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## LEF CONTROVERSY

### Effect Of Long-Term Deprenyl Treatment On Age-Dependent Changes In The Rat Brain

Recently, scientists at the Camerino in Italy explored the effects of deprenyl treatment on age-related microanatomical changes in the brains of male Sprague-Dawley rats. Deprenyl was given by subcutaneous injection in two doses (1.25 mg/kg/day and 5 mg/l daily) for 5 months (from 19-to- 24-months of age), with age-matched untreated rats used as controls and 11-month-old rats used as an adult reference group<sup>25-26</sup>

They found that the number, den- density, and metabolic activity of neurons and glial cells were decreased with age in untreated rats in the hippocampus (which plays a key role in learning and memory), the frontal cortex (which is involved in information processing), and the cerebellar cortex (which coordinates movement and balance).

They also observed that deprenyl (at 5 mg, but not 1.25 mg) prevented the decline in neuronal activity in certain areas of the brain, but not in others. The drug was particularly effective in preserving hippocampal neurons and Purkinje neurons in the cerebellar cortex. The lower dose of deprenyl (1.25 mg/kg/day), which did not affect MAO-B activity, prevented the age-related buildup of aging pigment (lipofuscin), but did not prevent the loss the neurons. Their conclusion was that *"treatment with L-deprenyl is able to counter some microanatomical changes typical of the aging brain. Some of these facts are probably not related to the inhibitory MAO-B activity of the compound."*<sup>26</sup>

#### DEPRENYL BOOSTS SOD AND CATALASE LEVELS

Deprenyl has antioxidant properties, but it can also boost levels of the body's own antioxidant enzymes *superoxide dismutase* (SOD) and catalase in the brains of laboratory rats. The studies demonstrating these effects were conducted by M.C. Carrillo and associates at the Tokyo Metropolitan institute of Gerontology in Japan.<sup>27-28</sup>

The Japanese scientists gave 6- month-old Fisher-344 rats daily sub- cutaneous injections of 2 mg/kg of deprenyl for 3 weeks, while control animals received saline injections. They found a 300% increase in SOD and a 60% increase in *catalase* in the substantia nigra, but not in the hippocampus or cerebellum. They noted that:

*"Our present results thus show that deprenyl's effect is rather selective to certain brain regions. It is interesting to see some significant increase in SOD activities, especially that of Mn-SOD, in certain cortical regions of the cerebellum. On the other hand, there was essentially no effect of deprenyl on the enzyme activities in the liver. Since there is abundant MAO-B activity in the liver as well as in the hippocampus, it seems unlikely that the ability of deprenyl to increase SOD activity is dependent on the presence of MAO-B."*<sup>27-28</sup>

#### EFFECT OF DEPRENYL ON NIGRAL NEURONS IN PARKINSON'S DISEASE

Although the tissue culture and animal studies suggesting that deprenyl has a neuroprotective effect on brain neurons are impressive, none of them provide direct evidence of the effect of deprenyl on neurons in the brains of Parkinson's patients. There is one study, however, by researchers at the University of Turku in Finland, that speaks volumes on the subject.<sup>29</sup>

Since substantia nigra neurons are destroyed in Parkinson's disease and the pathologic hallmark of the disease is neural lesions called Lewy bodies, the Finnish scientists studied a randomly selected sample of 25 brains from patients who had died of Parkinson's disease. Ten of the 25 patients had received P deprenyl and L-Dopa and 15 had received L-Dopa alone. They then counted the neurons and Lewy bodies in the medial section of the substantia nigra of all 25 brains.

They found that:

*"The present results show that the number of medial nigral neurons is greater and the number of Lewy bodies per neuron is smaller in those Parkinson's disease patients who had been treated with selegiline in combination with levodopa as compared with patients who had received levodopa alone. These findings indicate that the degeneration of the substantia nigra is less severe in patients who had had selegiline treatment."*<sup>29</sup>

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