Effect of rasagiline on balance in Parkinson's disease as measured by computerized posturography

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Keywords: rasagiline, balance, posturography, Parkinson's disease

Abstract:

Background:

Falls occur in a majority of Parkinson's disease (PD) patients. Balance disturbance can be measured by computer dynamic posturography. The effect of monoamine oxidase inhibition on PD patients as measured by computer dynamic posturography has not been previously studies.

Methods:

The study will test the hypothesis that therapy with rasagiline improves balance in PD patients as measured by computerized dynamic posturography. 5 subjects will be randomized to rasagiline or placebo and 5 further subjects will be randomized to rasagiline as adjuvant therapy versus placebo. Subjects will be analyzed by computerized dynamic posturography testing. The device measures body sway under varying visual and vestibular cues and is used for assessment of balance. Subjects will be evaluated at baseline prior to taking first tablet as well as at 4 weeks and 8 weeks. In the adjuvant therapy arm, subjects will be evaluated on rasagiline but in a functional OFF state for their other PD medications. If the scores are normally distributed, we will determine whether data variance is approximately equal in all tested groups. If these conditions are met, data evaluation will continue using repeated measures ANOVA with between factor of drug (levels: rasagiline, placebo) and within factor of treatment (levels: before, after). Level of significance will be preset to 0.05.

Background:
Posturography testing for Parkinson's disease patients on monoamine oxidase (MAO) inhibitors in general has not been studied previously. In Wood's study of patients with Parkinson's disease, falls occurred in 68.3% of the subjects [1]. In Ebmeier's population study of idiopathic Parkinson's disease patients, signs of postural instability on clinical examination were among the factors listed in premature death [2].

Hypothesis

The hypothesis is that therapy with rasagiline improves balance in PD patients as measured by computerized dynamic posturography.

Methods:

Inclusion Criteria:

1. 18 years old or above
2. Clinical diagnosis of Parkinson disease by verified by movement disorders expert at the initial study visit with at least two cardinal signs of the disease (rest tremor, bradykinesia, rigidity, and postural instability).
3. For the monotherapy arm, patients must not be on amantadine, dopamine agonists, or levodopa. For the adjuvant therapy arm: Patients must be on a stable dose of their current medication for treatment of Parkinson disease which may include any combination of the following: amantadine, trihexiphenydil, dopamine agonist, and/or levodopa.
4. Patients may continue their stable dose of tricyclic, selective serotonin reuptake inhibitor, or serotonin norepinephrine reuptake inhibitor if they are on these medications at randomization.

Exclusion Criteria:

1. Catechol-O-Methyltransferase (COMT) inhibitor therapy use 30 days prior to start of study (both study arms).
2. Dopamine receptor blocker use (such as quetiapine) one week prior to taking study drug
3. For both monotherapy and adjuvant therapy arms: use of MAO inhibitor therapy including selegiline or rasagiline within 30 days prior to taking study drug and first posturography evaluation.

Study Visits:

Screening:
Patients will be evaluated by movement disorders expert who will confirm diagnosis of Parkinson disease as stipulated in inclusion criteria. Blood pressure and heart rate, as well as a complete Unified Parkinson Disease Rating Scale (UPDRS) evaluation will be performed.

Randomization:
Subjects will be randomized by facility pharmacy to either placebo or rasagiline 1 mg daily for 8 weeks. There will be 5 rasagiline monotherapy and 5 matching placebo subjects as well as 5 rasagiline adjuvant therapy and 5 matching placebo subjects.

Computerized dynamic posturography evaluation:
Subjects will be evaluated at baseline prior to taking first tablet as well as at 4 weeks and 8 weeks. In the adjuvant therapy arm, subjects will be evaluated on rasagiline but in a functional OFF state for their other PD medications.

Functional OFF will be defined as at least 24 hours post last dose of long acting dopamine agonist or levodopa extended or continuous release formulations, at least 8 hours post last dose of immediate release dopamine agonist, immediate release levodopa, or trihexyphenidyl.

