Neuroprotection by Rasagiline: A New Therapeutic Approach to Parkinson’s Disease?

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ABSTRACT

Neuronal death in Parkinson’s disease (PD) may originate from the reciprocal interactions of a restricted number of conditions, such as mitochondrial defects, oxidative stress and protein mishandling, which would favor a state of apoptotic cell death in the nigrostriatal pathway. The search for pharmacological treatments able to counteract the nigrostriatal degeneration, possibly by interfering with these phenomena, has recently raised considerable interest in rasagiline [R(+)-N-propargyl-1-aminoindan], a potent, selective, and irreversible inhibitor of monoamine oxidase B (MAO-B). Rasagiline, like selegiline, is a propargylamine, but is 10 times more potent. Unlike selegiline, rasagiline is not metabolized to amphetamine and/or methamphetamine and is devoid of sympathomimetic activity. Numerous experimental studies, conducted both in vitro and in vivo, have shown that rasagiline possesses significant protective properties on neuronal populations. The pro-survival effects of the drug appear to be linked to its propargyl moiety, rather than to the inhibitory effect on MAO-B. Rasagiline’s major metabolite, aminooindan — which possesses intrinsic neuroprotective activity — may also contribute to the beneficial effects of the parent compound.

Rasagiline has been recently evaluated in early PD patients, with results that are consistent with slowing the progression of the disease. Therefore, the neuroprotective activity shown by the drug under experimental conditions may be reflected in the clinic, thus providing new perspectives for the treatment of PD.