Does cycling cadence affect interlimb symmetry in pedaling power in individuals with Parkinson’s disease?

Student Name, Harsh H. Buddhadev, Jun G. San Juan, David N. Suprak
Department of Health and Human Development, Western Washington University, Bellingham, Washington, United States of America

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Correspondence Address:
Harsh H. Buddhadev, PhD
Department of Health and Human Development
201H Carver Academic Facility, MS 9067,
516 High Street, Bellingham, WA 98225
Telephone: +1 (360) 650-4115
Fax: +1 (360) 650-7447
Email: harsh.buddhadev@wwu.edu

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Abstract

Cycling at higher pedaling rates leads to symptomatic improvement in patients with Parkinson’s disease (PD). However, these patients show inter-limb asymmetry in pedaling power when cycling at their slow self-selected cadence. The effects of higher pedaling cadence on symmetry of effort between limbs is unknown. We compared the effect of pedaling cadence on symmetry of crank power output in individuals with PD versus healthy controls. Fifteen participants with PD and 15 healthy controls performed 2-minute bouts of stationary cycling at three cadences (50, 65, 80 rpm) at 60W and self-selected workload. Power output contribution of each limb towards total crank power output was computed over 60 crank cycles from the effective component of pedal force, which was perpendicular to the crank arm.

Keywords: Ergometer, neurorehabilitation, UPDRS

Word Count:
Introduction

Parkinson’s disease (PD) is a common progressive neuromuscular condition affecting more than 10 million individuals worldwide \(^1-3\) and costs the healthcare system in the United States 14 billion dollars annually \(^4\). In patients with PD, degeneration of the dopaminergic neurons within the substantia nigra leads to substantial reduction in dopamine production \(^5-6\) resulting in symptoms such as resting tremors, bradykinesia or akinesia, rigidity, and postural imbalance \(^7-11\). These symptoms adversely affect the ability of these patients to perform activities of daily living such as maintaining balance and walking. In addition, these clinical features in patients with PD are generally more pronounced on side compared to the other, thereby leading to asymmetry in performing motor tasks such as walking and cycling \(^12-13\).

Cycling at is a commonly prescribed mode of neurorehabilitation for patients with PD \(^9,\ 13-14\). Generally, patients with PD are prescribed stationary cycling at high cadences (i.e. 80-90 rpm) three times per week with sessions ranging from 30-60 minutes \(^9, 15-16\). Post-cycling sessions, patients experience immediate and long terms improvements such as decrease in resting tremor, bradykinesia, and rigidity \(^9, 17-18\), and enhancement in executive function \(^19\). Cycling cadence is a very critical variable for effectiveness of pedaling as an intervention for patients with PD. Several studies have shown that symptomatic improvement is only observed at higher and not lower preferred cadences of patients with PD \(^9, 14, 17, 20\). Researcher have speculated that cycling at higher cadences alleviates symptoms of PD by promoting changes in neural drive by increasing both motor output and sensory input \(^14, 16\).

Penko et al.\(^13\) found that individuals with PD are asymmetrical when pedaling at their self-selected cadences. Specifically, these individuals exerted lesser power with their more affected leg and compensate by exerting greater power with their less affected side. Generally,
self-selected cadence of patients with PD were low (59 ± 13 rpm)\textsuperscript{9,14,16-17,21}, whereas symptomatic improvements were observed at higher pedaling cadences (80-90 rpm)\textsuperscript{9,14,16-17,21}.

Previous research in healthy subjects has shown that pedaling at higher cadences reduces asymmetry in power output. However, no previous research has investigated whether asymmetry of power output between lower limbs in cycling changes when pedaling at higher compared to lower cadences in patients with PD. Similar to healthy subjects, pedaling at higher cadences could also reduce interlimb asymmetry in power output for patients with PD. However, this hypothesis has not yet been tested. Interlimb asymmetry in effort would place asymmetrical stresses on the lower extremity joints on each side\textsuperscript{22,23}. By reducing interlimb asymmetry in cycling, effectiveness of pedaling could potentially be improved for rehabilitation of patients with PD.

