Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

A Model-Based Approach for Assessing Parkinsonian Gait and Effects of Levodopa and Deep Brain Stimulation

Catherine Cho, Yasuhiro Osaki, Mikhail Kunin, Bernard Cohen, C. Warren Olanow, Theodore Raphan, *Member, IEEE*

Abstract— **Gait and balance disturbances are amongst the most disabling features of Parkinson's disease (PD), and are not adequately controlled with currently available medical and surgical therapies. Development of objective quantitative measures of these abnormalities would greatly help in the assessment and the development of therapeutic interventions. Recently, we developed a methodology, using dynamical system theory, for testing gait with a state-of-the-art motion-detection system (OPTOTRAK 3020, Northern Digital, Inc.). We also developed a model of the dynamics of the foot that predicts the stance and swing phase dynamics of normal walking. In the present study, we determined whether model parameters were altered in subjects with PD when they were tested ON/OFF levodopa (LD) and ON/OFF deep brain stimulation (DBS) in a 2x2 matrix.**

I. INTRODUCTION

The locomotor gait cycle is divided into swing and stance phases [1], [2]. During the stance phase the weighted limb supports the weight of the body and moves it forward. During the swing phase, the unweighted limb swings forward to complete the step at heel contact. Together these comprise the stride length. Walking velocity is the product of stride length and stride frequency. In normal spontaneous gait, increments in walking velocity are predominantly dependent on increasing stride length, although increases in step frequency contribute to a lesser degree at higher walking velocities [3].

In PD, the stride does not lengthen sufficiently with higher walking velocities [4]-[6]; hence, the step rate increases to compensate in an effort to maintain gait velocity [7]-[9]. As a consequence, the angular excursion is reduced at the hip, knee, and ankle. The reason for these deficiencies is not clear and may be related to reduced plantar flexion at full weight acceptance, which could result in diminished push-off at the end of the stance phase [10]. Decreased force, decreased velocity, and slowed execution of the anticipatory postural adjustments for self-generated stepping have also been observed with isolated gait initiation difficulties in PD [10]-[12].

Training and supplying visual cues during overground locomotion can increase stride length to near normal values in PD patients [7], [9], [10]. However, when attention is diverted and PD subjects are required to multitask, motor function deteriorates, and stride length shortens as gait reverts to the abnormal state [4], [13]. Age and dementia can also be associated with diminished stride length and reduction in gait velocity [14], [15].

The benefits of LD and DBS have been well established for rigidity, bradykinesia, and tremor in PD patients [16], [17]. However, the effects of LD and DBS on locomotion are not well understood. Quantification is critical for standardizing the effects of drugs and DBS. Recently, we have found precise relationships between foot movements during the stance and swing phases that are critical for maintaining efficient and stable gait [18]-[20]. The purpose of this study was to utilize a model that we developed for predicting the dynamics of the stance and swing phases during normal walking to assess parkinsonian gait during ON/OFF DBS and LD in a 2x2 matrix. The model allows for quantitative assessment of the therapeutic value of the various treatments. It has the potential for assessing a wide range of treatments of PD that might affect gait and for determining targets for the development of new therapies that might improve PD gait.

II. METHODS

A. Subjects

Two male and one female subjects with PD, who were receiving LD and had previously undergone DBS, participated in this study after signing an IRB approved informed consent. Subject demographics are summarized in Table 2.1. All were right-handed with a right dominant leg

TABLE 2.1
SUBJECT DEMOGRAPHICS

	Subject 1	Subject 2	Subject 3
Age/Gender	55/M	65/M	62/F
PD Duration	12 yr	7 yr	24 yr
DBS Surgery	11 mo	4 mo	5 mo
Levodopa	250 mg	150 mg	100 mg

Manuscript received July 7, 2006. This work was supported in part by the National Institutes of Health under Grants DC05222, DC05204 and grants from the Bachman Strauss Dystonia and Parkinson Foundation and the Bendheim Parkinson Center.