Subjects will undergo computerized dynamic posturography testing via apparatus manufactured by Neurocom, Inc. This device is clinically used for measurement of balance impairment. It measures body sway under varying visual and vestibular cues [3]. Motor control test (MCT) measuring body sway during small translations of the support surface will also be used.

Conclusion of study:
Subjects will stop taking rasagiline or placebo once their 8 week supply runs out.

Power analysis to determine the number of subjects
To estimate number of subjects needed for the posturography test, we performed a power analysis using the software G*power [4]. For inputs, data from the effect of dopamine depleter tetrabenazine on posturography in Huntington's disease was used [5].

The strategy composite score here during the tetrabenzine ON state was 79.2, during tetrabenzine OFF state it was 63.5. Averaged SD for these two outcomes was 11.5 and the total sample size was 10. These data were used to calculate the anticipated effect size. This input provided the Effect Size f = 0.6826087 (Table 1).

Input of the effect size value into the G*power with requested α=0.05 and power (1-β)=0.9, weighing in the repeated measurements (before and after rasagiline) with very low correlation among repeated measures resulted in returned total sample size of 10 subjects Table 1 (please see the table of calculated inputs and outputs below). This total number will be randomized into 2 groups of subjects: rasagiline monotherapy and placebo study arm. Similarly, there will be 10 subjects in the study arm with rasagiline as an adjuvant therapy versus placebo.

F tests - `ANOVA: Repeated measures, between factors`

Analysis: `A priori: Compute required sample size`

Input:	Effect size f	=	0.6826087
	α err prob	=	0.05
	Power (1-β err prob)	=	0.9
	Number of groups	=	2
	Repetitions	=	4
	Corr among rep measures	=	.1
Output:	Noncentrality parameter λ	=	14.337066
	Critical F	=	5.317655
	Numerator df	=	1.000000
	Denominator df	=	8.000000
	Total sample size	=	10
	Actual power	=	0.910691

Table 1. G*power software inputs and outputs for statistical power

General approach for statistical evaluation of the study data

The output of the posturography testing are computer-calculated scores. Though these scores are discrete (do not represent a continuous variable), they still may fit the requirements of parametric statistical tests. Thus, we will first test the raw scores for normal distribution using a Kolmogorov-Smirnov test versus dataset with known Gaussian distribution. If the scores are normally distributed, we will determine whether data variance is approximately equal in all tested groups. If these conditions are met, we will continue data evaluation using repeated measures ANOVA with between factor of drug (levels: rasagiline, placebo) and within factor of treatment (levels: before, after). Level of significance will be preset to 0.05. Since no multiple comparisons are planned, there will be no adjustments of p.

If we do not find the Gaussian distribution of scores or if the variances among the groups are unequal (difference of one order of magnitude or more), we will calculate non-parametric statistics to determine differences. For this purpose we will use Wilcoxon Signed Rank test and evaluate separately rasagiline and placebo groups with p preset to 0.05.

Abbreviations

COMT: Catechol-O-Methyltransferase

HD: Huntington's disease

MCT: Motor control test

PD: Parkinson's disease

References:

1. Wood BH, Bilclough, Bowron A. Incidence and prediction of falls in Parkinson's disease: a prospective multidisciplinary study. J Neurol Neurosurg Psychiatry 2002;72:721-725
2. Ebmeier KP, Calder SA, Crawford JR, et al. Mortality and causes of death in idiopathic Parkinson's disease: results from the Aberdeen whole population study. Scott Med J 1990;35:173–5.
3. Ondo WG, Almaguer M, Cohen H. Computerized posturography balance assessment of patients with bilateral ventralis intermedius nuclei deep brain stimulation. Mov Disord. 2006;21:22243–7.
4. Faul F, Erdfelder E, Lang AG, Buchner A. (G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods 2007:39(2), 175-191. https://doi.org/10.3758/BF03193146.
5. Fekete, R., Davidson, A., Ondo, W.G., and Cohen, H.S. Effect of tetrabenazine on computerized dynamic posturography in Huntington disease patients. Parkinsonism and Related Disorders 2012;18(7):896-8.

