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The Effects of Four-Week Beta-Alanine Supplementation on Muscular Performance, Submaximal Oxygen Consumption, and Body Composition in Parkinson's Patients

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THE EFFECTS OF FOUR-WEEK BETA-ALANINE SUPPLEMENTATION ON MUSCULAR PERFORMANCE, SUBMAXIMAL OXYGEN CONSUMPTION, AND BODY COMPOSITION IN PARKINSON’S PATIENTS

By

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This research study and thesis are dedicated to and in acknowledgement of all of the individuals throughout the world who live bravely with Parkinson’s disease every day, as well as the immeasurable support from their families and caregivers.
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ABSTRACT

Background: Parkinson’s Disease (PD) is a progressive, neurodegenerative condition most commonly affecting adults over 60 years of age. PD patients often experience an increase in muscular fatigability as well as a decrease in muscular strength and power output. Beta-alanine (BA) has been shown to decrease muscular fatigue by increasing intra-muscular carnosine levels. Carnosine is thought to improve measures of fatigue, strength, and power in populations ranging from elite athletes to the elderly by attenuating the decrease in pH within working skeletal muscle. Purpose: To examine the effect of 4 weeks of beta alanine (BA) supplementation on muscular performance, submaximal oxygen consumption (VO₂), and body composition in adults diagnosed with PD. Methods: In this double blind placebo controlled study, participants with PD were stratified by leg strength and randomly assigned to either a SRCarnoSyn ® (Sustained Release) beta-alanine group (BA; age, 68.0±9.2 years; 5 men, 4 women) or a maltodextrin placebo group (PL; age, 68.0±8.9 years; 8 men, 2 women). Both groups took two 800 mg pills, three times/day with meals (4800 mg/day). No other nutritional or exercise changes were introduced. Before and after four weeks of supplementation, the following laboratory tests were conducted: anthropometrics, body composition (DXA), anaerobic capacity (Wingate), submaximal oxygen consumption (YMCA), leg strength, power, and fatigue (Biodex), and a 6-minute walk test. Results: Significant group by time interactions were observed for total body fat percent (BA: 35.2±6.5 vs. 35.5±6.6%; PL: 30.2±8.0 vs. 29.3±8.1%, p=0.01); android fat percent (BA: 39.5±11.4 vs. 40.5±11.2%; PL: 34.3±11.7 vs. 32.4±12.9%, p=0.01); and total fat-free mass (BA: 51.6±9.9 vs. 51.0±10.2kg; PL: 53.0±8.9 vs. 53.9±9.4kg, p=0.004). In addition, significant group x time interactions were observed during the 180 degrees/sec isokinetic fatigue test for both the percent work relative to bodyweight
during flexion (BA: 57.5±15.4 vs. 55.2±13.6%; PL: 52.9±22.3 vs. 62.0±21.7%, p=0.02) and acceleration time during extension (BA: 67.8±19.9 vs. 72.2±23.9 msec; PL: 85.0±22.2 vs. 72.0±20.4 msec, p<0.05). The following significant time effects were measured: fat mass; six-minute walk test distance; isokinetic 60 degrees/second test: peak torque during flexion; average peak torque during; relative peak torque during flexion; total work during; average power during both extension and flexion; as well as deceleration time during extension; 180 degrees/second test: peak torque during extension; average peak torque during extension; relative peak torque during; total work during both and flexion; average power during both extension and flexion; acceleration time during both extension and flexion; as well as deceleration time during extension; isometric 60 degree test: peak torque away and relative average peak torque away; and the fatigue test; peak torque during extension; relative peak torque during extension; relative total work during extension; and acceleration time during extension. No other significant time effects were observed and no differences were observed between groups. **Conclusion:** Four weeks of BA supplementation did not improve markers of muscular performance, submaximal oxygen consumption, or body composition in patients with PD to a greater degree than PL.
INTRODUCTION

