RESEARCH ARTICLE

The Effects of Rasagiline on Cognitive Deficits in Parkinson's Disease Patients Without Dementia: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study

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ABSTRACT: Cognitive impairment can occur at all stages of Parkinson's disease. Rasagiline is a selective monoamine oxidase type-B inhibitor that enhances central dopaminergic transmission. Dopamine is thought to be involved in certain cognitive processes such as working memory. We assessed the effects of rasagiline on cognitive deficits in cognitively impaired, nondemented patients with Parkinson's disease. This was a randomized, double-blind, placebo-controlled prospective study. Patients with Parkinson's disease receiving stable dopaminergic treatment were assigned to receive rasagiline 1 mg/day or placebo for 3 months. Patients were eligible if they had impairment in 2 of 4 cognitive domains (attention, executive functions, memory, visuospatial functions) in the screening neuropsychological tests, yet did not fulfill criteria for Parkinson's disease dementia. Fifty-five patients were randomized; 48 patients completed the study. Patients in the rasagiline group showed significant improvement in digit span–backward compared with the placebo group ($P = .04$), with trends favoring rasagiline in digit span total and digit-ordering tests. Verbal fluency total score showed a significant difference in favor of rasagiline ($P = .038$), with trends favoring rasagiline in semantic fluency test and Stroop spontaneous corrections. The composite cognitive domain Z scores revealed a significant difference in favor of rasagiline compared with placebo in the attentional Z score ($P < .005$). There were no significant differences between the 2 groups in the other cognitive tests or cognitive domain Z scores. The monoamine oxidase type-B inhibitor rasagiline may exert beneficial effects on certain aspects of attention and executive functions in nondemented patients with Parkinson's disease with cognitive impairment. © 2011 *Movement* Disorder Society

Key Words: Parkinson's disease; cognitive impairment; treatment; rasagiline; attention

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Parkinson's disease (PD) is a neurodegenerative disorder primarily associated with progressive loss of dopaminergic neurons in the substantia nigra. Cognitive impairment associated with PD ranging from mild impairment to overt dementia can occur at all stages of the disease. Although dementia is commonly a late clinical feature of PD, subtle cognitive dysfunction can be found already early in the disease course.[1] The presence of cognitive impairment is associated with increased risk for subsequent dementia.[2,3] The pattern of cognitive impairment in nondemented patients with PD typically includes deficits in executive functions, memory, visuospatial functions, and attention.

Several studies in PD patients receiving dopaminergic treatment suggested that dopaminergic substitution may have positive effects on some cognitive abilities.[4,5] In particular, dopaminergic treatment may improve frontal lobe–related tasks such as working memory and executive functions.[6] However, the effect of dopaminergic drugs on cognition in PD is complex; different studies have reported to improve, deteriorate, or not affect cognitive performance.[7] The conflicting results may be a result of the neuropsychological tests used for assessing cognition and more so of the patient population included, in particular regarding disease stage and the amount of dopaminergic denervation in various parts of the brain.

Rasagiline is a second-generation, selective, irreversible monoamine oxidase type-B (MAO-B) inhibitor, indicated for the treatment of motor symptoms in both early- and moderate- to late-stage PD. By inhibiting the breakdown of dopamine, rasagiline prolongs its synaptic residency time and thus enhances central dopaminergic transmission.[8]

The effects of rasagiline on cognitive functions in patients with PD have not been reported. The objective of this study was to assess the effects of rasagiline (1 mg/day) on cognitive deficits in cognitively impaired but not demented patients with PD.

Patients and Methods

This was a 12-week randomized, multicenter, double-blind, placebo-controlled prospective study conducted in 4 centers in Turkey. Patients were recruited from the Movement Disorders Outpatients Clinics, Department of Neurology, Istanbul Faculty of Medicine, Dokuz Eylul University, Faculty of Medicine, Ondokuz Mayis University, Faculty of Medicine, and Marmara University, Faculty of Medicine. All patients were examined by neurologists who are movement disorder specialists. Patients were randomly assigned in a ratio of 1:1 to receive rasagiline 1 mg/day or placebo for 12 weeks. Cognitive and behavioral assessments were performed at baseline, week 4, and week 12.