The purpose of this study is to examine the effects of pedaling cadence on interlimb asymmetry in crank power output in patients with PD compared to healthy control. We hypothesize that: 1) interlimb asymmetry in power output will be greater for patients with PD compared to healthy controls, and; 2) interlimb asymmetry in power output will decrease at higher cadences.

### Methods

**Study design:** In this cross-sectional, case-controlled study differences in interlimb asymmetry in crank power outputs at different cadences were assessed during low-intensity stationary cycling between patients with PD and age-and-sex matched control subjects. All experimental data were collected in single data collection session.

**Participants:** Sixteen individuals with idiopathic PD and twenty age-and-sex matched healthy controls were recruited from the surrounding community. Sample size was calculated
using GPower 3.1 software based on index of asymmetry data reported by Penko et al. A total sample size of 16 participants (8 per group) was needed to achieve a statistical power of 0.8 to detect a large effect size (Cohen’s $f=0.53$) for group main at an alpha level of 0.05.

A local neurologist screened the individuals with PD. Only individuals with Hoehn and Yahr stage II-III when “off” anti-parkinsonian medication were eligible to participate. These individuals were also assessed by the neurologist on the day of their testing using the Movement Disorders Society’s revision of Unified Parkinson’s Disease Rating Scale (UPDRS) while “off” anti-parkinsonian medication for at least twelve hours prior to examination. UPDRS is a reliable and valid test to assess the severity of Parkinson’s disease. This scale was used to determine which lower extremity was more affected based on UPDRS motor examination of tremor, rigidity, and leg agility score on each side. These tests were scored on a scale from 0-4. A score of 0 indicates a normal, unaffected individual, where a score of 4 indicates a high severity of PD. These data were used to identify the limb that was more affected by PD.

All of the participants completed a health history and physical health questionnaire to screen for exclusion criteria and obtain information about their current physical activity status and cycling experience. Exclusion criteria included any muscular, orthopedic, neurologic, and/or cardiovascular disorders that limited an individual’s ability to pedal on an ergometer at low to moderate intensities. The Western Washington University Institutional Review Board approved the study, and all participants gave written informed consent before participating.

**Data Collection:** In a single test session, participants completed 8 three-minutes pedaling trials at cadence of 50, 65, 80 rpm at an experimentally controlled power output (i.e. 60 W) and self-selected power output in a random order. These chosen cadences fell within the range of self-selected cadences (i.e. 50-70 rpm) and therapeutically prescribed cadences.
(i.e. 75-90 rpm)\textsuperscript{9, 14, 16, 21} of individuals with PD.

All pedaling trials were conducted on an electronically braked Velotron Dynafit

ergometer cycle ergometer (Racer-Mate Inc., Seattle, WA) which is shown to be accurate and

reliable for measuring power output during cycling\textsuperscript{27, 28}. Power output of each leg was
determined using an instructed force pedal system (Sensix, Poitiers, France) which

synchronously measures pedal forces in all planes of motion via strain gauges and pedal and

crank orientation via optical encoders. Prior to arrival of participants, the calibration of the

Velotron ergometer was verified by performing the Accuwatt calibration check test (Racer-Mate

Inc., Seattle, WA) and instrumented force pedals were initialized to ensure they were calibrated

accurately with respect to manufacturer settings.

Subjects were then asked to change into spandex clothing and shoes provided by the

researchers. The subject’s weight and height were measured in pounds and inches, respectively,

using a standard balance beam scale with stadiometer. Subjects then completed a five-minute

warm-up at 20 W resistance and a self-selected cadence on the Velotron cycle ergometer\textsuperscript{13, 15}. Three to five minutes of rest followed the warm-up where participants sat on the cycle

ergometer. Following this warm-up, participants completed three-minute trials under each of the

three randomly ordered workload-cadence conditions (60 W 50 rpm, 60 W 65 rpm, 60 W 80

rpm). Following the fixed power output pedaling conditions, participants repeated the three 3-

minute trials of the same cadences in random order at self-selected power output. A rest interval

of three to five minutes separated each condition.