Parkinson’s disease (PD) is a progressive neurodegenerative condition with no known cure. According to the Parkinson’s Disease Foundation there are approximately 60,000 new diagnoses of PD every year in the United States, with an incidence rate of nearly 1 in 500 (70). It is estimated that up to 10 million people worldwide are living with PD. The potential for PD to become a national health crisis is significant since PD is a disease of older adults (96% of all PD patients are over 50 years of age) (70) and the average life expectancy of adults in the US continues to increase (15). The symptoms of PD are numerous, but include four major motor complications which impact patients’ functionality the most. These include bradykinesia, postural instability, rigidity, and tremor. Collectively, these symptoms make voluntary movement like walking, talking, and other activities of daily living (personal hygiene, dressing oneself, driving a car, etc.) very difficult or impossible for some patients. Secondary motor symptoms of PD include impaired gross and fine motor control, lack of facial expressions, and freezing or accelerations of gait. Additionally, non-motor symptoms like muscle fatigue and thus, decreases in muscle strength and power, only exacerbate the other symptoms of PD. Without many of these abilities or the energy to perform them, PD patients cannot maintain their independence and must rely on caregivers (13, 15, 29, 32, 35, 43, 68).

The goal of PD treatment is to decrease the major motor symptoms enough that functionality can be kept as high as possible, while keeping treatment side effects like dyskinesias to a minimum. However, many pharmacological treatments can have equally debilitating side effects which affect functionality. As such, very few of the non-motor symptoms of PD receive much consideration or treatment. The most impactful (depression, sleep disturbances, cognitive disorders) are treated symptomatically. The treatment of many
other symptoms simply has to be bypassed. Moreover, the medical costs incurred can become burdensome to many, demonstrating the importance of finding alternative non-pharmacological methods for improving PD symptoms and overall well-being and reducing negative side effects. If the symptoms of muscular fatigue were treated, functionality may be maintained longer or possibly improved. Interestingly, there is some evidence from non-clinical populations to suggest that beta alanine (BA) supplementation may be a viable alternative to improve functionality. BA is a non-essential amino acid used to synthesize endogenous muscle carnosine. Carnosine acts as a proton buffer in the muscle, thereby reducing fatigue that would occur if the ions were allowed to accumulate (9).

BA has been shown to improve measures of muscular fatigue in healthy/athletic populations (12). Other research studies have only recently begun to examine the potential of supplementation with BA in special populations like the elderly (19, 55).

The only reported side effect from the consumption of BA are reports of paresthesia (a tingling or flushing sensation) often felt in the extremities or face following consumption (9). Paresthesia sensation intensity and duration can vary based on the amount of supplement consumed, especially relative to body mass, and other factors like time since eating or personal perception. In particular, consumption of a large BA dose and time elapsed since the last meal were both positively associated with more intense sensations of paresthesia (18). However, the sensations are not permanent and generally dissipate within 1-2 hours of consumption (9). Interestingly, the advent of slow release or “sustained-release” BA supplement pills has been shown to reduce or eliminate this side effect (10, 28).

Given that BA appears to improve physical work capacity and exercise tolerance in elderly individuals with no side effects (19, 33), it is possible that patients with PD may benefit
from BA supplementation. To date, no studies have examined the effect of BA supplementation in individuals with PD.

**Purpose**

The purpose of the present study was to examine the effect of 4 weeks of beta alanine (BA) supplementation on muscular performance, submaximal oxygen consumption (VO\(_2\)), and body composition in adults diagnosed with PD.

**Specific Aims and Hypotheses**

**Specific Aim 1:** Evaluate the effects of 4 weeks of BA supplementation versus a placebo (PL; maltodextrin) on muscular strength and power in PD patients.

Muscular strength and power were measured via:

- Thirty-second maximal power test using a cycle ergometer (Monark Exercise AB, Vansbro, Sweden)
- Maximal isometric and isokinetic knee flexion/extension on a dynamometer (BioDex Medical Systems, Shirley, New York)

**Hypothesis 1:** The BA group will increase muscular strength and power while the PL group will have no changes.

**Specific Aim 2:** Evaluate the effects of 4 weeks of BA supplementation versus a PL on submaximal VO\(_2\) in PD patients.

- Submaximal VO\(_2\) was measured using the YMCA protocol on a cycle ergometer.
**Hypothesis 2:** The BA group will show an improvement and the PL group will have no change in submaximal VO$_2$.

**Specific Aim 3:** Evaluate the effects of 4 weeks of BA supplementation versus a PL on muscular and functional fatigue/endurance in PD patients.