Subjects

The diagnosis of PD was based on the UK Parkinson Society Brain Bank criteria for clinical diagnosis.[9] Exclusion criteria were: diagnosis of dementia due to PD according to *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR), criteria,[10] diagnosis of current major depression or psychosis according to DSM-IV-TR criteria, presence of any other neurodegenerative disorder other than PD, history of PD surgery, and presence of any unstable or untreated systemic disorder such as diabetes, cardiac failure, or renal failure. Patients on psychoactive drugs or any other medications that could alter cognitive status were not permitted. Patients must have had at least 5 years of education and have been free of severe verbal or motor disability that would interfere with neuropsychological testing. All patients were to be on stable PD medication for at least 3 months prior and throughout the study. Anticholinergic drugs were prohibited. The severity of clinical symptoms was assessed using the Hoehn and Yahr scale[11] and motor status was evaluated with the Unified Parkinson's Disease Rating Scale (UPDRS) part III–Motor.[12] In fluctuating patients both motor and cognitive functions were assessed in the "on" state. Patients were required to be in the mild to moderate stages of the disease, with Hoehn–Yahr score ranging from 1 to 3. Patients with major depression were excluded by clinical interview and using the Geriatric Depression Scale (cutoff score, 13).[13] This study was approved by the Ethics Committee of the Istanbul Faculty of Medicine. Informed written consent was obtained from all subjects before study-related procedures were initiated.

Patients were considered to be cognitively impaired but not demented if they fulfilled the following criteria: subjective cognitive complaints such as forgetfulness, word finding difficulties, or inattentiveness; preserved daily living activities; impairment in at least 2 of 4 cognitive domains in the screening neuropsychological tests; and not fulfilling criteria for dementia due to PD according to DSM-IV criteria. For screening purposes, 4 cognitive domains (global attention, executive functions, memory, and visuospatial functions) were assessed. Impairment in a domain was defined as a performance 1.5 standard deviations below the normative mean score for age and education. The following tests were used: digit span for attention, letter fluency test for executive functions, logical memory subscale from the Wechsler Memory Scale–Revised for memory, and the line orientation test for visuospatial function.

Neuropsychological Testing

Cognitive functions were evaluated by selected neuropsychological tests representing each cognitive domain including global attention, executive functions, memory, language, and visuospatial functions. Individual tests included digit span–forward and –backward from the Wechsler Adult Intelligence Scale[14] and digit ordering test[15] for global attention; verbal fluency tests (K-A-S for letter fluency and category naming for semantic fluency),[16] clock drawing test,[17] Stroop test,[18] and Trail Making Test (TMT) A and B[19] for executive functions; verbal learning test and visual recognition test from the Wechsler Memory Scale–Revised[20] for memory, and the 30-item abbreviated Turkish version of the Boston Naming Test for language[21] and the Benton facial recognition and Benton line orientation tests for visuospatial functions.[22,23]

Primary analysis in week 12 was based on change from baseline. This was an exploratory trial, and there was no a priori defined primary end point. The individual test scores and 5 cognitive domain subscores were analyzed separately. Differences between the 2 groups were compared in week 12 in change from baseline on the individual neuropsychological tests. *Z* scores were calculated for each domain in order to harmonize different units used in different cognitive tests, as well as to assess potential effects on a given domain as a whole. As the number of tests in different domains varied, depending on the spectrum of cognitive processes inherently present in that domain, we chose the representative tests (or subscores) on their face value for each presumed cognitive subfunction for a given domain. Domain *Z* scores were calculated by combining the following tests in each domain: attention *Z* score, digit span total + digit ordering test; executive *Z* score, verbal fluency total + clock drawing test + Trail Making Test B-A + Stroop spontaneous corrections; memory *Z* score, verbal recall + verbal recognition + verbal learning + visual immediate recall + visual delayed recall; visuospatial *Z* score, Benton line orientation test + Benton facial recognition test; language *Z* score, Boston Naming Test total score. *Z* scores of selected tests for each domain were calculated according to the following formula: $Z =$ (data point mean)/standard deviation. Domain *Z* scores were obtained by summing the calculated *Z* scores of selected tests.

Post hoc analysis of differences between the 2 groups in change from baseline was conducted in week 4 in order to assess the onset of any effects.

Other Evaluations

Effects of study medications on mood were evaluated using the Geriatric Depression Scale (GDS), on anxiety using the State Anxiety Inventory (STAI-TX),[24] and on motor functions using UPDRS part III by comparing the changes from baseline to the end of the study.

