

## Rasagiline-associated Hypersexuality

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### Abstract

**Introduction:** Hypersexual behavior has been reported in patients with Parkinson disease, particularly when treated with dopamine agonists. The effect on sexual behavior of monoamine oxidase inhibitors type B (MAO-B) is less clear cut.

**Aims:** This article reports a case of hypersexuality that appears to be induced by rasagiline therapy, a MAO-B inhibitor.

**Methods:** A 86-year-old man, with Parkinson disease, was initially treated with rasagiline alone at a dose of 1mg/day. After 1 month, he began on presenting hypersexuality. This behavior stopped within 2 weeks after rasagiline discontinuation. Then, Parkinson disease was treated with levodopa 50 mg/day, benserazide 12.5 mg three times a day and entacapone 200 mg twice daily. No hypersexuality reappeared.

**Results:** The time sequence of the start of the drug rasagiline and onset of the sexual behavior and of the rapid improvement after rasagiline discontinuation is consistent with drug-related hypersexuality. This effect could be attributed to dopamine potentiation properties of rasagiline. However, in our patient, levodopa did not produce the adverse effect. We can assume that rasagiline increases preferentially central dopamine at the medial preoptic area, which is the main integrative site for male sexual behavior. We can also hypothesize that rasagiline induces stimulation of serotonin receptors subtypes that enhance sexual functioning.

**Conclusion:** This is the first case report, to our knowledge, of hypersexuality secondary to rasagiline taken alone and not in combination with another antiparkinsonian therapy, in which there were no other confounders such as prior therapy with levodopa. Prescribers and users of rasagiline should be alert to the possibility of such adverse reactions to be more able to assess and treat these disabling sexual problems.

**Keywords:** Parkinson disease; Rasagiline; Hypersexuality

### Introduction

Parkinson disease treatments are well known to produce impulsive control disorders like hypersexuality [1]. Pathological increased sexual desire and aberrant sexual behaviour have previously been reported in Parkinson disease patients receiving dopamine agonists and MAO-B inhibitors including rasagiline [2-5], but not in patients treated de novo with rasagiline. We hereby report a case of hypersexuality that appears to be induced by rasagiline therapy.

### Case Description

A 86-year-old white man, with a medical history of Parkinson disease, was admitted to the department of neurology for motor symptoms aggravation. He was initially treated with rasagiline alone at a dose of 1mg/day. He had no premorbid history of abnormal sexual behavior. The medical history was cardiac insufficiency treated with ramipril. After 1 month of initiating his medication, he began on presenting hypersexuality. He had heightened sexual desire and increased demands to have sexual intercourse. Laboratory investigations revealed mild renal impairment. These behaviors stopped within 2 weeks after rasagiline discontinuation. Then, Parkinson was treated with Levodopa 50 mg and benserazide 12.5 mg three times a day, in combination with entacapone 200 mg twice daily. Fludrocortisone at 50 mg per day was introduced to treat persistent hypotension. No hypersexuality reappeared.

### Discussion

Rasagiline is a selective irreversible monoamine oxydase B (MAO-B) inhibitor given orally to treat Parkinson motor symptoms. This drug is usually well tolerated with headache, insomnia, xerostomia, abdominal discomfort, nausea, and diarrhea most commonly reported side effects.

Since a psychiatric examination was not realized, the available data only allow a broad diagnosis of paraphilia. The medical and personal history of this patient did not suggest any underlying mental disorder. The time sequence of the start of the drug rasagiline and onset of the sexual behavior is consistent with drug-related hypersexuality. Although no rechallenge was attempted, the rapid improvement after rasagiline discontinuation seems to indicate an association of the sexual behavior disorder with the drug use.

Moreover, no other one of its treatments could explain this adverse effect. Ramipril, alone or in combination with rasagiline, has not been shown to enhance sexual function. In ONTARGET trial, treatment with Ramipril did not ameliorate erectile function [6]. And finally, exposure to rasagiline may be slightly increased by renal impairment. For this event the Naranjo adverse drug reaction score indicates that it is probable that there was an adverse drug effect.

A number of animal studies have suggested that dopamine promotes sexual functions. Although testosterone is considered the main mediator of sexual desire in men and women, central nervous system dopaminergic and serotonergic pathways seem to play an important role. In particular, brain dopamine systems (incerto-hypothalamic and mesolimbic) that link the hypothalamus and limbic system appear to form the core of the excitatory system [7].

The effect of rasagiline on sexual behavior may be explained by inhibiting monoamine oxidase B, with resultant increases in endogenous dopamine content. However, in our patient, levodopa therapy without rasagiline did not produce the adverse effect. Rasagiline could preferentially increase central dopamine at the medial preoptic area, which is the main integrative site for male sexual behaviour [8].

Another approach is the involvement of the serotonergic system. Some evidence suggests that activation of the 5-HT<sub>2</sub> receptor impairs sexual functioning and stimulation of the 5-HT<sub>1A</sub> receptor facilitates sexual functioning [9]. The improvement observed after the intake of antidepressant drug sertraline (a selective serotonin reuptake inhibitor) in other cases of Parkinson Disease patients who experienced paraphilia while being treated with selegiline leads Meco et al. to hypothesize that the serotonergic system may also be involved in the development of paraphilia in patient affected by Parkinson disease [10]. When considering the pharmacological properties of rasagiline, unselective inhibition of MAO-A cannot be completely excluded. Administered chronically, hippocampal and midbrain tissue levels of serotonin in rats increased after rasagiline daily doses augmentation [11]. In our case, exposure to rasagiline may stimulate serotonin receptors subtypes which enhance sexual functioning.

## Conclusion

Although the mechanism of rasagiline induced hypersexuality is still speculative, rasagiline has been associated with hypersexuality independently of another Parkinson Disease treatment. Sexuality is a basic human right and a significant determinant of quality of life. Prescribers should assess sexual dysfunction in routine care of Parkinson disease treatment and users of drug rasagiline should be alert to the possibility of such adverse reactions. The explanation of how this drug might have an impact on sexual desire could help to drug development in the treatment of hypoactive sexual desire disorder. This case has been reported to the French National Health Authorities (registered as number GR12-00102).

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