Although the renin-angiotensin system (RAS) was classically considered as a circulating system that regulates blood pressure, many tissues are now known to have a local RAS. Angiotensin, via type 1 receptors, is a major activator of the NADPH-oxidase complex, which mediates several key events in oxidative stress and inflammatory processes involved in the pathogenesis of major aging-related diseases. Several studies have demonstrated the presence of RAS components in the basal ganglia, and particularly in the nigrostriatal system. In the nigrostriatal system, RAS hyperactivation, via NADPH-oxidase complex activation, exacerbates oxidative stress and the microglial inflammatory response and contributes to progression of dopaminergic degeneration, which is inhibited by angiotensin receptor blockers and angiotensin converting enzyme inhibitors. Several factors may induce an increase in RAS activity in the dopaminergic system. A decrease in dopaminergic activity induces compensatory upregulation of local RAS function in both dopaminergic neurons and glia. In addition to its role as an essential neurotransmitter, dopamine may also modulate microglial inflammatory responses and neuronal oxidative stress via RAS. Important counterregulatory interactions between angiotensin and dopamine have also been observed in several peripheral tissues. Neurotoxins and proinflammatory factors may also act on astrocytes to induce an increase in RAS activity, either independently of or before the loss of dopamine. Consistent with a major role of RAS in dopaminergic vulnerability, increased RAS activity has been observed in the nigra of animal models of aging, menopause and chronic cerebral hypoperfusion, which also showed higher dopaminergic vulnerability. Manipulation of the brain RAS may constitute an effective neuroprotective strategy against dopaminergic vulnerability and progression of Parkinson’s disease.

REFERENCES