Statistical Analysis

Statistical analysis was conducted using SPSS for Windows (version 15.0; SPSS Inc., Chicago, IL). The chi-square test was used for the comparison of independent categorical variables. For the comparison of independent numerical variables, the independent-samples *t* test was used when the data were normally distributed and the Mann–Whitney *U* test when the distribution was not normal. The paired-sample *t* test was used to determine differences between 2 dependent groups when the data were normally distributed and the Wilcoxon test when they were not. $P \leq .05$ was considered statistically significant.

TABLE 1. Clinical and demographic features of study groups

	Rasagiline (n = 23)	Placebo (n = 25)	*P*
Age (y)	65.17 ± 9.5	67.56 ± 10.13	ns
Sex (female/male)	6/17	9/16	ns
Education (y)	8.13 ± 4.16	8.40 ± 3.91	ns
Duration of PD (y)	4.09 ± 2.54	3.96 ± 2.26	ns
Hoehn & Yahr score	2.00 ± 0.69	1.64 ± 0.60	ns
UPDRS-part III score	23.09 ± 9.96	18.84 ± 8.62	ns
Geriatric Depression Scale score	8.00 ± 4.00	7.08 ± 4.26	ns
State Anxiety score	31.76 ± 7.48	31.25 ± 8.75	ns

All data are shown as mean ± standard deviation; ns, nonsignificant

Results

Fifty-five patients were randomized, and 48 patients (15 female, 33 male) completed the study, 23 in the rasagiline 1 mg/day group and 25 in the placebo group. There were only a few adverse events reported (2 patients reported headache and 1 low-back pain), and none of the patients discontinued because of adverse events. Seven subjects dropped out during the study because they were unable to comply with study procedures; they were not included in the statistical analysis. Mean age was 66.4 ± 10.4 years (range, 42–81 years), mean time from diagnosis was 4 ± 2.4 years (range, 1–10 years), and mean Hoehn–Yahr score was 1.8. Twenty-one patients in the rasagiline group and 23 patients in the placebo group were receiving L-dopa preparations, and 13 patients in each group were on dopamine agonists. There were only a few patients receiving antidepressants; the numbers were similar in both groups. There were no patients receiving sedatives, hypnotic drugs, or antipsychotics. No significant differences were observed between the 2 groups in any of the baseline characteristics. Clinical features and demographic data at baseline are summarized in Table 1.

Neuropsychological Tests

Neuropsychological test results are shown in Tables 2 and 3. At baseline there were no statistically significant differences between the 2 groups in the profile and severity of cognitive impairments. In the attentional tests, patients in the rasagiline group showed significant improvement in digit span–backward compared with the placebo group in week 12 ($P = .04$), with trends favoring rasagiline in digit span total ($P = .058$) and the digit ordering test ($P = .052$). In the executive function tests, verbal fluency total score showed a significant difference in favor of rasagiline compared with placebo ($P = .038$), with trends favoring rasagiline in semantic