- Muscular fatigue was measured using maximal isokinetic concentric knee flexion/extension with no gravity correction on a dynamometer (BioDex Medical Systems, Shirley, New York)
- Functional fatigue/endurance was measured using the 6-minute walk protocol.

**Hypothesis 3:** The BA group will show improved measures of muscular and functional fatigue/endurance while the PL group will have no changes.

**Specific Aim 4:** Evaluate the effects of 4 weeks of BA supplementation versus a PL on body composition in PD patients.

- Lean and fat mass were measured using dual x-ray absorptiometry (DXA).

**Hypothesis 4:** The BA group will improve their body composition (increased lean mass and/or decreased fat mass) and the PL group will have no changes.
Assumptions

The following assumptions were made in this study:

1. Participants consumed at least 80% of their supplement (BA or PL), as directed for 28 days (±2 days).

2. Participants put forth their maximal effort during both the baseline and post-supplementation testing sessions.

3. Participants provided truthful answers on all questionnaires and logs.

4. All laboratory equipment provided reliable results and was used properly by researchers.

5. Participants followed instructions provided by researchers.

Delimitations

Delimitations included the following:

1. The study included a total of 19 men and women who were previously diagnosed with PD and were able to ambulate without the use of an assistive device (walker, cane, etc.). This correlates with a score of 3 or lower out of 5 on the Unified Parkinson’s Disease Rating Scale (UPDRS).

2. Individuals with major cardiovascular or respiratory issues, musculoskeletal injuries or complications that would prevent exercise testing with reasonable accommodations were excluded.

3. Individuals who were currently taking nutritional supplements with known ergogenic
The major limitations included the following:

1. The inability to control participants’ diet, physical activity, and supplementation adherence outside of testing sessions.

2. Participants did not have identical disease progression, nor were they at equal fitness levels.

3. Participants who had taken performance supplements in the past might have detected whether they were taking the supplement or not.

Definition of Terms

**Akinesia** – absence of voluntary movement

**Alpha synuclein** - protein which forms inclusions (Lewy body) in dopaminergic neurons of PD patients; assists in maintaining presynaptic vesicles in dopaminergic neurons

**Basal ganglia system** – a complex network of brain structures and systems responsible for processing and integrating functions like motor control

**Beta alanine (BA)** – a non-essential amino acid; rate-limiting component of carnosine synthesis; a common ergogenic aid

**Bradykinesia** – the condition of slowed or delayed onset and completion of voluntary movement

**Carnosine** - beta-alanyl-l-histidine; a dipeptide formed by the combination of beta alanine and l-histidine; acts as an important intramuscular buffer; also plays a role as an antioxidant and protein glycation inhibitor.

**Dopamine** - neurotransmitter; produced by neurons in the substantia nigra pars compacta (SNPC); responsible for lowering inhibitory factors within the motor cortex to allow for the initiation of voluntary movement; its absence results in the development of PD.

**Histidine** – essential amino acid; combines with BA to form carnosine
**Fatigue** – (muscular); decrease in ability to sustain previous level of exertion, speed, strength, power, etc. due to multiple factors including changes in muscle pH and internal buffering capacity

**Functionality/Functional capacity** – ability of a PD patient to walk, talk, and perform activities of daily living (personal hygiene, dressing, driving a car, grocery shopping, house chores, etc.), as normally as possible

**Lewy body** - formed in dopaminergic neurons of PD patients; composed of alpha synuclein protein aggregations

**Postural instability** – primary motor symptom of PD; impaired balance and ability to recover from balance disruptions; contributes to falls and shuffling gait

**Power** – ability of an muscle to rapidly generate force

**Rigidity** – (also: **Hypertonia**); primary motor symptom of PD; stiffness of limb(s) as the result of excessive muscle tone

**Strength** – maximal force produced by a muscle

**Substantia nigra pars compacta** – region of the midbrain containing dopaminergic neurons; death of neurons in this area is the cause of PD

**Tremor** – primary motor symptom of PD; an involuntary movement (shaking/trembling), usually of the hands; disappears during voluntary movement of the affected area
REVIEW OF LITERATURE

Introduction

Parkinson’s disease (PD) is the second most common neurologic disease diagnosed in adults, with more affected individuals than amyotrophic lateral sclerosis (Lou Gehrig’s), multiple sclerosis, and muscular dystrophy, combined. PD is a progressive, degenerative disease with no known cure. As many as 10 million individuals worldwide may suffer from PD and current treatments are only targeted at delaying or managing its major debilitating symptoms. Alternative treatment, such as supplementation with beta alanine (BA) may alleviate some of the less well-known but still detrimental side effects of PD, such as increased muscular fatigue and a reduction in physical functioning. This review will provide an understanding of PD, current treatment strategies, as well as some recent novel treatment approaches. This will be followed by an introduction showing how BA reduces muscular fatigue and improves strength/power in healthy individuals. Finally, the use of BA in special populations, and thereby its potential benefit in PD patients will be examined.