Declarations

Ethics Approval and Consent to Participate

The study was not registered as no patients were enrolled. The study was approved by the New York Medical College Office of Research Administration Institutional Review Board under tracking number L-10,768.

Consent for Publication

Not applicable

Competing Interests

RF has served as a consultant for Teva Neuroscience, Inc.

Funding

There was no funding for this study.

Author Contributions

RF Conception, writing of manuscript.

Data Availability

Given the absence of funding, data gathering could not commence. No data was gathered.

Acknowledgements

None

Figure Legends

Table 1. G*power software inputs and outputs for statistical power

Consent Form for Participation in Research
New York Medical College

Affiliate: NYMC

Name of Patient/Subject :

Address:

Chart Number:

Title of Research Project: Effect of rasagiline on balance in Parkinson's disease

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Note:

☐ **This project involves the experimental use of a new drug/device/procedure called:**

☒ **This project does not involve the experimental use of a new drug/device/procedure.**

Explanation of Research Project:

1. Purpose of the study:

This study is designed to test whether the medication rasagiline improves balance in patients with Parkinson's disease (PD). Rasagiline is a medication that is FDA approved for the treatment of PD. The duration of the study is 8 weeks. The study consists of an initial screening visit, followed by computerized posturography measurement at baseline, and 4 weeks as well as 8 weeks after taking rasagiline or placebo (sugar pill). Computerized posturography is an FDA approved device with a moving platform that measures how much a person's body moves or sways in response to changes in the position of the platform.

Falls are an important problem in Parkinson's disease and may be experienced by up to 68% of patients with the disease. Problems with balance and resulting injuries from falls were identified as a risk factor for early death in Parkinson's disease. The computerized posturography device is able to measure degree of impairment of balance and may be able to show the effect of the study medication on balance.

Study Qualification: You qualify for the study if you have a diagnosis of Parkinson's disease.

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9/8/15 TO 9/7/16

2. Risks and discomforts:
Each computerized posturography testing session should last less than half an hour. Subjects are strapped into a harness to prevent them from injuring themselves if they were to fall during the test. The risks of the study are the same as those for rasagiline, which is a drug widely used for treatment of PD and include rare possibility of a reaction called serotonin syndrome requiring hospitalization (no fatal cases have been reported in rasagiline post-marketing experience), possible allergic reaction to the medication itself or coating of the tablet, and "tyramine reaction" causing high blood pressure if a person eats aged cheese such as Stilton cheese with a high tyramine content. Rasagiline can also increase blood concentration of an antibiotic (ciprofloxacin). Patients with PD have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population and should follow with a dermatologist. There is also a risk of serotonin syndrome, defined as a dangerous episode of very high blood pressure, fever, and shock that may need treatment in the emergency room and rarely may be life threatening.

Since rasagiline or placebo ("sugar pill") are provided by the study, additional rasagiline and similar medications, including selegiline, are not allowed 30 days prior to the study and during the study. In the adjuvant (additional) therapy arm of the study, you will be allowed to take trihexyphenidyl, amantadine, dopamine agonists such as ropinirole and pramipexole, and carbidopa/levodopa. You will not be allowed to take entacapone during the study, which may cause a worsening of symptoms. You will not be allowed to take dopamine receptor blocking medications such as Seroquel (quetiapine). This class of medications is not typically used for Parkinson's disease treatment.

3. Benefits: This study may help us understand if rasagiline can treat balance problems in Parkinson's disease. There is not a direct benefit to the study participant.

4. Alternatives: The alternative is not to participate in the study. Subjects may elect to receive no treatment or consider a number of FDA approved medications for Parkinson's disease if they do not enroll in this study.