TABLE 2. Results of efficacy analysis

Variable	Baseline score	Change in week 12	Between-group difference in week 12	
	Mean ± SD		Estimate ± SE	*P* value
		Attention		
Digit span–forward				
Rasagiline	4.39 ± 0.89	0.26 ± 0.86	0.14 ± 0.25	0.792
Placebo	4.6 ± 1.04	0.12 ± 0.88		
Digit span–backward				
Rasagiline	3 ± 0.8	0.30 ± 1.02	0.58 ± 0.28	0.04
Placebo	3.52 ± 0.82	−0.28 ± 0.89		
Digit span total				
Rasagiline	7.39 ± 1.31	0.57 ± 1.44	0.73 ± 0.36	0.058
Placebo	8.12 ± 1.54	−0.16 ± 1.07		
Digit Ordering Test				
Rasagiline	26.17 ± 9.76	2.96 ± 6.94	3.79 ± 1.9	0.052
Placebo	29.29 ± 9.29	−0.83 ± 6.07		
		Executive functions		
Semantic verbal fluency				
Rasagiline	16.35 ± 4.78	1.45 ± 4.44	2.17 ± 1.41	0.06
Placebo	15.32 ± 5.96	−0.72 ± 5.16		
Lexical verbal fluency				
Rasagiline	19.43 ± 10.15	3.14 ± 6.78	2.62 ± 1,81	0.156
Placebo	21.88 ± 8.78	0.52 ± 5.66		
Verbal fluency total				
Rasagiline	35.78 ± 13.24	4.59 ± 8.42	4.79 ± 2.24	0.038
Placebo	37.20 ± 12.29	−0.20 ± 6.91		
Clock drawing test				
Rasagiline	7.83 ± 3.08	0.52 ± 2.79	0.48 ± 0.66	0.489
Placebo	7.92 ± 2.64	0.04 ± 1.70		
Trail Making Test A				
Rasagiline	89.13 ± 42.47	3.09 ± 45.72	2.65 ± 10.82	0.861
Placebo	85.2 ± 32.83	0.44 ± 27.81		
Trail Making Test B				
Rasagiline	242.75 ± 138.72	10.13 ± 128.33	−1.13 ± 39.78	0.669
Placebo	212.22 ± 86.03	11.25 ± 94.09		
Trail Making Test B-A				
Rasagiline	152.9 ± 110.39	8.13 ± 98.56	−2.50 ± 32.14	0.939
Placebo	131.89 ± 76.31	10.63 ± 82.55		
Stroop time difference				
Rasagiline	67.05 ± 50.67	−8.27 ± 34.29	7.42 ± 8.84	0.406
Placebo	92.42 ± 40.55	−15.70 ± 24.43		
Stroop error				
Rasagiline	5.64 ± 9.61	−1.27 ± 8.67	0.38 ± 2.08	0.47
Placebo	3.5 ± 3.96	−1.65 ± 4.79		
Stroop spontaneous corrections				
Rasagiline	5.45 ± 3.8	−0.59 ± 2.56	1.89 ± 1.02	0.056
Placebo	8 ± 5.78	−2.48 ± 4.07		
		Memory		
Verbal immediate recall				
Rasagiline	3.87 ± 1.66	−0.17 ± 1.61	−0.49 ± 0.52	0.546
Placebo	3.44 ± 1.26	0.32 ± 1.93		
Verbal delayed free recall				
Rasagiline	8 ± 3.36	0.7 ± 2.57	−0.02 ± 0.93	0.561
Placebo	7.6 ± 3.69	0.72 ± 3.71		
Verbal recognition				
Rasagiline	5.43 ± 3.16	−0.35 ± 2.42	−0.51 ± 0.89	0.573
Placebo	5.4 ± 2.53	0.16 ± 3.60		
Verbal delayed recall + recognition				
Rasagiline	13.43 ± 2.11	0.35 ± 2.04	−0.53 ± 0.64	0.505
Placebo	13 ± 2.48	0.88 ± 2.35		
Verbal learning score				
Rasagiline	77.65 ± 18.2	−1.96 ± 16.99	0.24 ± 4.42	0.956
Placebo	77.56 ± 20.59	−2.20 ± 13.55		

Variable	Baseline score	Change in week 12	Between-group difference in week 12	
	Mean ± SD		Estimate ± SE	*P* value
Visual immediate recall				
Rasagiline	6.74 ± 3.6	1.04 ± 2.25	0.48 ± 0.73	0.514
Placebo	7.44 ± 3.16	0.56 ± 2.79		
Visual delayed recall				
Rasagiline	5.3 ± 3.31	2.26 ± 2.47	0.98 ± 0.90	0.283
Placebo	5 ± 4.06	1.28 ± 3.62		
Visual recognition				
Rasagiline	2.11 ± 1.2	0.47 ± 1.17	0.11 ± 0.40	0.501
Placebo	2.36 ± 1.36	0.36 ± 1.36		
Visuospatial functions				
Benton line orientation				
Rasagiline	17.48 ± 5.36	1.96 ± 3.18	1.32 ± 1.02	0.202
Placebo	19.16 ± 4.97	1.21 ± 3.34		
Benton facial recognition				
Rasagiline	41.3 ± 5.05	1.57 ± 4.71	−0.31 ± 1.50	0.835
Placebo	43.08 ± 4.81	0.58 ± 4.22		
Language				
Boston Naming Test total score				
Rasagiline	22.83 ± 3.59	1.65 ± 1.37	0.19 ± 0.52	0.957
Placebo	23.08 ± 3.37	1.46 ± 2.11		
Mood				
Geriatric Depression Scale				
Rasagiline	8 ± 4.2	−0.52 ± 4.43	−0.16 ± 1.37	0.86
Placebo	7.08 ± 4.26	−0.36 ± 5.02		
Anxiety-State score				
Rasagiline	31.76 ± 7.48	−1.67 ± 8.18	−3.37 ± 2.37	0.164
Placebo	31.25 ± 8.75	1.70 ± 6.94		
Anxiety-Trait score				
Rasagiline	35.38 ± 7.41	−0.76 ± 6.43	−2.11 ± 1.96	0.288
Placebo	33.79 ± 7.28	1.35 ± 6.10		
UPDRS				
Part II				
Rasagiline	10.09 ± 4.95	−2.17 ± 3.95	−0.53 ± 1.09	0.539
Placebo	9.68 ± 3.97	−1.64 ± 3.59		
Part III				
Rasagiline	23.09 ± 9.96	−4.35 ± 5.21	−2.15 ± 1.34	0.116
Placebo	18.84 ± 8.62	−2.20 ± 4.05		

