AGING-RELATED CHANGES IN THE NIGRAL ANGIOTENSIN SYSTEM ENHANCES PROINFLAMMATORY AND PRO-OXIDATIVE MARKERS AND 6-OHDA-INDUCED DOPAMINERGIC DEGENERATION

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Introduction: Aging, the most prominent risk factor for Parkinson's disease, is associated with a proinflammatory and pro-oxidant state that may increase the vulnerability of dopaminergic neurons. Angiotensin II (AII), via type 1 (AT1) receptors, is an important known inflammation and oxidative stress inducers.

Aims: We have studied the age-related changes in the nigral angiotensin system and in the proinflammatory and pro-oxidant state that could lead to increased vulnerability of dopaminergic neurons.

Methods: We compared the expression (mRNA and/or protein) of AII receptors, the NADPH subunit p47, interleukin (IL)-1β and tumor necrosis factor (TNF)-α in the nigra of young adults and aged rats; we also studied the effect of treatment with 6-OHDA and the AT1 antagonist candesartan on the observed proinflammatory changes and dopaminergic degeneration, using real-time PCR, western-blot, ELISA and immunohistochemistry.

Results: In aged rats, we observed increased activation of the NADPH oxidase complex and increased levels of the proinflammatory cytokines IL-1β and TNF-α, which indicate pro-oxidative, proinflammatory state in the nigra. We also observed enhanced 6-OHDA-induced dopaminergic cell death in aged rats. This is associated with increased expression of AT1 receptors and decreased expression of AT2 receptors, and is reduced by treatment with the AT1 antagonist candesartan.

Conclusions: Our results indicate that brain angiotensin is involved in changes that may increase the risk of Parkinson's disease with aging. Furthermore, the results suggest that manipulation of the brain angiotensin system may constitute an effective neuroprotective strategy against aging-related risk of dopaminergic degeneration.