5. Confidentiality: Research related information will be kept in a locked cabinet at 19 Bradhurst Ave, Suite 2850, Hawthorne, NY and will be treated confidentially. In addition, study subjects will be assigned a number. To the extent possible, study subjects will be referred to by their number, further protecting confidentiality. The aggregate study results will be reported in a medical journal and at medical meetings.

6. Device: This study uses computerized dynamic posturography. This is an FDA approved device. Briefly, it is a platform which moves slightly and is accompanied by a screen (visual surround). The patient is tested in multiple settings, with eyes open or closed, with and without movement of the platform, and with and without movement of the screen. A computerized device measures body sway during each of these conditions. For safety, you will be strapped into a harness to prevent you from falling if you were to lose postural stability.

7. Contact: Subjects may contact the principal investigator with questions or in the event of an injury at 914-345-1313.

8. Additional risks: There are no well controlled studies of rasagiline in pregnant women. Therefore, women who expect to become pregnant should not enroll in the study.

9. Termination: Subjects who do not follow the clinical protocol, including but not limited to non-adherence to instructions during the posturography testing and not reporting to study visits may be terminated from the study.

10. Costs: You may incur a parking fee at Westchester Medical Center when going to pick up the medication from the pharmacy. You may avoid this fee by using free parking at 19 Bradhurst Ave and taking the shuttle to Westchester Medical Center.

Your participation in this study should not result in any costs other than those associated with the treatment of your disease. The study sponsor will supply study drug and cover the posturography procedures at no cost to you.

Tests and procedures that are part of regular care for your disease will not be paid by the study sponsor. You or your insurance carrier will be charged or held responsible for the costs of that care. Some insurance companies or government health care programs may limit what they will pay for certain routine services that are performed in a research study, in which case you may be responsible.

11. Withdrawal: The study medication can be stopped at time of withdrawal from the study. We ask that subjects return unused medication back to Westchester Medical Center Pharmacy.

12. Significant findings: Given that the study is blinded, we will not be able to provide direct feedback about the effectiveness of study medication to individual subjects during the study.

13. Number of subjects: 20

14. Internet: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Consent Form for Participation in Research (continued)

Research-related Injury
New York Medical College and its affiliated institutions (Metropolitan Hospital Center, Westchester Medical Center, Westchester Institute for Human Development, Terence Cardinal Cooke Health Care Center, and Richmond University Medical Center) do not provide financial compensation for injury or illness resulting from participation in research, but essential medical care is available. Unless the sponsor provides otherwise, payment for treatment of any injury or illness resulting from participation in research will be assumed by you personally or through your medical insurance. You should contact the investigator in the event of a research-related injury.

Confidentiality
This consent form and your medical records are subject to review by representatives of New York Medical College, the study sponsor, cooperative study groups, and State and federal regulatory agencies, including the Food and Drug Administration (FDA). Additionally, if they are involved, Metropolitan Hospital Center and the Health and Hospital Corporation of New York City or Westchester Medical Center may review this consent form and your medical records. If this investigation is published, you will not be identified by any personal data. You will be given a copy of the signed consent form. Other copies will be kept in confidential files in the investigator's office and (if appropriate) with your medical chart. Additionally, the HIPAA Authorization form associated with this study, that you will be asked to sign, discusses what use will be made of your information.

Voluntary participation
Your signature indicates that you understand this consent form and freely consent to participate in this study. You are free to refuse or to discontinue participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled.

Offer to answer questions
You may call the investigator if you have any questions about your participation in the study. You may call the Office of Research Administration at (914) 594-4480 if you have questions about your rights as a research subject.

