**Prénom, Nom**

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**Titre**

ROLE DES ACIDES GRAS POLYINSATURES DANS LE DEVELOPPEMENT CEREBRAL NORMAL ET PATHOLOGIQUE

**Abstract**  
**POLYUNSATURATED FATTY ACIDS ROLE IN NORMAL AND PATHOLOGICAL BRAIN**

**DEVELOPMENT**

The perinatal dietary intake in n-3 and n-6 polyunsaturated fatty acids (PUFAs n-3 and n-6), also known as ‘omega-3’ and ‘omega-6’, is essential for brain development. As these lipids cannot be *de novo* synthesized by the body, they must be provided by the diet according to a ratio of one n-3 PUFA for four n-6 PUFAs. Western diet has dramatically evolved over the past 70 years, towards excessive omega-6 consumption and reduction in omega-3 intake. This correlated with an increasing number of children with neurodevelopmental pathologies. However, the link between perinatal nutrition and neurodevelopment remains poorly understood.

The main objective of my thesis was to study the cellular and molecular mechanisms by which a reduction in perinatal n-3 PUFA dietary intake alters neural networks shaping, focusing on the interactions between glial cells (namely microglia and oligodendrocytes) and

neurons.

Our results show that perinatal n-3 PUFA deficiency leads to 1) an alteration of microglial and oligodendrocytes functions during brain development; 2) an increase in microglia-mediated dendritic spines pruning and deficits in myelination process; 3) the establishment of dysfunctional neural networks in the hippocampus and prefrontal cortex; 4) deficits in learning, sociability and occurrence of anxiety behaviors.

Moreover, n-3 PUFA deficiency during the perinatal period exacerbates the deleterious effects of a prenatal maternal immune activation (MIA). Low n-3 PUFA intake 1) increases the maternal and fetal inflammatory response to MIA; 2) increases the duration and extent of MIA effects on neuronal morphology and microglia-neuron interactions; 3) alters the inflammatory reactivity of intestinal lymphocytes, that persists at adulthood 4) induces memory deficits and hyperactivity in offspring in adulthood.

Overall, the present work specified some of the mechanisms by which n-3 PUFA deficiency affects the developing brain by highlighting its detrimental effect on microglia andoligodendrocytes function and showing how its sensitizes the brain to other

developmental insults.

**KEY WORDS:** PUFA, BRAIN DEVELOPMENT, MICROGLIA, OLIGODENDROCYTE,

NEURAL NETWORKS, BEHAVIOR, PRENATAL INFLAMMATION.

**Jury**

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**Publications**

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**Book Chapter:**

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**Soumis**

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