During these six cycling conditions, data were synchronously captured for bilateral pedal

forces and orientation, and crank position using instrumented force pedals at a sampling

frequency of 240 Hz during the last two minutes of each three-minute experimental condition.
Verbal encouragement was provided along with a visual screen that participations could look at to maintain their assigned cadence. Participants finished with a five-minute cool-down at 20 W resistance and a self-selected cadence.\(^{13,15}\)

**Data analysis:** The crank position, pedal orientation, and pedal force data were low pass filtered at 4 Hz using a fourth order recursive Butterworth filter. The pedal forces were transposed to the crank coordinate system using pedal force and orientation, and crank position data using the Sensix I-Crankset software (Poitiers, France). The anterior-posterior and normal components of pedal forces were then used to compute resultant sagittal pedal forces. Effective component of force is the only component of force that creates the angular impulse to rotate the crank. The effective force was computed as the component of the resultant force perpendicular to the crank arm using trigonometric methods described in previous studies.\(^{29,30}\) Effective crank torque on each side for a complete crank cycle was computed as a product of the component of the effective pedal force and length of crank arm (0.1725 m). The crank power on each side was computed as a product of effective crank torque and crank angular velocity. The data for crank power on each side were then averaged over 60 crank cycles.

Based on the average crank power output measured for each limb, the Symmetry Index (SI) was calculated for each 360-degree crank cycle. The equation to compute symmetry index is based on previous research\(^{13,31}\) and it is as follows:

\[
Symmetry \ Index \ (SI) = \frac{(Unaffected \ limb - Affected \ limb)}{(Unaffected \ limb + Affected \ limb)/2}
\]

Values from this equation can be used to quantify the magnitude of contribution from each limb. A positive value indicates a greater contribution from the unaffected limb, while a negative value indicates a greater contribution from the affected limb.\(^{13}\) This equation can be modified to
evaluate the contribution of left versus right lower extremity contribution, or dominant versus non-dominant leg power. For the control group, leg dominance was determined by asking which leg they preferred to kick a ball.\(^{32,33}\)

\[
Symmetry Index (SI) = \left( \frac{Dominant - Nondominant limb}{Dominant limb + Nondominant limb} \right)/2
\]

**Statistical analysis:** Two-factor mixed model analysis of variance (ANOVAs) (limb condition (4) x cadence (4)) with repeated measures on cadence were used to test the effects of limb condition on index of asymmetry and total, average, and relative crank power output. For between group contrasts, limb condition for the Parkinson’s disease group (i.e. more affected and less affected leg) was not equivalent to the limb condition for healthy controls (dominant and non-dominant leg). Therefore, limb condition variable with four levels (PD-more affected, PD-less affected, control dominant, and control non-dominant) was used for the between group contrast. The statistical design used in the current study is identical to the one used by Hunt et al.\(^{10}\), contrasting interlimb asymmetry in ACL-deficient individuals and healthy controls. Alpha was set at .05. Significant main effects and interactions were further analyzed using univariate ANOVAs and t-test, respectively. Effect sizes (Cohen’s f) are reported for primary dependent variables. Small, medium, and large effect sizes correspond to Cohen’s f-values of 0.1, 0.25, and 0.40, respectively.\(^{24}\) All statistical procedures were performed using SPSS (Version 21).
Review of literature

Cycling at higher pedaling rates leads to symptomatic improvement in patients with Parkinson’s disease (PD). However, these patients show inter-limb asymmetry in pedaling power when cycling at their slow self-selected cadence. The effects of higher pedaling cadence on symmetry of effort between limbs is unknown. This chapter will introduce the reader to relevant information about PD, neurorehabilitation via cycling, assessment of symmetry in cycling, and cycling cadence (a mechanical variable that affects both symptoms and symmetry in cycling). This pertinent review of literature provides evidence to support the testing protocol and procedures used in the current study.

Overview of Parkinson’s disease

Etiology

Parkinson’s disease (PD) is the second most common, progressive neuromuscular condition, after Alzheimer’s disease, affecting more than 10 million individuals worldwide \(^{1-3, 34}\). Both the prevalence and the incidence of the disease increases with age. For individuals age 60 years or higher, the incidence of PD is 1-2\% \(^{34-35}\). Though the prevalence rates compared between sexes has shown to be insignificant, more males have been reported to have the disease \(^{34}\), with incidence showing significance in the age range of 60-69 and 70-79 \(^{36}\). The exact cause for the disease is unknown, but studies have shown that both genetic and environmental factors play a role in the development of PD \(^{34-35, 37-38}\).