Catherine Cho is with the Department of Neurology, Mount Sinai School of Medicine USA (phone: 212-241-7068; fax: 212-987-7363; e-mail: catherine.cho@mssm.edu).

Yasuhiro Osaki is with the Department of Neurology, Mount Sinai School of Medicine, USA. (e-mail: osaki@tracer.med.osaka-u.ac.jp).

Mikhail Kunin is with the Department of Computer and Information Science, Brooklyn College, City University of New York, (e-mail: kunin@nsi.brooklyn.cuny.edu).

Bernard Cohen is with the Department of Neurology, Mount Sinai School of Medicine, USA. (e-mail: bernard.cohen@mssm.edu).

C Warren Olanow is with the Department of Neurology, Mount Sinai School of Medicine, USA. (e-mail: warren.olanow@mssm.edu).

Theodore Raphan is with the Department of Computer and Information Science, Brooklyn College, City University of New York and the Department of Neurology, Mount Sinai School of Medicine, (e-mail: raphan@nsi.brooklyn.cuny.edu).

and had subjective and objective features of gait dysfunction despite therapy. PD therapies were stable for at least one month prior to testing. Each subject had received bilateral DBS surgery of the subthalamic nucleus (STN), which was performed at least 4 months prior to testing. Stimulation settings (voltage, frequency, pulse width) were maintained at a stable level for at least one month prior to testing.

B. Methodology for Testing Gait

Movements of the foot, shank, and head were recorded using the OPTOTRAK 3020 video motion analysis system (Northern Digital, Ontario, Canada). The system sensed pulses coming from active infrared (IR) markers (LED's), and tracked the three-dimensional position of each LED, storing this information in a computer file. The total number of markers determines the sampling rate. In this study, 21 markers were utilized, allowing a sampling rate of 100 frames/s. When the OPTOTRAK system is positioned 4 m from the subject, the accuracy of translational measurement is 0.3 mm (manufacturer's specification) with an accuracy in pitch and yaw of 0.1 deg (See [3], [18] for a full description of the OPTOTRAK characteristics and the methods for calibration and data acquisition).

C. Normalization of length and Temporal Vectors

The data were normalized by transforming them into dimensionless quantities that could be compared across subjects with different body sizes [21]. Quantities that had dimension of length, i.e., coordinate location in space, were normalized to individual leg length l_0, the distance between the greater trochanter and the heel markers. The coordinate location was, therefore, given in terms of "leg-length." Acceleration was normalized with respect to the equivalent acceleration of gravity, a_g. As the period of a naturally oscillating leg is $2\pi\sqrt{l/a_g}$, where l is the distance from the hip to the center of mass of the leg ($0.4l_0$) [22], time was normalized with respect to $2\sqrt{0.4}\pi\sqrt{l_0/a_g}$, which is the natural oscillation period of a leg whose length is l_0. This equalizes the duration of gait cycles for short and tall persons. The average l_0 for the normal subjects was 0.84 m [20]. Therefore the consequent normalization time was 1.16 s, which was referred to as a "leg-period".

The velocity, which has the dimension of length over duration, has the normalization factor equal to $\sqrt{l_0 a_g}$. This velocity, which is considered to be 1.0 "Froude number" [21], has been used to normalize the gait kinematics across a wide range of species and gravitational environments [23], [24].

D. Experimental protocol

Parkinsonism was assessed using Part III of the Unified PD Rating scale (UPDRS), a standardized means of assessing PD disability. The gait subscore (items 26-30 of the UPDRS) was also tabulated.

PD gait was characterized using treadmill walking for at least 30 seconds over a range of velocities. Treadmill walking approximates normal overground walking if subjects are properly trained [25]. Walking velocities in previous studies on normal subjects ranged from 0.6 – 2.1 m/s. However, PD subjects were not able to achieve these velocities, and walked at 0.6, 0.9, and 1.2 m/s under four conditions: 1) OFF medication/OFF stimulation, 2) ON medication/OFF stimulation, 3) OFF medication/ON stimulation, and 4) ON stimulation/ON medication. OFF medication was defined as no anti-parkinsonian medication for at least the preceding 12 hours prior to testing. ON medication was defined as the best response after administration of anti-parkinsonian therapy. OFF stimulation was tested when the stimulator had been turned off for at least 30 minutes. ON stimulation was tested when the stimulator had been turned on for at least 30 minutes. Clinical and treadmill assessments were performed after 30 minutes in each condition to "wash out" any effects of stimulation in Condition 2 and to allow medication and stimulation to have maximal effects during Conditions 3 & 4.