For comparison of independent numerical variables, the independent-samples *t* test was used when the data were normally distributed and the Mann–Whitney *U* test when the distribution was not normal.

fluency test ($P = .06$) and Stroop spontaneous corrections ($P = .056$). There were no statistically significant differences between the 2 groups in the other attentional and executive function tests. The composite cognitive domain Z scores revealed a significant difference in favor of rasagiline compared with placebo in the attention domain Z score ($P < .005$). There were no significant differences between the 2 groups in cognitive tests assessing language, visuospatial function, and memory, as well as in the other composite cognitive domain Z scores.

The post hoc analysis in week 4 of differences in change from baseline revealed that the significant differences observed at the end of the study were already apparent in the digit ordering test ($P = .016$), verbal fluency total score ($P = .010$), and Stroop spontaneous corrections ($P = .002$). In addition, there was a significant difference between the 2 groups in Benton line orientation test ($P = .027$) and verbal fluency semantic score ($P = .020$) favoring rasagiline.

Other Measures

In week 12, there were no significant differences between the 2 groups in change from baseline in the GDS depression and Anxiety-State or Trait scores. At baseline UPDRS part III scores were slightly higher (worse motor function) in the rasagiline group. In week 12 the scores were lower than at baseline in both groups, with the decrease (improvement) larger in the rasagiline group, but the difference between the 2 groups was not statistically significant.

TABLE 3. Changes in composite cognitive domain *Z* scores

	Baseline *Z* score	Change in week 12	Between-group difference in week 12	
Variable	Mean ± SD		Estimate ± SE	*P* value
Attention				
Rasagiline	−0.43 ± 1.58	0.16 ± 0.85	0.93 ± 0.32	0.005
Placebo	0.46 ± 1.78	0.10 ± 1.16		
Executive functions				
Rasagiline	−0.43 ± 2.51	0.39 ± 2.23	0.60 ± 0.67	0.377
Placebo	0.07 ± 1.72	−0.21 ± 1.19		
Memory				
Rasagiline	0 ± 2.65	0.34 ± 2.19	0.20 ± 0.51	0.703
Placebo	0 ± 3.04	0.25 ± 2.57		
Visuospatial functions				
Rasagiline	−0.36 ± 1.74	−0.11 ± 0.97	0.21 ± 0.33	0.526
Placebo	−0.33 ± 1.36	0.2 ± 0.9		
Language				
Rasagiline	−0.04 ± 1.04	0.08 ± 0.41	0.06 ± 0.14	0.687
Placebo	0.04 ± 0.98	−0.02 ± 5.00		

For the comparison of independent numerical variables, the independent-samples *t* test was used when the data were normally distributed and the Mann–Whitney *U* test when the distribution were not normal.
Attention Z score, digit span total + Digit Ordering Test; executive functions *Z* score, verbal fluency total + clock drawing test + Trail Making Test B-A + Stroop spontaneous corrections; memory Z score, verbal delayed recall + verbal recall and recognition + verbal learning + visual immediate recall + visual delayed recall; visuaospatial functions *Z* score, Benton line orientation test + Benton facial recognition test; language *Z* score, Boston Naming Test total score.