Parkinson’s Disease

Parkinson’s disease (PD) is a progressive, neurodegenerative condition affecting approximately 1% of all adults over 60 years of age (70). The progression of PD has classically been associated with individuals of low bodyweight (3, 11); although recent research suggests that PD patients may have an obesity prevalence 50% greater than a reference population of the same age (3). The symptoms of PD vary, dependent upon the progression, or “stage,” of the disease (Figure 1). The primary motor symptoms associated with PD include tremor, bradykinesia, postural instability, and hypertonia. These symptoms are the hallmark of PD and are also responsible for the decline
in a patient’s ability to function normally. There are also several lesser-known, yet equally debilitating non-motor symptoms. Most notably, PD patients often experience an increase in muscular fatigability which ultimately affects their ability to care for themselves and perform daily functions (32).

<table>
<thead>
<tr>
<th>Stage 0</th>
<th>No signs of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Unilateral disease</td>
</tr>
<tr>
<td>Stage 1.5</td>
<td>Unilateral plus axial involvement</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Bilateral disease, without impairment of balance</td>
</tr>
<tr>
<td>Stage 2.5</td>
<td>Mild bilateral disease; recovery on pull test</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Mild to moderate bilateral disease; some postural instability; capacity for living independent lives</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Severe disability; still able to walk or stand unassisted</td>
</tr>
<tr>
<td>Stage 5</td>
<td>Wheelchair bound or bedridden unless aided</td>
</tr>
</tbody>
</table>

**Figure 1. Hoehn and Yahr Scale (Modified version)** (48).

Even as the second most commonly diagnosed neurological disease, the pathology of PD is not fully understood by medical and scientific communities, thus, giving the clinically recognized diagnosis of “idiopathic Parkinson’s disease”. The average age for a clinical diagnosis of PD is 50 years old, and its presence in younger individuals is uncommon (43). Both men and women are susceptible to developing PD, however it seems to affect men more frequently than women (15).

Different forms of PD exist, which are the result of environmental or genetic causes; however they are rare and outside the scope of this review. There is a consensus that PD develops before clinical symptoms present and that its diagnosis must often results from a
process of elimination. Similarly the treatment of PD is not precise, but rather a balance between maintenance of physical function and minimization of negative side effects.

Treatment plans for PD patients only address the most severe non-motor symptoms. With proper medication in most patients, the progression of motor symptoms can be significantly delayed. Subsequently, with a treatment-induced increase in functional time and a decrease in major symptoms, patients often explore new treatment options targeting other common symptoms such as physical fatigue and decreased endurance in daily activities. In regards to treatment modalities, of particular interest to many patients is the use of non-pharmacological sources to attenuate common symptoms.

**Pathophysiology**

The difficult nature of understanding and treating PD is primarily due to the complicated brain structures affected by the disease. The substantia nigra, a structure within the midbrain (mesencephalon), is presumed to be the lesion site in PD. In post-mortem examinations of PD patients, the melanin-containing neurons of the substantia nigra pars compacta (SNPC) are often found to have degraded significantly (Figure 2).

