Resveratrol Promotes Remyelination in Cuprizone Model of Multiple Sclerosis:

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Abstract

Multiple sclerosis (MS) is a demyelinating neurodegenerative disease, representing a major cause of neurological disability in young adults. Resveratrol is a stilbenoid polyphenol, known to pass blood brain barrier and exhibit antioxidant, anti-inflammatory, and neuroprotective effects in several brain injuries. Cuprizone model of MS is particularly beneficial in studying demyelination/remyelination. Our study examined the potential neuroprotective and pro-remyelination effects of resveratrol in cuprizone-intoxicated C57Bl/6 mice. Mice were fed with chow containing 0.7% cuprizone for 7 days, followed by 3 weeks on 0.2% cuprizone diet. Resveratrol (250 mg/kg/day, p.o.) was given for 3 weeks starting from the second week. At the end of the experiment, animals were tested on rotarod to evaluate changes in balance and motor coordination. Mice were then sacrificed to measure the brain content of glutathione, lipid peroxidation products, adenosine triphosphate, and phospho-inhibitory subunit of nuclear factor κB-α. The activities of cytochrome oxidase and superoxide dismutase were also assessed. The gene expression of myelin basic protein, 2',3'-cyclic nucleotide 3' phosphodiesterase, oligodendrocyte transcription factor-1 (Olig1), NF-κB p65 subunit, and tumor necrosis factor-α was also estimated. Luxol fast blue/periodic acid-Schiff stained brain sections were blindly scored to assess the myelin status. Resveratrol effectively enhanced motor coordination and balance, reversed cuprizone-induced demyelination, improved mitochondrial function, alleviated oxidative stress, and inhibited NF-κB signaling. Interestingly, resveratrol increased Olig1 expression that is positively correlated to active remyelination. The present study may be the first to indicate a pro-remyelinative effect for resveratrol which might represent a potential additive benefit in treating MS.

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