Discussion

The objective of this study was to assess the effects of rasagiline on cognitive functions in cognitively impaired but not demented patients with PD. An extensive battery of neuropsychological tests that assess all cognitive domains was administered. The results revealed that rasagiline may confer some beneficial effects on certain aspects of cognition in this patient population. The effects became apparent in week 4 and were maintained at the end of the study in week 12. These effects were confined to several tests of attention and executive functions; there were no benefits in tests of memory, language, and visuospatial functions. The composite cognitive domain *Z* scores revealed a benefit in attention, but not in other domains. Some of the cognitive tests that showed significant differences between the 2 groups in week 4 did not do so in week 12. Whether the results on these tests represents a transient effect or chance effects cannot be concluded.

Attentional and executive dysfunctions are among the most prominent cognitive deficits in PD and may be among the earliest signs of cognitive deterioration.[2,3,25] The mechanisms underlying early cognitive impairment in PD probably involve impaired activity in frontostriatal circuits subserving cognitive functions.[26] Dopaminergic deficit is the main neurochemical impairment in PD. In addition to having motor effects, dopamine is thought to be involved in certain cognitive processes such as working memory and attention[7,27,28] that are associated with prefrontal functions. Dopamine levels have been found to be reduced in prefrontal cortices of patients with PD.[29] In nondemented patients, dopaminergic substitution treatment is described to improve certain aspects of attention and executive functions such as working memory.[30,31] As the primary effect of rasagiline is to improve the efficiency of dopaminergic transmission, the results are compatible with improved dopaminergic function in the prefrontal cortex, which is known to be depleted of dopamine early in the disease process.[32] The 2 cognitive tests in which there was significant improvement in the rasagiline group, verbal fluency and digit span, are those that rely on the integrity of the frontal lobe. The verbal fluency test was originally developed to assess fluency in aphasic patients, but impaired verbal fluency is also a sign of executive dysfunction. Digit span, especially its backward version, heavily relies on attention and working memory. Biochemical deficits underlying cognitive impairment in PD, however, are complex, and dopaminergic deficit alone does not account for the whole spectrum of cognitive dysfunction; consequently, its substitution is not expected to improve all deficits.

Previous studies have demonstrated that inhibition of MAO-B, the main enzyme that metabolizes dopamine in the brain, may also increase dopaminergic transmission in the frontal-striatal pathways, in addition to potentiating dopaminergic transmission in the nigrostriatal system. Several studies showed that the MAO-B inhibitor selegiline provided some beneficial

effects on cognition in patients with PD.[33,34] Another MAO-B inhibitor in clinical development, safinamide was also suggested to show some cognitive benefits in nondemented PD patients.[35] Although not previously reported in humans, the beneficial effects of rasagiline on learning and memory have been described in animals.[36]

Dopamine is also involved in the modulation of mood, and treatment with L-dopa has been described to improve anxiety and depression in patients with PD.[37] In our study there was no apparent effect of rasagiline on depression and anxiety scores. However, the potential effects of rasagiline on these symptoms were not adequately assessed in this study, as patients with scores indicating major depression were excluded. Good tolerability and low rates of adverse events with rasagiline were consistent with the results of previous large-scale trials.

Although the improvement from baseline in the UPDRS Motor score was greater in the rasagiline group, the difference between the 2 groups did not reach statistical significance. This was partly because of the relatively small sample size. In addition, patients were not recruited on the basis of the severity of their motor impairment; instead, they were recruited on the basis of cognitive involvement. Hence, they were relatively stable in terms of motor function and did not have much room for additional improvement in this regard.

The strengths of this study include its randomized, placebo-controlled design, extensive assessment of all cognitive domains, and inclusion of a carefully selected patient population with evidence of both subjective and objective cognitive impairment. Patients with PD dementia were deliberately excluded, as dopaminergic drugs may worsen cognitive functions in patients with dementia,[38] although no significant worsening under L-dopa treatment was also reported.[39] Limitations of the study include its relatively small sample size and large number of tests that resulted in a high number of statistical testing. Therefore, nominally significant differences should be interpreted with caution, and individual statistical significances should not be overinterpreted; instead, direction and consistency of differences should be considered. As our patient sample did not include those with dementia, the results cannot be generalized to demented PD patients.

In summary, our results suggest that the MAO-B inhibitor rasagiline may confer beneficial effects on certain aspects of attention and executive functions in nondemented PD patients with cognitive impairment. These results justify performing larger-scale placebo-controlled trials in this patient population. Such studies may include assessment of rasagiline's effects on the course of cognitive decline, as it has been suggested to have disease-modifying effects on motor function in early-stage PD patients.[40]

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