The LD dose was determined by the anti-PD regimen before surgery since the LD requirement often drops after the stimulation parameters are optimized. LD during testing was given as carbidopa/levodopa that was crushed and suspended in soda to expedite the time to ON.

III. Results

A. Clinical Assessments

Clinical measurements are summarized in Table 3.1. Higher scores correspond to more severe parkinsonism.

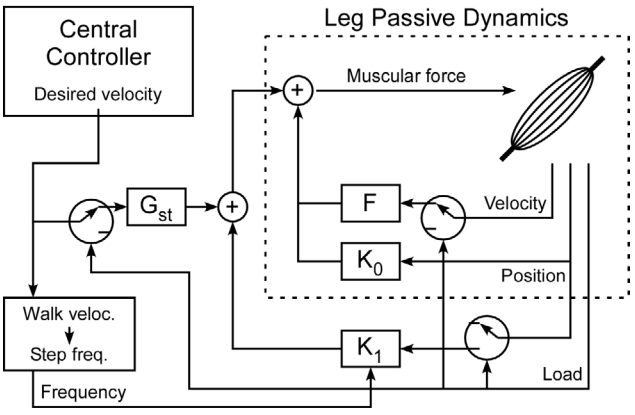
TABLE 3.1
CLINICAL ASSESSMENTS OF SUBJECTS

UPDRS III/ Gait Subscore	S 1	S 2	S 3
M- S-	63/10	43/10	38/11.5
M+ S-	63/11	39/9	12.5/1
M- S+	34/7	16/3	24/5
M+ S+	8/2	21/7	22/4.5

B. Conceptual Basis for Parameterization of PD Gait

The conceptual basis for comparing PD gait to that of normals is embodied in a simple model of foot dynamics during walking on a treadmill [18]-[20] (Fig. 3.1).

FIG. 3.1
MODEL OF FORWARD FOOT MOVEMENT DURING LOCOMOTION



The model assumes that when there is a load on the foot during the stance phase, the foot velocity is controlled by a velocity feedback governed by a damping parameter, F, which maintains foot velocity equal to that of the treadmill. When the foot is lifted from the treadmill, the load is reduced to zero, and the feedback is switched from a velocity dependent mechanism to a position dependent mechanism governed by a parameter, K_1, which is an active feedback control law. This modifies the passive dynamics of the foot, determined by a parameter, K_0. The summation of parameters K_1 and K_0 determine the dynamics of the swing and the phase-plane behavior of forward foot velocity vs. foot position.

To assess the kinematics and dynamics of stance and swing phases, the phase-plane trajectories (Toe Velocity vs. Position) (Fig. 3.2) and main sequence relationships (Peak-Toe Velocity vs. Range of Toe Translation) (Fig. 3.3) were evaluated. Fig. 3.2a shows an average phase-plane plot of toe movement in 6 normal subjects [18]-[20]. These are characterized by a constant velocity during the stance phase and an approximately semicircular trajectory during the swing phase (Fig. 3.2). The peak velocity of the swing phase was dependent on walking velocity. Phase-plane plots for the three subjects while walking at up to three velocities generally followed these trajectories under all conditions (Fig. 3.2b-g). Trajectories of Subject 1 while OFF medication/OFF stimulation could not achieve the third walking velocity (Fig. 3.2b), but had fairly normal plots at lower velocities (Fig. 3.2b, c). When ON medication/ON stimulation, this subject was able to achieve the higher walking velocity and had approximately normal trajectories (Fig. 3.2c). The trajectories of Subject 2 show that the range of normal swinging could not be achieved (Fig. 3.2d, e). However, Subject 2 achieved an approximately normal peak velocity for the forward foot movement (Fig. 3.2d, e). The trajectories of Subject 3 were close to normal, independent of medication/stimulation (Fig. 3.2f, g).

