype and motility in the post-natal developing brain. This was paralleled by an increase in pro-inflammatory cytokines expression at PND21 and to modification of neuronal plasticity-related genes expression. Overall, our findings show for the first time that a dietary n-3 PUFAs deficiency from the first day of gestation leads to the development of a pro-inflammatory condition in the central nervous system that may contribute to neurodevelopmental alterations.