Soluble beta amyloid triggers alteration in noradrenaline system: involvement of nitric oxide

M.G. Morgese[1], M. Colaianna[2], P. Tucci[1], V. Cuomo[3], L. Trabace[1]

[1] Dept. of Clinical and Experimental Medicine, School of Medicine, University of Foggia, Italy
[2].Dept of Pathology and Immunology, School of Medicine, Geneva , Switzerland
[3] Dept of Physiology and Pharmacology 'V. Erspamer', University of Rome 'La Sapienza', Italy

Despite the consolidation of the amyloid hypothesis, the main component of senile plaques in Alzheimer's disease (AD), recently the potential physiological role of beta amyloid (BA) has been recognized. Indeed, it has been reported that the peptide is physiologically produced during normal cell cycle via proteolysis of a high molecular weight precursor. BA is theoretically produced in several cell compartments, but it has been reported that its main production occurs down the secretory and endolysosomal pathways. Moreover, BA is secreted from the cell via neurotransmission. Therefore, the intracellular level of BA is altered according to neuronal activity in absence of gross sign of neurotoxicity. On the other hand, novel evidence report that neurodegenerative conditions, such as AD, involve nitric oxide (NO) in their pathogenesis. NO also holds potent neuromodulatory effects in brain regions, such as prefrontal cortex (PFC), hippocampus (HIPP) and nucleus accumbens (NAC), involved in AD. Moreover, we have recently found that BA alters noradrenergic transmission 7 days after its administration. Thus, here we decided to evaluate the effect of an acute BA injection on noradrenaline (NA) content before and after pharmacological manipulations of nitrergic system in the above mentioned areas. Our data showed that 2 hours after i.c.v. soluble BA administration, NA levels were significantly increased in all areas considered. Moreover, such increase was accompanied by higher iNOS mRNA along with increased NOx concentrations, suggesting that the effects of BA on noradrenergic system could be associated to altered NO release. Interestingly, pharmacological treatment confirmed our hypothesis since pre-treatment with NOS inhibitors, 7-NI and L-NIL, completely reversed such alteration. Surprisingly, the same effect was obtained with pre-treatment with a potent NO-donor, SNAP and by using a NO-precursor, L-Arginine (L-Arg). However, only in NAC, co-administration of L-Arg was not able to reverse BA effect. Taken together, our data suggest that NO pathway is involved in BA action on noradrenergic transmission and NO plays a critical role in such alteration.