_____ _____
Subject's Signature Date

_____ _____ _____
Signature of person authorized to consent for subject or witness if consentor is illiterate or unable to sign Position Date

_____ _____
Signature of person obtaining consent Date

Name of Principal Investigator: Dr. Robert Fekete Telephone Number: 914-345-1313

Name of Sponsor: N/A

The Committee for Protection of Human Subjects is the Institutional Review Board for New York Medical College, Metropolitan Hospital Center, Westchester County Health Care Center, Westchester Institute for Human Development, Terence Cardinal Cooke Health Care Center and Richmond University Medical Center

RevORA Sept 2011
Not Valid Without the Committee Stamp of Certification

NYMC IRB Approval
9/8/15 TO 9/7/16

Consent Form for Participation in Research
New York Medical College

Affiliate:

Name of Patient/Subject :

Address:

Chart Number:

Title of Research Project: Effect of tetrabenazine on Stroop test in Huntington disease

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Note:

☐ **This project involves the experimental use of a new drug/device/procedure called:**

☒ **This project does not involve the experimental use of a new drug/device/procedure.**

Explanation of Research Project:

This study involves tetrabenazine, which is the only FDA approved medication for treatment of Huntington disease chorea. You qualify for the study if you have genetically confirmed Huntington disease.

The study is meant for patients who are not currently taking tetrabenazine or those who have not taken tetrabenazine in the last three days. The study involves two evaluations called the Stroop test. This is a test of visual function that consists of reading words and naming colors. It should take less than five minutes to administer each set of tests. You will have one test in the morning, followed by another test six hours later. You will be given one dose of 12.5 mg of tetrabenazine just after the first test and also three hours later.

Risks and discomforts: There are no invasive procedures. Tetrabenazine has known side effects of depression, slowed movements (parkinsonism), and restlessness (akathisia). These side effects are known to resolve after tetrabenazine is stopped. Usually side effects are associated with high doses; therefore, it would be unlikely for them to occur at the dosage given in this study.

Nursing staff at Terence Cardinal Cooke will check in on subjects during regularly scheduled nursing rounds to ensure safety when the drug is stopped and look for above mentioned known side effects when the drug is restored. There were no reported side effects from stopping tetrabenazine in previous research studies. The prinicpal investigator will be notified if any unexpected side effect occurs when the drug is stopped or if known side effects occur when the drug is restarted. Subjects can also use a call bell system to summon staff during the study.

Benefits: This study may help us understand if low dose tetrabenazine can help patients with Huntington disease correctly process visual information.

Alternatives: You may elect not to participate in this study. .

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9/15/14 TO 9/14/15

Costs: Your participation in this study should not result in any costs other than those associated with the treatment of your disease. The study sponsor will supply study drug and cover treatment and procedures related to the study at no cost to you. Some tests and procedures that are provided as part of regular care will not be paid for by the study sponsor. You or your insurance carrier will be charge or held responsible for costs of that care. Some insurance companies or government health care programs may limit what they will pay for certain routine services that are performed in a research study, in which case you may be responsible.

Financial Disclosure and Conflict of Interest: There is no financial benefit to the study subject. Dr. Fekete is a consultant for Lundbeck, LLC which makes tetrabenazine.

Confidentiality: Research related information will be kept in a locked cabinet at Munger Pavilion, 4th Fl, Valhalla, NY 10595 and will be treated confidentially. In addition, study subjects will be assigned a number. To the extent possible, study subjects will be referred to by their number, further protecting confidentiality. The aggregate study results will be reported in a medical journal and at medical meetings.

Contact: Subjects may contact the principal investigator with questions or in the event of a problem at 914-345-1313.

