

An Omega-3 PUFA/Vitamin A enriched diet to prevent cognitive deficits induced by the Social Instability Stress

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Early-life stress in humans and rodents has been shown to represent a neurodevelopmental risk with implications to subsequent cognitive abilities during adulthood. Likewise, poor nutritional habits are closely intertwined with mood regulation, stress perception and stress responses (Hoeijmakers et al., 2015). Evidence suggests that a healthy diet, rich in polyphenols, B-vitamins, omega-3 polyunsaturated fatty acids (ω -3 PUFAs) and vitamins, exerts favourable effects on cognitive performance, stress reactivity and neuroinflammation (Bazinet & Layè, 2014). This study aims to investigate the effects of an ω -3 PUFAs (0.545g/100g)/Vitamin-A (45 IU/g) enriched diet in the negative effects of chronic stress on cognition and anxiety. Male Wistar rats fed with normal or supplemented diet were submitted to the social instability stress protocol (McCormick, 2010) that includes a combination of repeated 1h daily isolation in a small container followed by pairing with a new partner and new cage after the restraint. As rodents use social bonds to moderate stress, the advantage of this model is that the social instability blunts habituation to repeated isolation. The stressful procedure is repeated for 15 days starting on post-natal day (PND) 30. The behavioural repertoire of the animals was accessed at the end of stress protocol, i.e. during adolescence (PND 45-50,) as well as in adulthood (PND 70-75) using a battery of tests comprehensive of several domains affected by stress: mood (sucrose preference), anxiety (open field, elevated plus maze) and cognition (novel object recognition). Results from stressed animals were compared with a control group fed with normal chow and that did not received stressful manipulations. Diet supplementation with ω -3 PUFAs/Vitamin-A prevented the reductions in food consumption and body weight gain caused by the exposition of adolescent rats to social instability stress. While no significant effects were observed during adolescence, chronic stress induced cognitive deficits late in life. The dietetic intervention prevented the deficit observed in the recognition but not the spatial location test in adulthood. No signs of anhedonia were observed since there were no differences in sucrose preference among groups. Surprisingly, stressed rats seems to spend more time in the center of the open field arena and in the open arms of the elevated plus maze. These effects did not reach statistical significance, but suggests a low anxiety state. In summary, we demonstrated long-term effects of chronic social instability stress during adolescence and that an ω -3 PUFAs/Vitamin-A enriched diet can prevent the cognitive decline observed in adulthood. This work was supported by Joint Programming Initiative – A Healthy Diet for a Health Life (AMBROSIAC).

(1) Hoeijmakers et al. (2015) *Front Mol Neurosci.* 7:103

(2) Bazinet and Layè (2014) *Nat Rev Neurosci.* 15(12):771-85

(3) McCormick (2010) *Physiol Behav* 99(2):194-203.

