Pre- and post-natal exposure to polyunsatured fatty acid enriched diet: impact on depression development in adult offspring

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Several studies show that nutrients can influence disease risks beginning in fetal life until to old age. The n-3 and n-6 long-chain polyunsaturated fatty acids (PUFAs), the so called omega-3 and omega-6, are derived from short-chain PUFAs present in food. The high ratio of omega-6 to omega-3 has been associated with health deficits, including psychiatric disorders (DiLeone, 2011).

Fatty acids influence membrane composition and many signalling pathways in cells and high cerebral concentrations of long-chain PUFAs are present. In particular, fetal neuronal development needs optimal levels of omega-3 fatty acid to drive normal brain development and function. Moreover, some evidence indicate that deficit in neuronal development can influence the onset of psychiatric disorder in adulthood, such as depression (Manji et al., 2003).

Therefore, the first aim of this study was to investigate the depressive-sensitive or depressive-resistant phenotype in male offspring by manipulating omega 3 and 6 levels in maternal diet. To evaluate the depressive behaviour the Forced Swimming Test (FST) was used and biochemical, neurochemical and neuroendocrine factors known to be involved in depression development were studied.

Furthermore, we have previously demonstrated that an acute injection intracerebroventricular of soluble amyloid-beta peptide 42 (sAbeta) is associated to depressive-like behavior in rats. In particular, we found that sAbeta induces a number of neurochemical [(reduced serotonin, brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) levels in prefrontal cortex (PFC) and neurobehavioural (increased immobility time in FST)] alterations compatible with a depressive state (Colaianna et al., 2010). Therefore, a further aim of the present work was to test the hypothesis that these diets might prevent pro-depressant effects of sAbeta.

We have used two specific diets to mimic lifelong omega-3/omega-6 imbalance of PUFAs in rats according to the procedures previously described (Lafourcade et al., 2011). In particular, after mating, female rats were fed with either a diet containing 6% fat in the form of peanut oil and rapeseed oil called 'omega-3 rich diet' or an isocaloric diet containing 6% fat in the form of only peanut oil called 'omega-3 poor diet' throughout gestation and lactation. A control group was fed with a balanced diet. Experiments were performed on adult offspring, fed with the same pre-natal diet.

In animals fed with the 'omega 3 poor diet', we found that the immobility frequency in FST was increased (pro-depressant effect). Accordingly, plasmatic levels of corticosterone were higher than controls.

The 'omega 3 poor diet' does not affect sAbeta depressant-effect in FST. Conversely, the 'omega 3 rich diet' seems to reverse the effects of sAbeta and mRNA NGF levels in PFC were increased. In conclusion, our data show that 'omega 3 poor diet' sensitizes animals to depressive stimuli. Moreover, the 'omega 3 rich diet' acts like antidepressant compounds in sAbeta-treated rats.

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DiLeone (2011). *Nature Neuroscience* 14: 271–272.
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