![Figure 2. Transverse view of the substantia nigra pars compacta in a healthy individual versus Parkinson’s patient](71).
The neurons within the SNPC produce dopamine, a potent neurotransmitter, with melanin being a non-reactive byproduct of the process. The presence of protein accumulations, or inclusions called Lewy bodies, within the same neurons are also indicative of PD. While the exact damage that Lewy bodies cause is not well known, their constituent protein, alpha synuclein, is highly involved in the maintenance of vesicles within the presynaptic terminal and the release of dopamine. Lewy bodies are therefore a hallmark of PD, and research on their precise effects on decreased dopamine production and release is inconclusive. Similarly, excess levels of calbindin (calcium-transport protein) and iron have been implicated as possible contributing neurotoxins. It is the absence of dopamine production that causes the four major motor symptoms and later diagnosis of PD. PD is considered a disease of the basal ganglia system because the SNPC projects primarily into the nuclei of the basal ganglia via the striatum (central processing station). Since the basal ganglia serves as a primary integration site for signals from the motor cortex and association cortex, the loss of dopaminergic input from the SNPC greatly affects the basal ganglia’s integrated output, and in particular, the basal ganglia’s output to the motor cortex. This subsequent imbalance of inhibitory and excitatory action within the basal ganglia is what causes the actual stimuli to occur which results the major symptoms experienced by those with PD.

**Clinical Signs and Symptoms**

The primary neuromuscular symptoms most commonly associated with PD are resting tremor, bradykinesia, hypertonia, and postural instability. Collectively, these symptoms are considered “Parkinsonism.” Resting tremor is an involuntary movement that disappears when a patient initiates voluntary movement within the affected limb(s). Unlike other disorder-related tremors, the resting tremor seen in PD patients is not associated with the initiation of
movement, commonly displayed in cerebellar disorders. Bradykinesia may manifest itself in the early stages of PD as muscular weakness or stiffness within the affected limb(s). Hypertonia is often experienced as a rigid or stiff limb(s). In combination with these symptoms, postural instability can result in impaired balance and a stooped, shuffling gait as the disease progresses. The initial presentation and progression of these symptoms are unique to each individual. However, many individuals who are later diagnosed with PD experience decreased or loss of sense of smell, frequent constipation, rapid eye movement (REM) sleep disorders (exceptionally vivid dreams, sleepwalking), and orthostatic hypotension many years before a PD diagnosis is made.

These pre-diagnosis symptoms eventually arise in almost all cases of PD, becoming non-motor symptoms of the disease and usually worsen over time. Secondary motor symptoms, the result of primary motor symptoms include: a mask-like facial expression (hypomimia), difficulting speaking (dysarthria), trouble swallowing (dysphagia), excessive salivation (sialorrhoea), small cramped handwriting (micrographia), shuffling gait, gait quickening (festination), gait freezing, involuntary twisting from muscular contractions (dystonia), and abnormal blinking (glabellar reflexes). Finally, independent of perpetual muscle fatigue, the non-motor symptoms of PD are extensive and beyond the scope of this review. These symptoms include, but are not limited to impulse control disorders, cognitive and mood disorders, and autonomic dysfunction (10, 29, 32, 66, 68).

**Diagnosis and Progression**

Diagnosis of PD before it has significantly advanced is difficult, especially in mild cases or early in its onset. This is because the primary motor symptoms, which are evident in more advanced cases of PD, may not be detectable or may mimic other neurologic conditions. Within
the SNPC, typically more than 50% of the dopaminergic neurons have died before Parkinsonism presents (32). This delay of symptom onset despite neuronal death is due largely to the plasticity of the brain’s neurochemical processes. By slowing its uptake of dopamine within the striatum of the basal ganglia, the transport systems within dopaminergic neurons can preserve decreasing supplies of the neurotransmitter.

The classification or “staging” of PD is commonly performed using the Unified Parkinson’s Disease Rating Scale (UPDRS), which is a 3 to 5-part test used to track an individual’s disease progression. Within the UPDRS, the Hoehn and Yahr scale is used to describe the current progression of the disease with a numeric value ranging from 1 to 5. A modified version of the scale (Figure 1) includes descriptions at the half-mark (1.5 and 2.5) to allow for more accurate staging.

**Current Treatment Strategies**

There is no known cure for PD. Current treatment strategies are used to delay the disease’s progression and treat those symptoms which most adversely affect a patient’s ability to function. The most common treatment strategies currently used for the management of PD symptoms are pharmacologic agents. Treatment plans almost always include dopamine antagonists, MAO-B inhibitors, and/or levodopa (L-DOPA)/carbidopa. All of these medications are usually used at some point and often in conjunction with one another.

