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Meeting abstract

Chronic administration of rotenone induces Parkinsonian symptoms and increases levels of nitric oxide in rat brain

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Background

Parkinson's disease (PD) is one of the most widespread neurodegenerative diseases. A reduction of complex I activity has been demonstrated in mitochondria of PD patients. Recently, it was shown that chronic subcutaneous exposure to low doses of rotenone (an inhibitor of mitochondrial NADH dehydrogenase and a commonly used pesticide) caused highly selective nigrostriatal dopaminergic lesions. However, while the behavioural effects of rotenone administration are well characterised, the mechanisms underlying rotenone action are unclear. Recent studies are regarding nitric oxide (NO) as universal neuronal messenger in the pathophysiology of neurodegenerative diseases. The aim of this work is to study mechanisms underlying oxidative damage of the various brain areas of rats produced by rotenone and to investigate a possible role of NO and lipid peroxidation (LPO) processes during chronic rotenone administration.

Materials and methods

Rotenone at a dose of 1.5 mg/kg i. p. or vehicle (natural oil, 1 ml/kg) was administered to male Sprague-Dawley rats daily for 10, 20, 30 and 60 days and NO and LPO were measured in the frontal and prefrontal cortices, striatum and nucleus accumbens (NAc). NO generation was directly measured using electron paramagnetic resonance spectroscopy. Specific indexes of LPO (i.e., thiobarbituric acid reactive substances, TBARS) were measured spectrophotometrically. Catalepsy was tested by measuring the descent latency after 30 and 60 days using a bar and grid test.

Results

NO levels in all studied brain structures of rats after the first rotenone injection were not different from those of the control group. In striatum and frontal cortex the level of NO was increased on day 30 and day 60. In our study on day 1 and 20 there were slight increases of TBARS in the striatum and frontal cortex, but on day 30 and 60 the amount of TBARS was two times greater as compared to control in these regions. Rotenone-treated animals showed a prolonged descent latency as compared to control animals after 60 injections of rotenone only. An increase of descent latency from day 30 to 60 was not observed.

Conclusion

The findings indicate that chronic administration of rotenone at the low dose 1.5 mg/kg significantly enhances the NO generation in all studied brain areas, especially in the NAc and striatum. Moreover, the results provide the first direct evidence that rotenone increases NO tissue levels. The results of this study should advance the under-

standing of the mechanism of action for pesticides in the pathogenesis of PD.