

# ***In utero* exposure to omega-3 and omega-6 polyunsaturated fatty acid enriched diet: neurobiochemical and behavioral effects in the female rat offspring**

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Recent evidence pointed out that the prevalence of depression has reached epidemic proportions in last decades. Such an increase has been linked to many environmental factors, among these the influence of dietary factors has gained great attention. In particular, it has been reported the omega-3 polyunsaturated fatty acid (omega-3 PUFA) content in diet was inversely correlated to the development of depressive symptoms. Furthermore, such association was substantial and stronger only among women (Beydoun et al., 2015). Thus, the aim of the present work was to study the effect of pre- and post-natal (7 weeks) exposure to diets differently enriched in omega-3 and omega-6 PUFA, as well as omega-3/ omega-6 –balanced, on immobility time displayed on the forced swimming test (FST), along with several neuroendocrine quantification in female rats.

Results showed that, in female offspring rats, omega-6 PUFA enriched diet induced an increase in immobility time in the FST and such an effect was accompanied by higher estradiol levels. Conversely, omega-3 PUFA enriched diet caused a significant decrease in plasmatic corticosterone measurement.

We have previously shown that soluble beta amyloid (sAbeta), intracerebrally injected in rats, can evoke a depressive-like status, by increasing the immobility time in the FST, as well as by reducing cortical brain derived neurotrophic factor and nerve growth factor proteins and mRNA content. In addition, reduced cortical serotonin (5-HT) levels were found (Colaïanna et al, 2010). In the same animal model, we also described an altered hypothalamic–pituitary–adrenal axis function with higher cortical and hippocampal concentrations of noradrenaline and lower plasmatic corticosterone (Morgese et al., 2014). Further scope of our research was to evaluate if PUFA diet exposure was able to interfere with the pro-depressive effect of sAbeta. In particular, we found that the depressive effect, previously shown in male rats, was also evidenced in female animals. Moreover, we found that either omega-3 and omega-6 PUFA enriched diet reduced the immobility time in sAbeta-treated female rats compared to balanced diet. In addition, omega-3 PUFA enriched diet decreased adrenocorticotrophic hormone content only in sAbeta-treated rats. Interestingly, high omega-3 PUFA diet increased cortical 5-HT levels in sAbeta-treated rats compared to controls.

Taken together, our data suggest a possible protective role of omega-3 PUFA in the stress response and in the development of depressive-like symptoms induced by sAbeta.

Beydoun et al. (2015). *Am J Epidemiol.* May 1;181(9):691-705.

Colaïanna et al. (2010). *Br J Pharmacol.* Apr;159(8):1704-15.

Morgese et al. (2014). *Curr Pharm Des.* 20(15):2539-46.