NYMC IRB Approval

9/15/14 TO 9/14/15

Consent Form for Participation in Research (continued)

Research-related Injury
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Offer to answer questions
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NYMC IRB Approval
9/15/14 TO 9/14/15

Subject's Signature _____ Date _____

Signature of person authorized to consent for subject or witness if consentor is illiterate or unable to sign _____ Position _____ Date _____

Signature of person obtaining consent _____ Date _____

Name of Principal Investigator: Robert Fekete Telephone Number: 914-345-1313

Name of Sponsor:

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Consent Form for Participation in Research
New York Medical College

Affiliate: NYMC

Name of Patient/Subject :

Address:

Chart Number:

Title of Research Project: Effect of rasagiline on balance in Parkinson's disease

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Note:

☐ **This project involves the experimental use of a new drug/device/procedure called:**

☒ **This project does not involve the experimental use of a new drug/device/procedure.**

Explanation of Research Project:

1. Purpose of the study:

This study is designed to test whether the medication rasagiline improves balance in patients with Parkinson's disease (PD). Rasagiline is a medication that is FDA approved for the treatment of PD. The duration of the study is 8 weeks. The study consists of an initial screening visit, followed by computerized posturography measurement at baseline, and 4 weeks as well as 8 weeks after taking rasagiline or placebo (sugar pill). Computerized posturography is an FDA approved device with a moving platform that measures how much a person's body moves or sways in response to changes in the position of the platform.

Falls are an important problem in Parkinson's disease and may be experienced by up to 68% of patients with the disease. Problems with balance and resulting injuries from falls were identified as a risk factor for early death in Parkinson's disease. The computerized posturography device is able to measure degree of impairment of balance and may be able to show the effect of the study medication on balance.

Study Qualification: You qualify for the study if you have a diagnosis of Parkinson's disease.

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9/15/14 TO 9/14/15

2. Risks and discomforts:
Each computerized posturography testing session should last less than half an hour. Subjects are strapped into a harness to prevent them from injuring themselves if they were to fall during the test. The risks of the study are the same as those for rasagiline, which is a drug widely used for treatment of PD and include rare possibility of a reaction called serotonin syndrome requiring hospitalization (no fatal cases have been reported in rasagiline post-marketing experience), possible allergic reaction to the medication itself or coating of the tablet, and "tyramine reaction" causing high blood pressure if a person eats aged cheese such as Stilton cheese with a high tyramine content. Rasagiline can also increase blood concentration of an antibiotic (ciprofloxacin). Patients with PD have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population and should follow with a dermatologist. There is also a risk of serotonin syndrome, defined as a dangerous episode of very high blood pressure, fever, and shock that may need treatment in the emergency room and rarely may be life threatening.

Since rasagiline or placebo ("sugar pill") are provided by the study, additional rasagiline and similar medications, including selegiline, are not allowed 30 days prior to the study and during the study. In the adjuvant (additional) therapy arm of the study, you will be allowed to take trihexyphenidyl, amantadine, dopamine agonists such as ropinirole and pramipexole, and carbidopa/levodopa. You will not be allowed to take entacapone during the study, which may cause a worsening of symptoms. You will not be allowed to take dopamine receptor blocking medications such as Seroquel (quetiapine). This class of medications is not typically used for Parkinson's disease treatment.

3. Benefits: This study may help us understand if rasagiline can treat balance problems in Parkinson's disease. There is not a direct benefit to the study participant.

4. Alternatives: The alternative is not to participate in the study. Subjects may elect to receive no treatment or consider a number of FDA approved medications for Parkinson's disease if they do not enroll in this study.

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6. Device: This study uses computerized dynamic posturography. This is an FDA approved device. Briefly, it is a platform which moves slightly and is accompanied by a screen (visual surround). The patient is tested in multiple settings, with eyes open or closed, with and without movement of the platform, and with and without movement of the screen. A computerized device measures body sway during each of these conditions. For safety, you will be strapped into a harness to prevent you from falling if you were to lose postural stability.

7. Contact: Subjects may contact the principal investigator with questions or in the event of an injury at 914-345-1313.

8. Additional risks: There are no well controlled studies of rasagiline in pregnant women. Therefore, women who expect to become pregnant should not enroll in the study.

9. Termination: Subjects who do not follow the clinical protocol, including but not limited to non-adherence to instructions during the posturography testing and not reporting to study visits may be terminated from the study.