Neurophysiology

Parkinson’s disease is characterized by changes in the brain, more specifically the basal ganglia. The basal ganglia are a group of subcortical nuclei that are highly connected with many
areas of the brain including the cortex, thalamus, and brain stem. These nuclei are associated
with many functions of life including voluntary movement, cognition, and emotion. Synaptic
pathways between the basal ganglia and the cortical systems are affected by dopaminergic status,
and dysfunction in these connections may lead to Parkinson’s disease symptomology 5, 38.

Within the basal ganglia is a structure known as the substantia nigra, which plays a role
in movement and reward. Degeneration of the dopaminergic neurons within the substantia nigra
pars compacta leads to as much as a 90% reduction in dopamine in the striatum, depriving the
basal ganglia of the dopamine that it requires to initiate and facilitate movement and postural
control required of daily living. Thus, leading to many of the motor and non-motor signs and
symptoms observed in PD 3, 6, 34, 37. de Lau et al. 1 speculated that dysfunction at the muscular
level, such as mitochondrial dysfunction, oxidative stress, and protein mishandlings, may play a
role in the pathogenesis of PD.

Symptomology

PD is characterized by motor and non-motor symptoms. As the disease progresses, it
becomes an increasing social and economic burden on those affected. Four cardinal motor
symptoms associated with PD are resting tremors, bradykinesia or akinesia, rigidity, and postural
imbalances. Resting tremors are an involuntary oscillatory movement produced when a limb is
fully supported against gravity and the muscles involved are not active 7. Bradykinesia or
akinesia are defined as a slowness or absence in movement initiation and execution. There is also
an observed reduction in its amplitude of movement up until complete cessation of the
movement 8. Diminished levels of dopamine and associated reduced motor control output in
patients with PD, is suggested to influence bradykinetic movements and impaired sensory
integration 9. Rigidity refers to an increase in resistance when passively stretching a muscle 10.
As PD progresses, patients begin to exhibit abnormal body posture, including an increase in flexion of the head and cervical spine, an increase in thoracic kyphosis, and other postural imbalances that greatly affect daily life. Even though these symptoms are very common in patients with PD, some of these symptoms are not always observed. The current criteria for the diagnosis of PD includes the presence of at least two of these motor symptoms. The non-motor symptoms include sensory deficits, insomnia, and emotional problems such as depression, lack of facial expression, a slowing of gastrointestinal function, and reduction in the sense of smelling.

**Diagnosis and Classification**

*Unified Parkinson’s Disease Rating Scale*

Though there lacks a reliable and valid tool for these assessments, the Unified Parkinson’s Disease Rating Scale (UPDRS) has been widely used to assess many factors of PD including activities of daily living (ADLs), motor symptoms, mentation, and treatment complications in these patients. Ramaker et al. reports high internal consistency, inter-rater reliability, and a moderate construct validity. The UPDRS has specific use in PD, covers many arrays of the widespread scope of PD in differing severities, as well as clinimetric properties, especially in ADLs, and motor examination. In 2009, the release of the Movement Disorder Society-UPDRS (MDS-UPDRS) improved the older version of the test to cover multiple groups at differing levels of severity. The MDS-UPDRS consists of four parts: I: non-motor experiences of daily living; II: Motor experiences of daily living; III: Motor examination; IV: Motor complications. Patient and caregiver or administrator complete questions in each section on a rating scale of zero to four, with zero being normal, one being slight, two being mild, three being moderate, and four being severe. The MDS-UPDRS rates sixty-five items,
taking the patient and caregiver approximately thirty minutes to complete \textsuperscript{42}.

\textit{Hoehn and Yahr scale}

The Hoehn and Yahr scale has been widely accepted and utilized in the research of PD \textsuperscript{18}.\textsuperscript{43-44} In a research setting, the Hoehn and Yahr scale is primarily used to define inclusion/exclusion criteria \textsuperscript{43}. The scale consists of five stages, with each stage increasing in the severity of the disease.

