Regulation of Preprotachykinin-A Gene Expression in an Animal Model of Alzheimer’s Disease


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Alzheimer’s disease is a neurodegenerative disorder of the CNS characterized by deposition of neuritic plaques and neurofibrillary tangles with consequent neuron death. Clinically it is characterized by a progressive loss of memory and impairment of learning capacity (Selkoe 1997; Seabrook et al. 1999).

Substance P (SP) is a neurotransmitter related to memory functions and learning properties, highly expressed in several brain areas from forebrain to hindbrain (Rattan and Tejwani 1992; Alvarez et al. 1997). For example, the nucleus basalis of Meynert (NBM) is highly sensitive to memory enhancement effects of SP. SP also interacts with the cholinergic ascending system of the NBM that is implicated in memory functions. Patients with Alzheimer’s disease show a marked loss of cholinergic neurons from the NBM to the cortex and diminished brain SP immunoreactivity (Cleary et al. 1995; Nag et al. 1999).

On the basis of these findings, the aim of this study was to verify the presence and the distribution of preprotachykinin-A (PPT-A) mRNA in discrete brain areas in an animal model of Alzheimer’s disease.

Twenty male Albino Wistar rats weighing ~340 g were implanted SC with miniosmotic infusion pumps (Alzet type) that deliver the mixed neurotoxins to the hippocampus via a catheterized cannula (Morimoto et al. 1998).

Experimental animals included four groups (five animals each group). The first group (vehicle) was infused with a saline solution. The second group was infused with a solution of 0.075 μg/μl of β-amyloid (fragment 1–40) and 0.01875 μg/μl of ibotenic acid (A dose). The third group was infused with a solution of 0.15 μg/μl of β-amyloid (fragment 1–40) and 0.0375 μg/μl of ibotenic acid (B dose). The fourth group was infused with a solution of 0.224 μg/μl of β-amyloid (fragment 1–40) and 0.0562 μg/μl of ibotenic acid (C dose). Finally, on Day 10, rats were sacrificed by decapitation and the brains were removed and then stored for in situ hybridization. Semi-quantitative ISH histochemistry examined PPT-A mRNA levels in the bed nucleus of the stria terminalis (BNST) in the medial preoptic area (MPA).

The infusion of the two neurotoxins β-amyloid (fragment 1–40) and ibotenic acid induced a 24.29% statistically significant reduction in basal hybridizable PPT-A mRNA in the BNST brain area after administration with dose A, as well as a 19.26% and a 16.85% statistically significant decrease after administration with dose B and dose C compared to CON rats, respectively (Figure 1).

The same figure shows a 30.7% statistically significant lower level of PPT-A mRNA in MPA after dose A, whereas PPT-A mRNA levels were shown to be sig-
nificantly lower by 22.00% and by 19.01% after dose B and dose C in MPA in β-amyloid (fragment 1–40) and ibotenic acid-treated animals compared to CON rats.

The decrease in PPT-A mRNA levels shown in the present study might contribute to the loss of memory and impairment of learning capacity seen in AD, thus suggesting a role of the tachykinergic system as a putative co-factor in the etiopathogenesis of AD.

Acknowledgment

Supported by the Fondazione Cassa di Risparmio, Provincia di Maceratao.

Literature Cited