Dopamine antagonists exert their effects by binding with the post-synaptic receptors in dopaminergic neurons. This extends the usefulness of the dopamine that is present despite a decrease in its overall concentration. MAO-B inhibitors act by blocking the metabolism of dopamine (by MAO-B), thereby increasing the neurotransmitter’s half-life. The most well-known
medication for the treatment of PD is levodopa or L-DOPA. L-DOPA is the biologic precursor to dopamine; although its use is delayed as long as possible and its dosage kept low. This is because no more than 10% of the ingested L-DOPA will cross the blood-brain barrier to become usable dopamine. The remainder is metabolized throughout the body, resulting in unwanted side effects such as dyskinesias.

**Novel Treatment Approaches**

In a recent comprehensive review, creatine supplementation was implicated as a potentially effective tool in treating neurodegenerative conditions, particularly by positively affecting existing intracellular bioenergetic deficits. There may also be a neuroprotective effect that occurs from creatine supplementation in PD patients (1, 2). Animal models have shown a decrease in dyskinesias from L-DOPA therapy when a 2% creatine diet is administered. However, these improvements were only seen after one month of diet supplementation prior to beginning L-DOPA treatment (65).

Exercise has also been suggested as an alternative treatment method for PD, as well as maintenance of lean body mass. A cross-sectional study of PD patients reported that the benefits from exercise or physical therapy were more related to the patient’s self-efficacy than the progression or stage of their disease (16).

Bolyrev et al. (2008), explored whether carnosine supplementation could improve the effects of L-DOPA drug therapy in PD patients (7). Participants consumed a total of 1.5 g of carnosine, 3 times per day for 30 days. Researchers found that the basic therapy and carnosine group showed greater improvements in their scores of neurological measures using the UPDRS. The same group also studied the effects of carnosine as an antioxidant to minimize mitochondrial dysfunction in PD patients, and reported that carnosine was inefficient as an antioxidant.
action of carnosinase, a metabolic enzyme found outside of the skeletal muscle, on carnosine makes its supplementation inefficient (8).

**Beta-Alanine**

To date, the effects of BA supplementation in PD patients has not been investigated. BA is a naturally occurring non-essential amino acid consumed in most diets. It is found primarily in meat products, with particularly high concentrations present in beef and poultry sources, like turkey and chicken. Vegetarians are particularly susceptible to low intramuscular carnosine levels because their diet lacks animal sources of carnosine (17). Commercially available BA, however, is typically synthesized in a laboratory from non-animal sources. Current annual production BA for use as a dietary is estimated to be around 100,000 kilograms (45).

When consumed as a sport supplement, BA is used to increase intramuscular carnosine (beta-alanyl-l-histidine), which acts as an endogenous intramuscular buffering agent. During muscular contractions, protons or hydrogen ions (H+) are produced as a byproduct of glycolysis. While the ions can be cleared and used to form lactate, they accumulate rapidly during the anaerobic phase of physical activity (approximately 10 seconds up to 2 minutes). This rapid accumulation decreases the pH of the exercising muscle. The acidification of the muscle is what causes muscular fatigue which is proposed to be attenuated with supplementation of BA (through the action of carnosine; see below for a detailed explanation) (25, 45). Whether this mechanism occurs to a different and potentially greater degree in PD patients has not yet been evaluated

Extensive research on the efficacy of BA supplementation in young, healthy and sport populations has been conducted with particular attention to high-intensity exercise such as that performed by power/sprint athletes, which will be discussed later in this review. Because BA
eliminates similar symptoms of muscular fatigue and decreases in strength and power (physical capabilities) seen in healthy populations through carnosine supplementation it is plausible that BA supplementation may improve the same symptoms in PD patients.

**Beta Alanine vs. Carnosine**

Supplementation with BA rather than carnosine, to increase intramuscular carnosine levels is recommended for several reasons. First, the muscular uptake of ingested carnosine is limited due to metabolic action on carnosine. Most ingested carnosine is broken down into its constituent amino acids (the nonessential amino acid BA and the essential amino acid L-histidine) by the action of the enzyme carnosinase before it is taken up by muscular tissue, making supplementation inefficient and not cost-effective (1, 21, 27).