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11. Withdrawal: The study medication can be stopped at time of withdrawal from the study. We ask that subjects return unused medication back to Westchester Medical Center Pharmacy.

12. Significant findings: Given that the study is blinded, we will not be able to provide direct feedback about the effectiveness of study medication to individual subjects during the study.

13. Number of subjects: 20

14. Internet: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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Consent Form for Participation in Research (continued)

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NYMC IRB Approval
Date 9/15/14 TO 9/14/15

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Signature of person obtaining consent _____ Date _____

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Telephone Number: 914-345-1313

Name of Sponsor:

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1. Purpose of the study:

This study is designed to test whether the medication rasagiline improves balance in patients with Parkinson's disease (PD). Rasagiline is a medication that is FDA approved for the treatment of PD. The duration of the study is 8 weeks. The study consists of an initial screening visit, followed by computerized posturography measurement at baseline, and 4 weeks as well as 8 weeks after taking rasagiline or placebo (sugar pill). Computerized posturography is an FDA approved device with a moving platform that measures how much a person's body moves or sways in response to changes in the position of the platform.

Falls are an important problem in Parkinson's disease and may be experienced by up to 68% of patients with the disease. Problems with balance and resulting injuries from falls were identified as a risk factor for early death in Parkinson's disease. The computerized posturography device is able to measure degree of impairment of balance and may be able to show the effect of the study medication on balance.

Study Qualification: You qualify for the study if you have a diagnosis of Parkinson's disease.

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7/11/16 TO 7/10/17

2. Risks and discomforts:
Each computerized posturography testing session should last less than half an hour. Subjects are strapped into a harness to prevent them from injuring themselves if they were to fall during the test. The risks of the study are the same as those for rasagiline, which is a drug widely used for treatment of PD and include rare possibility of a reaction called serotonin syndrome requiring hospitalization (no fatal cases have been reported in rasagiline post-marketing experience), possible allergic reaction to the medication itself or coating of the tablet, and "tyramine reaction" causing high blood pressure if a person eats aged cheese such as Stilton cheese with a high tyramine content. Rasagiline can also increase blood concentration of an antibiotic (ciprofloxacin). Patients with PD have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population and should follow with a dermatologist. There is also a risk of serotonin syndrome, defined as a dangerous episode of very high blood pressure, fever, and shock that may need treatment in the emergency room and rarely may be life threatening.

Since rasagiline or placebo ("sugar pill") are provided by the study, additional rasagiline and similar medications, including selegiline, are not allowed 30 days prior to the study and during the study. In the adjuvant (additional) therapy arm of the study, you will be allowed to take trihexyphenidyl, amantadine, dopamine agonists such as ropinirole and pramipexole, and carbidopa/levodopa. You will not be allowed to take entacapone during the study, which may cause a worsening of symptoms. You will not be allowed to take dopamine receptor blocking medications such as Seroquel (quetiapine). This class of medications is not typically used for Parkinson's disease treatment.

3. Benefits: This study may help us understand if rasagiline can treat balance problems in Parkinson's disease. There is not a direct benefit to the study participant.

4. Alternatives: The alternative is not to participate in the study. Subjects may elect to receive no treatment or consider a number of FDA approved medications for Parkinson's disease if they do not enroll in this study.

5. Confidentiality: Research related information will be kept in a locked cabinet at 19 Bradhurst Ave, Suite 2850, Hawthorne, NY and will be treated confidentially. In addition, study subjects will be assigned a number. To the extent possible, study subjects will be referred to by their number, further protecting confidentiality. The aggregate study results will be reported in a medical journal and at medical meetings.

6. Device: This study uses computerized dynamic posturography. This is an FDA approved device. Briefly, it is a platform which moves slightly and is accompanied by a screen (visual surround). The patient is tested in multiple settings, with eyes open or closed, with and without movement of the platform, and with and without movement of the screen. A computerized device measures body sway during each of these conditions. For safety, you will be strapped into a harness to prevent you from falling if you were to lose postural stability.

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