THE NEUROPROTECTIVE EFFECT OF RASAGILINE, A MAO-B INHIBITOR, ON THIAMINE DEFICIENCY-INDUCED NEURODEGENERATION IN RATS

M. Rehavi¹, V. Dror¹, Y. Assaf², A. Fattal-Valevski³, S. Eliash¹

¹Physiology and Pharmacology, ²Neurobiochemistry, ³Tel-Aviv Sourasky Medical Center, Tel-Aviv University, Tel-Aviv, Israel

Introduction: Selective neurodegeneration accompanied by mitochondrial dysfunction characterizes neurodegenerative disorders such as Alzheimer’s and Parkinson’s diseases. Thiamine deficiency (TD) in rats is a model for the study of cellular and molecular mechanisms that lead to selective neuronal loss caused by chronic oxidative deficits.

Aims: To study the effect of rasagiline, a MAO-B inhibitor, on the in-vivo progression of thiamine deficiency-induced neurodegeneration in rat.

Methods: Rats were fed a thiamine-deficient diet accompanied by injections of the central thiamine antagonist, pyrithiamine. The progression of the neurodegeneration processes, with and without co-administration of rasagiline, was characterized using neurobehavioral tests and histopathology as well as several MRI techniques.

Results: Rats exposed to TD protocol developed neurodegeneration over a period of 12 to 14 days along with neurological impairments, cognitive deficits and neuropathological lesions. Decrease in the fractional anisotropy (FA) was found on day 10, a presymptomatic stage, in the inferior colliculi and in the thalamus, while the earliest detectable changes in the T₂ parameter occurred on day 12. FA values in the thalamus remained low after thiamine restoration, suggesting irreversible disarrangement and replacement of neuronal structures. FA values in the frontal cortex significantly increased on days 14 and 31. An enlargement of the lateral ventricles was observed and persevered during the recovery period. Rasagiline both ameliorated and delayed neuronal injury. It improved cognition, decreased the severity of the histopathological changes and diminished the neuropathological lesions significantly.

Conclusions: In TD model of neurodegeneration, rasagiline provides a significant neuroprotection which could have implications for clinical neurodegenerative disorders.