ESTROGEN AND ANGIOTENSIN INTERACTION IN THE SUBSTANTIA NIGRA. RELEVANCE TO POSTMENOPAUSAL PARKISON’S DISEASE

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Introduction: Epidemiological studies have reported that the incidence of Parkinson’s disease (PD) is higher in postmenopausal than in premenopausal women. Several studies have revealed that estrogen (E2) has protective effects against dopaminergic toxins but the mechanism by which protects has not been clarified.

Aim: Investigate the effect of ovariectomy and E2 replacement on the nigra renin-angiotensin system (RAS) and on dopaminergic degeneration.

Methods: In a first series of experiments adult female Sprague-Dawley rats were injected intrastriatally with 6-OHDA or saline (controls) and treated with E2 and/or candesartan. Then they were killed for immunohistochemical studies: localization of RAS components in dopaminergic neurons and glial cells, and quantification of dopaminergic cell death. Estrogen was administered in silastic implants filled with 17β-estradiol benzoate. Candesartan was injected subcutaneously 0.05mg/kg/day from 10 days before 6-OHDA injection until death. In a second series of experiments rats were killed by decapitation three weeks after ovariectomy and the mesencephalon processed for investigation on RAS activity by western blot, ACE (angiotensin converting enzyme) and NADPH activity and RT-PCR studies.

Results: E2 replacement or treatment with Candesartan significantly reduced the loss of dopaminergic neurons in ovariectomized rats treated with 6-OHDA. In substantia nigra, we observed downregulation of the ACE activity, NADPH complex activity and AT1 receptor expression, as well as upregulation of AT2 receptor expression in ovariectomized rats treated with E2 in comparison with ovariectomized rats.

Conclusions: Manipulation of brain RAS may be an efficient approach for the prevention or coadjutant treatment of PD in E2 deficient women.