Imipramine and amitriptyline ameliorate the rotenone model of Parkinson's disease in rats

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Abstract

Amitriptyline (AMI), a commonly prescribed tricyclic antidepressant (TCA) to parkinsonian patients, specifically showed a significant delay in dopaminergic therapy initiation and improvement in motor disability in parkinsonian patients. Moreover, it was recently shown that AMI has neuroprotective properties; however, the mechanisms underlying this effect in Parkinson's disease (PD) are not fully understood. The current study aimed to investigate the possible neuroprotective mechanisms afforded by AMI in the rotenone model of PD and to assess whether another TCA member, imipramine (IMI), shows a corresponding effect. Rats were allocated into seven groups. Four groups were given either saline, dimethyl sulfoxide, AMI or IMI. Three rotenone groups were either untreated or treated with AMI or IMI. Rats receiving rotenone exhibited motor impairment in open field and rotarod tests. Additionally, immunohistochemical examination revealed dopaminergic neuronal damage in substantia nigra. Besides, striatal monoamines and brain derived neurotrophic factor levels were declined. Furthermore, oxidative stress, microglial activation and inflammation were evident in the striata. Pretreatment of rotenone groups with AMI or IMI prevented rotenone-induced neuronal degeneration and increased striatal dopamine level with motor recovery. These effects were accompanied by restoring striatal monoamines and brain-derived neurotrophic factor levels, as well as reducing oxidative damage, microglial activation and expression of proinflammatory cytokines and inducible nitric oxide synthase. The present results suggest that modulation of noradrenaline and serotonin levels, up-regulation of neurotrophin, inhibition of glial activation, anti-oxidant and anti-inflammatory activities could serve as important mechanisms underlying the neuroprotective effects of the used drugs in the rotenone model of PD.

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