The modified Hoehn and Yahr scale is as follows: \textsuperscript{41}

Stage 0: No signs of disease

Stage 1.0: Symptoms are very mild; unilateral involvement only

Stage 1.5: Unilateral and axial involvement

Stage 2: Bilateral involvement without impairment of balance

Stage 2.5: Mild bilateral disease with recovery on pull test

Stage 3: Mild to moderate bilateral disease; some postural instability; physically independent

Stage 4: Severe disability; still able to walk or stand unassisted

Stage 5: Wheelchair bound or bedridden unless aided

\textbf{Pharmacological management with Levodopa}

Since PD remains a progressive and thus far, a non-curable disease, rehabilitation has focused on decreasing the rate of progression as well as aiding in alleviating the side-effects that are common from the debilitation disease. For nearly the past half century, the use of the drug Levadopa (L-dopa) has been used to help alleviate the symptoms of PD. Further research found that administration of L-dopa in lab animals led to an excretion of dopamine in the urine, suggesting that dopamine levels were elevated \textsuperscript{9,45-46}. As the disease progresses though,
complications arise from Levodopa including either inadequate dopaminergic tone, where the drug wears-off or there are dose failures, or excessive dopaminergic tone that can cause levodopa-induced dyskinesia\(^\text{46}\). Though alternative medication can be used once L-dopa begins to have negative side-effects, alternative medications are used when tolerance increases \(^\text{46}\).

**Neurorehabilitation for PD**

PD is identified as a dysfunction in sensorimotor integration, leading to common symptoms such as bradykinesia and other atypical movement. Alternative rehabilitation methods have been researched and how they can positively elicit changes in the symptoms seen in PD \(^\text{2-3, 8-9, 14}\). Neurorehabilitation programs are an increasingly favorable method for the rehabilitation of PD \(^\text{47}\). Huang et al. \(^\text{47}\) also stated since the mechanism for the symptoms of PD, including weakness and fatigue, are unknown and often subjective, challenges arise when constructing neurorehabilitation programs. Though exercise has shown to combat other side-effects such as sleep deprivation and depression, finding a regimen that can improve kinesthetic deficits as well can be difficult \(^\text{17}\). Many studies have shown an increased attention to interventions that promote changes in neural drive \(^\text{9, 13}\). These studies have shown that an increase in not just motor output, but sensory input may play a role in these motor improvements, and since drugs like levodopa do not improve these kinesthetic deficits, neurorehabilitation interventions like these are greatly needed \(^\text{14}\). High intensity exercise has been highly suggested as a method to increase neural drive and promote neural plasticity as well as neuroprotection against dopaminergic cell loss \(^\text{14}\). Though the exact method is still undetermined, non-invasive trans-magnetic stimulation has been used to show a decrease in the dysfunction of corticomotor excitability in people with PD \(^\text{48}\). These changes in corticomotor excitability could be at the base of symptomatic improvements.
Neurorehabilitation through cycling

An increasing interest in cycling specifically has occurred in researches studying the effects of neurorehabilitation interventions for PD. Penko et al. stated that pedaling is a bidpedal motor task, similar to walking, that requires the same principles of lower extremity coordination, so quantifying pedaling kinetics can give a more precise measurement of lower extremity function. The exact protocol for cycling has been studied largely by researchers hoping to find a protocol that improves kinesthetic deficits the most. Alberts et al. stated that in order for the patients to gain a benefit from exercise, the rate of the exercise must be increased to trigger a release of neurotrophic factors and possibly dopamine.