The main sequence plots of peak velocity vs. range of toe translation in both the X and Z direction had an approximately linear relationship (Fig. 3.3), confirming the normal trends apparent in the toe phase-plane trajectories. The only abnormality was the limited range of toe translation in the subjects, which was unaffected by medications and/or stimulation. Subject 1 had smaller main sequence slopes than normals for both X and Z directions (Fig. 3.3a, b), although at the lower range of velocities, the slopes fell close to the normal main sequence plot. Subject 2 had similar characteristics, although it was confined to a small region of position-velocity space (Fig. 3.3c, d). Subject 3 was normal in all respects and could achieve the higher velocities and ranges during the swing phase than the other subjects (Fig. 3.3e, f). Again, there was no change in the main sequence relationships either due to the medication, DBS, or both.

In all subjects, the data representing the oscillation frequency of the foot as a function of frequency of stepping could be fit by the model with the same parameter K, which is the sum K_0+K_1, as a function of stepping frequency (Fig. 3.4),

FIG. 3.2
PHASE-PLANE PLOTS OF ALL SUBJECTS AT DIFFERENT WALKING VELOCITIES

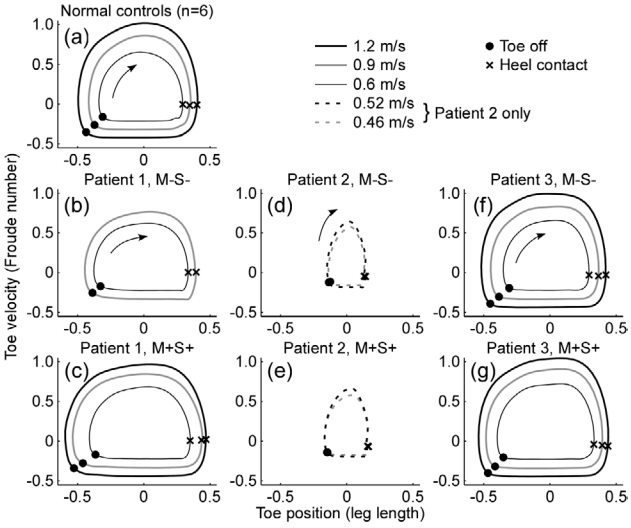
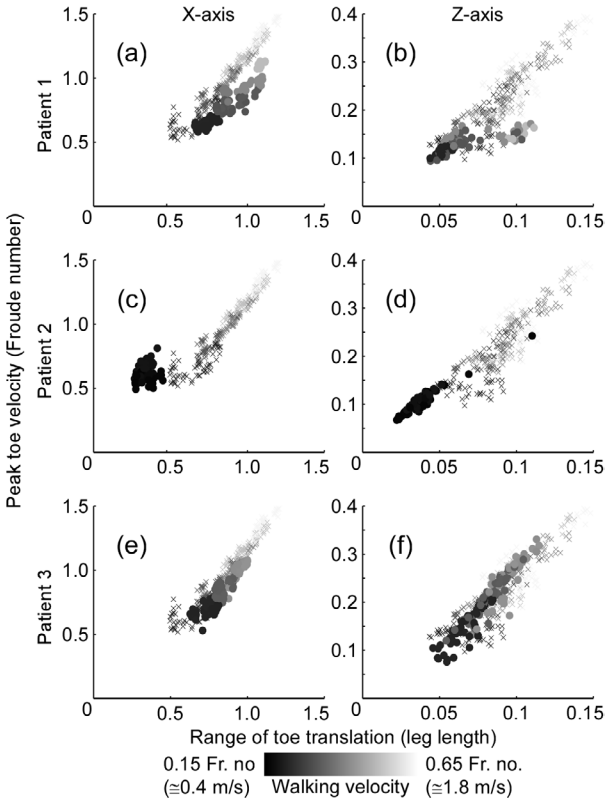
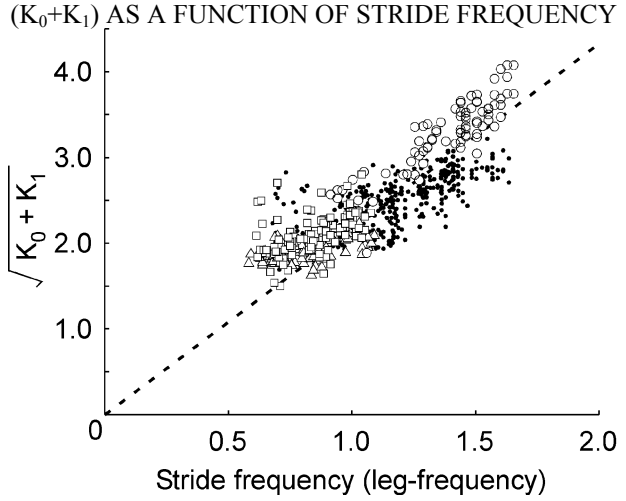


