Soluble beta amyloid as bridge between Depression and Alzheimer's disease: evidences from an animal

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Depression and Alzheimer's disease (AD) have reached epidemic proportions in last decades. Indeed, an overlap between these neuropathological events hypothesized, such as depressive state has been pointed as an early manifestation of AD. In our experience, we have demonstrated that central soluble beta amyloid 1-42 (Aβ) peptide induces a depressive like-behavior in rats, with altered hypothalamic pituitary adrenal (HPA) axis activation, reduced cortical serotonin and neurotrophin levels. In searching for new risk factors for these pathologies, maternal malnutrition is emerging as a potential cause factor for developing mental illness in later adulthood, including depression. Therefore, we have studied the effect of lifelong exposure to diets differently enriched in n-3, n-6 (poor in n-3), as well as n-6/ n-3 polyunsaturated fatty acids (PUFA) balanced, on immobility time displayed on the forced swimming test (FST), along with neuroendocrine quantification of HPA axis parameters in offspring rats. Our data showed that n-3 PUFA poor diet increased depressive- and anxiety-like behaviors accompanied by reduced cortical serotonin and enhanced plasmatic Aβ1-42 levels. In addition, plasmatic corticosterone and hypothalamic corticotropin releasing factor levels were significantly higher in animals fed with n-3 poor diet. Interestingly, chronic stress is a widely accepted risk factor for the development of both depressive symptoms and AD pathology. Indeed, high cortisol levels, and thus HPA axis hyperactivity, have been indicated as the most frequent alteration in patients affected by depression and AD. On the other hand, neuro-inflammation represents a common link between depression and AD and the cyclooxygenase II (COX-2) enzyme seems to play a crucial role. Thus, in our study, we tested in vivo the effect of sub-chronic celecoxib, a selective COX-2 inhibitor, on the Aβ-induced model of depression and we associated ex-vivo quantification of monoamines and Aβ in order to evaluate a possible mechanism of action. We found that celecoxib prevented the increase in immobility and the decrease in swimming frequency, as well as the reduction in serotonin content at prefrontal cortex level induced by the peptide. In addition, an Aβ-lowering effect was also evidenced. Taken together our results indicate that Aβ levels could represent a novel biomarker also for depression, and treatments or dietary interventions able to modify the peptide levels can be suitable therapeutic approaches for either AD or depression.