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Epigallocatechin-3-gallate, a green tea polyphenol, reduces MPTP-induced neurotoxicity by down-regulation of inducible nitric oxide synthase

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Objective: To examine the neuroprotective potential of epigallocatechin-3-gallate (EGCG), one of green tea polyphenols, and study the mechanism of action.

Background: Green tea polyphenols have free radical scavenging, antiinflammatory, and anticarcinogenic effects. Recently, neuroprotective actions of tea polyphenols have been described in the models of cerebral ischemia and 6-hydroxydopamine-induced neurotoxicity. In the present study, the neuroprotective potential of EGCG is examined in a MPTP Parkinson model.

Methods: Male C57Bl/6 mice (20-25g) were administered with EGCG (10 and 50mg/kg/d, i.p.) for 14 days. During the last 4 days of EGCG treatment, mice received 4 doses of MPTP (20mg/kg/d, i.p.) Mice treated with normal saline served as a negative control, and mice with MPTP only (20mg/kg/d for 4 days) as a positive control. Animals were sacrificed 7 days following above treatments. Immunohistochemical staining (N=7/each group) for tyrosine hydroxylase(TH) in the substantia nigra (SN), western blot (N=5/each group) for TH in the striatum, and for inducible nitric oxide synthase (iNOS) and nuclear factor kappa B (NF-kB) in the striatum and SN were performed.

Results: In the MPTP group, the number of nigral TH-positive cells and the amount of striatal TH protein were decreased by 25% compared with a negative control. In the EGCG group, the number of nigral TH-positive neurons was decreased only by 10%, and the amount of striatal TH protein by 5-10% of a negative control. Therefore, EGCG treatment rescued about 15% of nigral dopaminergic neurons from MPTP neurotoxicity. In the MPTP group, iNOS levels in the striatum and SN were increased by 15-20% compared with a negative control. Pretreatment with EGCG reduced the iNOS levels to the range of a negative control in both regions. NF-kB levels were increased by 20% in the SN in the MPTP group, and were normalized by EGCG pretreatment. There were no differences between 10 and 50mg/kg of EGCG dosage.

Conclusions: Neuroprotective potential of EGCG is demonstrated in this model. EGCG may exert its neuroprotective effect by inhibiting iNOS expression and down-regulation of NF-kB.