FIG. 3.3
MAIN SEQUENCE RELATIONSHIPS



independent of the administration of LD or the initiation of DBS. Thus, the foot followed the appropriate dynamic trajectory at initiation of the swing in all subjects. This occurred despite the fact that the trajectories of Subject 3 with medication/stimulation in the ON/OFF state were greatly affected by dyskinesia causing eversion of the right foot and subjective complaints of walking difficulties.

FIG. 3.4
CHANGES FEEDBACK CONTROL PARAMETER (K_0+K_1) AS A FUNCTION OF STRIDE FREQUENCY



IV. CONCLUSION

We quantified and analyzed locomotion in PD using a three-dimensional motion detection system (OPTOTRAK). *Regardless of testing condition, the major difficulty that impaired locomotion in the PD subjects was an inability to generate adequate toe lift and foot pitch.* The impaired toe clearance limited stepping both in forward and vertical directions, prematurely shortening stride length. Consequently, energy expenditure was increased because the foot was thrust into the treadmill surface at the end of the swing phase.

Contrary to current understanding of the gait disturbances in PD, the onset of swing-phase trajectories and the velocity profile as a function of foot position were normal in all PD subjects, regardless of severity of disease or mode of therapy. Furthermore, the peak-toe velocity as a function of walking velocity was essentially normal in all subjects, and the ability to walk at higher velocities did not improve with LD or DBS. However, in Subject 1, DBS with LD allowed for an increase in range and peak velocity in the X direction.

DBS and LD achieved their clinical effect by increasing the range of the main sequence and $K=K_0+K_1$. Further studies are needed to determine the characteristics in gait dysfunction that will result in clinically significant improvements with DBS, LD, or the combination of both modalities.

REFERENCES

[1] J. G. Nutt, C. D. Marsden, and P. D. Thomson, "Human walking and higher level gait disorders, particularly in the elderly," *Neurology*, vol. 43, pp. 268-279, 1993.

[2] V. T. Inman, "Human locomotion," *Can Med Assoc*, vol. 94, pp. 1047-1054, 1966.

[3] E. Hirasaki, S. T. Moore, T. Raphan, and B. Cohen, "Effects of walking velocity on vertical head and body movements during locomotion," *Exp Brain Res*, vol. 127, pp. 117-130, 1999.

[4] N. Giladi, R. Kao, and S. Fahn, "Freezing phenomenon in patients with parkinsonian syndromes," *Mov Disord*, vol. 12, pp. 302-305, 1997.

[5] Y. A. Grimbergen, M. Munneke, and B. R. Bloem, "Falls in Parkinson's disease," *Curr Opin Neurol*, vol. 17, pp. 405-15, 2004.