Mode of cycling

A wide array of protocols has been looked at regarding cycling, and can be classified into three distinct categories; Active, active-assisted, and passive. Active, also known as voluntary cycling, is performed by the patient alone, usually at a self-selected pace. Though individuals do see some improvements in symptomology from an active protocol, the other modes of exercise have been shown to elicit greater improvements. Active-assisted cycling involves the individual biking with the assistance of an able-bodied assistant on a tandem bicycle. The exact mechanism for a greater response in this mode is unknown, but it is hypothesized that patients in this mode cycle at a cadence higher than their preferred speed, and this intervention promotes an increase in afferent input to the central nervous system. Ridgel et al. found that patients in an active-assisted group showed a 13% greater increase in UPDRS scores than compared to a voluntary group. In a practical sense, active-assisted cycling may not be the best mode in terms of resources as well as at-home protocols. Not every individual will be able to have an able-bodied assistant help them during at-home sessions. Passive cycling, or
forced exercise (FE), has been researched to work around these limitations. During FE, the individual is assisted through a motorized bike that is set at a specific cadence. Patients are told to cycle with the cadence of the motorized bike, so it is not passive in the sense that the patient isn’t cycling, but they do not need to exert the force need to increase the cadence past their comfortable range. It has been proposed that FE promotes angiogenesis and synaptogenesis which begin to degenerate in Parkinson’s disease. Acute aerobic exercise, in this case through a forced-cycling regimen, has been shown to release neurotrophins such as brain-derived neurotrophic fact (BDNF) and glial-derived neurotrophic factor (GDNF) as well as dopamine, which aids in supporting neuroplasticity as well as protect against cell loss in the basal ganglia. The key to this difference between FE and VE is the increase in intrinsic feedback, given by the higher pedaling rate.

**Mechanical variables critical for cycling performance assessment**

*Cadence*

The specific modality of the cycling training program has been extensively studied as to which modality is the most beneficial, and there has been an increasing interest in speed-based training. Uygur et al. examined the effects of an acute cadence-derived protocol primarily on the symptoms of bradykinesia in Parkinson’s disease patients. Three groups were looked at; no exercise, voluntary cycling, and high cadence-low resistance (HC:LR) cycling. For the HC:LR group, the cycled at a self-selected pace, similar to the voluntary group, but during the first 15-seconds of minutes 5-24, they pedaled at a self-selected fast cadence. They found that subjects in the HC:LR group had significant improvement during a 4-square step test and 10-minute walk test, primarily in walking velocity. It is suggested that this exercise facilitates locomotor central pattern generators, which are generally impaired in the Parkinson’s disease population.
**Power output**

Power output as well as lower extremity function can be quantified using pedaling kinetics. Power output can be a direct measurement of lower extremity asymmetries by examining crank torque produced on the pedals. Penko et al. studied the effects that power output has on common asymmetries seen in PD subjects. They tested their subjects by having them cycle on a cycle ergometer beginning at 20W for three minutes at a self-selected pace. They then increased the power by 20W every two minutes until the fourth stage (eighth minute), when 40W increases were made until exhaustion. A symmetry Index was calculated to determine whether the affected limb was contributing more or less as power increased. They witnessed a decrease in the symmetry index as workload increased, indicating that symmetry was increasing. The results of their study helped support a claim for a therapeutic intervention that provides higher quality and quantity afferent information through the use of augmented pedaling motion, as seen in forced exercise.

**Measurement of cycling and its importance in rehabilitation**

**Asymmetry**

As PD progresses, individuals experience a decrease in gait function, postural stability, and coordination of voluntary movements. Every human exhibits some degree of asymmetry that mostly goes unnoticed throughout the gait cycle, but individuals with PD exhibit a greater degree of asymmetry that affects their activities of daily living. Asymmetry can be directly quantified by measuring the crank torque of a modified cycle. Identifying asymmetry in Parkinson’s disease patients would therefore provide a baseline to be later used to measure the effectiveness of an intervention. Primary goals of exercise regimens for PD individuals should be in reducing asymmetry, thus improving normal daily activity.
Index of asymmetry

Researchers have used the Symmetry Index as a method of evaluating the lower extremity kinematics and degree of asymmetry in cyclers. Penko et al. calculated the symmetry index using the equation below:

\[ \text{Symmetry Index (SI)} = \frac{\text{Unaffected limb} - \text{Affected limb}}{(\text{Unaffected limb} + \text{affected limb})/2} \]

Using this equation, the researchers could evaluate the degree of contribution from each limb, with a positive value indicating a greater contribution by the unaffected limb, and a negative number indicating a greater contribution from the affected limb. These variables could be modified to evaluate left versus right leg contribution. Penko and colleagues found that as the power increased during a maximal cycle ergometry test, the symmetry index decreased, indicating an increase in symmetry.
References


