

## Rasagiline Improves Metabolic Function and Reduces Tissue Injury in the Substantia Nigra in Parkinson's Disease: A Longitudinal In-Vivo Advanced MRI Study

**Authors :** Omar Khan, Shana Krstevska, Edwin George, Veronica Gorden, Fen Bao, Christina Caon, NP-C, Carla Santiago, Imad Zak, Navid Seraji-Bozorgzad

**Abstract :** Objective: To quantify cellular injury in the substantia nigra (SN) in patients with Parkinson's disease (PD) and to examine the effect of rasagiline of tissue injury in the SN in patients with PD. Background: N-acetylaspartate (NAA) quantified with MRS is a reliable marker of neuronal metabolic function. Fractional anisotropy (FA) and mean diffusivity (MD) obtained with DTI, characterize tissue alignment and integrity. Rasagiline, has been shown to exert anti-apoptotic effect. We applied these advanced MRI techniques to examine: (i) the effect of rasagiline on cellular injury and metabolism in patients with early PD, and (ii) longitudinal changes seen over time in PD. Methods: We conducted a prospective longitudinal study in patients with mild PD, naive to dopaminergic treatment. The imaging protocol included multi-voxel proton-MRS and DTI of the SN, acquired on a 3T scanner. Scans were performed at baseline and month 3, during which the patient was on no treatment. At that point, rasagiline 1 mg orally daily was initiated and MRI scans were obtained at 6 and 12 months after starting rasagiline. The primary objective was to compare changes during the 3-month period of "no treatment" to the changes observed "on treatment" with rasagiline at month 12. Age-matched healthy controls were also imaged. Image analysis was performed blinded to treatment allocation and period. Results: 25 patients were enrolled in this study. Compared to the period of "no treatment", there was significant increase in the NAA "on treatment" period (-3.04 % vs +10.95 %,  $p=0.0006$ ). Compared to the period of "no treatment", there was significant increase in following 12 month in the FA "on treatment" (-4.8% vs +15.3%,  $p<0.0001$ ). The MD increased during "no treatment" and decreased in "on treatment" (+2.8% vs -7.5%,  $p=0.0056$ ). Further analysis and clinical correlation are ongoing. Conclusions: Advanced MRI techniques quantifying cellular injury in the SN in PD is a feasible approach to investigate dopaminergic neuronal injury and could be developed as an outcome in exploratory studies. Rasagiline appears to have a stabilizing effect on dopaminergic cell loss and metabolism in the SN in PD, that warrants further investigation in long-term studies.

**Keywords :** substantia nigra, Parkinson's disease, MRI, neuronal loss, biomarker

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