[6] J. T. Davis, K. E. Lyons, and R. Pahwa, "Freezing of gait after bilateral subthalamic nucleus stimulation for Parkinson's disease," *Clin Neurol Neurosurg*, to be published, 2005.

[7] M. E. Morris, R. Iansek, T. A. Matyas, and J. J. Summers, "Stride length regulation in Parkinson's disease: Normalization strategies and underlying mechanisms," *Brain*, vol. 119, pp. 551-568, 1996.

[8] M. E. Morris, "Ability to modulate walking cadence remains intact in Parkinson's disease," *J Neurol Neurosurg Psych*, vol. 57, pp. 1532-1534, 1994.

[9] M. E. Morris, "Abnormalities in stride length-cadence relation in Parkinson gait," *Mov Disord*, vol. 13, pp. 61-69, 1998.

[10] E. Knutsson, "An analysis of parkinsonian gait," *Brain*, vol. 95, pp. 475-486, 1972.

[11] R. Rosin, H. Topka, and J. Dichgans, "Gait initiation in Parkinson's disease," *Mov Disord*, vol. 12, 1997.

[12] A. Burleigh-Jacobs, F. B. Horak, J. G. Nutt, and J. A. Obeso, "Step initiation in Parkinson's disease: influence of levodopa and external sensory triggers," *Mov Disord*, vol. 12, pp. 206-215, 1997.

[13] N. Giladi, "Freezing of gait in patients with advanced Parkinson's disease," *J. Neural Transm*, vol. 108, pp. 53-61, 2001.

[14] R. Elble, L. Hughes, and C. Higgons, "The syndrome of senile gait," *J. Neurol*, vol. 239, pp. 71-75, 1992.

[15] H. Vissar, "Gait and balance in senile dementia," *Age and Aging*, vol. 12, pp. 296-301, 1983.

[16] P. Krack, A. Batir, N. Van Blercom, S. Chabardes, V. Fraix, C. Ardouin, *et al.*, "Five-Year Follow-up of Bilateral Stimulation of the Subthalamic Nucleus in Advanced Parkinson's Disease," *N Engl J Med*, vol. 349, pp. 1925-1934, 2003.

[17] M. C. Rodriguez-Oroz, J. A. Obeso, A. E. Lang, J. L. Houeto, P. Pollak, S. Rehncrona, *et al.*, "Bilateral deep brain stimulation in Parkinson's disease: a multicenter study with 4 years follow-up," *Brain*, vol. 128, pp. 2240-2249, 2005.

[18] Y. Osaki, M. Kunin, B. Cohen, and T. Raphan, "Three-dimensional kinematics of the leg during treadmill walking," in *Society for Neuroscience*. Washington D.C., 2005.

[19] Y. Osaki, M. Kunin, B. Cohen, and T. Raphan, "Kinematics and Dynamics of Leg Movement During Treadmill Walking in Humans," in *ARO*. Baltimore, MD, USA, 2006, pp. 65.

[20] Y. Osaki, M. Kunin, B. Cohen, and T. Raphan, "Three-dimensional kinematics and dynamics of the foot during walking: A model of central control mechanisms," *Exp. Brain Res.*, submitted for publication, 2006.

[21] A. L. Hof, "Scaling gait data to body size," *Gait Posture*, vol. 4, pp. 222-223, 1996.

[22] H. Witte, H. Preuschoft, and S. Recknagel, "Human body proportions explained on the basis of biomechanical principles," *Z Morphol Anthropol*, vol. 78, pp. 407-423, 1991.

[23] A. E. Minetti, "Invariant aspects of human locomotion in different gravitational environments," *Acta Astronaut*, vol. 49, pp. 191-8, 2001.

[24] A. E. Minetti, "Walking on other planets," *Nature*, vol. 409, pp. 467, 469, 2001.

[25] M. P. Murray, G. B. Spurr, S. B. Sepic, G. M. Gardner, and L. A. Mollinger, "Treadmill vs. floor walking: kinematics, electromyogram, and heart rate," *J Appl Physiol*, vol. 59, pp. 87-91, 1985.