

## NITRIC OXIDE AND DOPAMINERGIC SYSTEM: NEUROCHEMICAL INTERACTIONS IN $\beta$ -AMYLOID INJECTED RATS

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In the pathogenesis of Alzheimer disease (AD) a critical role is played by deposits of  $\beta$ -Amyloid ( $A\beta$ )<sup>(1)</sup>. Recent evidences suggest that nitric oxide (NO) may be involved in neuronal cell death in AD<sup>(2)</sup>. In the present study, we explored the neuromodulatory role of NO on the neurochemical alterations associated with  $A\beta$  exposure in rat prefrontal cortex (PFC) and we investigate whether subchronic *in vivo* exposure to 7-nitro indazole (7-NI) or L-Arginine (Arg) would induce changes in the extracellular concentrations of dopamine (DA) in  $A\beta$  treated-rats. We measured the release of DA 2h after  $A\beta$  i.c.v. administration by using *in vivo* microdialysis technique. Basal extracellular concentrations of DA were significantly lower in  $A\beta$ -injected animals than that in vehicle-treated rats. Moreover, extracellular concentrations of DA were significantly lower in Arg-treated animals than that in vehicle-treated rats ( $F_{tr(2,14)}=6,78$ ;  $P<0.05$ ). On the contrary, 7-NI administration significantly increased DA levels with respect to the control group ( $F_{tr(2,14)}=6,78$ ;  $P<0.05$ ). *In vivo* microdialysis sampling showed that  $A\beta$ , administered via the dialysis probe, did not modify extracellular DA concentrations ( $F_{tr(1,15)}=7.25$ ,  $P<0.02$ ). However, the presence of  $A\beta$  significantly attenuated high  $K^+$ -induced increase in DA levels ( $P<0.05$ ). Nevertheless, the effects of locally applied  $A\beta$  on the extracellular concentrations of DA were determined for 4 h after administration of the peptide. The decrease in DA concentrations was still significant 4h after treatment. Then, we studied the efficiency of administration and diffusion of  $A\beta$  to brain parenchima. After 2h from the injection of  $A\beta$ , its immunoreactivity was detected within the ventricle system and on its walls. The peptide injected in the right ventricle was found at the site of injection and at other levels of the ventricular system. No gross signs of neurodegeneration were observed within the area of  $A\beta$  diffusion. In conclusion, these results suggest that dopaminergic transmission is affected by the NO production in  $A\beta$ -induced animal model of AD. Moreover, understanding the role of the nitrergic system might be of therapeutical importance in the treatment of this neurodegenerative disorder.

### References

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- (2) Trabace L., Kendrick KM. (2000) J Neurochem. 75(4):1664-74.