Increased amyloid-b $_{1-40}$ peptide in the hippocampus and frontal cortex of vitamin A-treated rats

Schnorr, C.E.; Oliveira, M.R. de; Rocha, R.F. da;, Behr, G.A.; Oliveira, M.W.S.; Pasquali, M.A. de B.; Moreira, J.C.F.

Programa de Pós-Graduação em Ciências Biológicas: Bioquímica, Dep. de Bioquímica, ICBS, UFRGS, RS, Brazil

Oral vitamin A (retinol palmitate) at moderate to high doses (25000-300000 IU/day) during either acute or chronic periods have been utilized in the treatment of some life threatening pathologies in the fields of dermatology and oncology. Furthermore, very-low-weight preterm infants receive vitamin A daily at 8500 IU/kg.day^{-1} during weight gain treatment. In spite of this, several side effects, for instance gastrointestinal disturbances, pseudo-tumor cerebri, and, more concerning, cognitive decline (anxiety and depression) have been attributed to excessive vitamin A intake, even when occurring therapeutically. We have previously demonstrated that retinol palmitate induced pro-oxidant effects on rat central nervous system. Additionally, anxiety-like, but not depression-related behaviors were observed in such animals submitted to vitamin A supplementation for 28 days. However, the exact mechanism by which vitamin A altered rat cognition remains under investigation. Then, based on the fact that vitamin A is a pro-oxidative agent and impairs mammalian cognition, we have analyzed here the levels of amyloid-β $_{1-40}$ peptide, TNF-α, and 3-nitrotyrosine (indirect or sandwich ELISA assay, depending on the parameter analyzed) in the hippocampus and frontal cortex of rats that received vitamin A at therapeutic doses (1000-9000 IU/kg.day^{-1}) for 3, 7, or 28 days and for 3 months through a gavage. Acute vitamin A supplementation did not alter the parameters herein investigated. However, we observed increased amyloid-β $_{1-40}$ peptide, TNF-α, and 3-nitrotyrosine contents in the brain of the rats that received vitamin A for 3 months. We suggest that such biochemical alteration may take an important role during the cognitive decline previously observed in both experimental animals and humans under vitamin A treatment.

Key words: 3-nitrotyrosin, amyloid-β $_{1-40}$ peptide, retinol palmitate, TNF-α
Supported by: CNPq.