![Chemical structure of carnosine and its constituent amino acids](image)

**Figure 3. Chemical structure of carnosine and its constituent amino acids** (34)

Since BA is the rate-limiting component of intramuscular carnosine synthesis, it is naturally present in much lower concentrations than histidine. BA is also taken up more quickly
by muscular tissue, making it the obvious choice for supplementation, as opposed to carnosine. The proposed mechanism of action of carnosine on the maintenance of intramuscular pH is by improving the muscle’s capacity for buffering hydrogen ions (H\(^+\)). This buffering capacity is important because it prevents the intramuscular acidification that leads to muscular fatigue and a loss of strength and power in the affected area (25, 57). The action of carnosine may be responsible for up to 10% of the entire buffering that occurs in working skeletal muscle (25). While BA supplementation is typically associated with high-intensity exercise performance, its use may be applicable for PD patients given their increased fatigability while performing physical tasks. Theoretically, a low- to moderate-intensity workload for a typical individual might be high- or maximal-intensity for the system of a PD patient. This concept has yet to be examined, but is a plausible basis for BA supplementation in PD patients.

**Figure 4. Proton production from ATP hydrolysis** (42)

It is clear that BA supplementation increases intramuscular carnosine content which can lead to improved muscle buffering capacity. However, if this increase translates to improved physical performance is less well documented. Levels of intramuscular carnosine have been
positively and directly associated with maximal anaerobic power performance, like that measured during the Wingate test (57). Muscle carnosine content can be determined several ways; however, the best method is through biopsies of the muscle tissue. Analyses of the muscle fiber types from biopsies have shown the highest carnosine concentrations in Type IIB, or fast-twitch, fibers. This has strengthened the association between BA supplementation and performance during sprint/power performances; activities which rely primarily on Type IIB fibers. These fibers are able to generate large amounts of force for a short period of time, fulfilling the demands of sprint/power movements. However, this results in a very rapid rise in intramuscular H⁺ ions in a matter of seconds. Thus, the inability to quickly and efficiently buffer the accumulating protons from the working skeletal muscle will cause fatigue and negatively impact physical performance (25, 45).

**Healthy Populations**

Improving the buffering capacity of skeletal muscle through BA supplementation has been studied extensively in healthy, typically young adult and trained athlete populations. Previous research has focused primarily on the ability of BA to improve sprint/power measurements during anaerobic exercise, which typically includes physical movements lasting 20 seconds to 2 minutes from the onset of exercise. This immediate short-duration physical activity, followed by prolonged rest may be applicable to PD patients in certain instances of their day-to-day physical activity. However, for most individuals, the nature of daily living necessitates that the ability to perform such activities still be possible even at the end of a day full of physical movement and accumulated fatigue. Thus, it is important that BA supplementation be useful for improving physical performance in later timeframes as well.
Van Thienen et al. (2009) studied sprint performance after BA supplementation by placing a final sprint phase at the end of a 2 hour endurance cycling test. The 8 week, double-blind study of young, moderate- to well-trained male cyclists used an increasing dose of BA or PL (maltodextrin) over the course of the study (2.0-4.0 g/day). It was reported that BA improved peak power output (+11.4%; 95% CI = +7.8 to +14.9%; P = 0.0001) and mean power output (+5.0%; 95% CI = +2.0 to +8.1%; P = 0.005) during the final sprint phase of the exercise test when compared to the PL group. Thus, it was demonstrated that BA supplementation could improve sprint performance, even at the end of an endurance event. This finding challenged the conventional notion that BA supplementation is only effective for improving performance during entirely anaerobic sprint/power-type tests (62).

Similarly, Sale et al. (2012) studied the effects of BA supplementation on the endurance of isometric force generated by the knee extensors in young, healthy males. Participants were asked to complete 5 isometric knee extension tests (IKET) to fatigue at 45% of their maximal voluntary isometric contraction (MVIC) force. Tests were performed both before and after 4 weeks of supplementation with either 6.4g/day (8 x 800mg) of BA (CarnoSyn®) or a PL (maltodextrin). After supplementation, BA significantly increased their IKET hold-time versus PL which decreased their IKET hold-time (BA: +9.7 ± 9.4 s, +13.2%, vs PL: −2.6±4.3 s, -4.0%; p < 0.05). The IKET times (seconds) were combined with each participant’s average force generated in Newtons (N) to calculate the impulse value (kN s\(^{-1}\)), which allowed for participant dependent differences. BA significantly improved compared to PL (BA: +3.7±1.3 kN s\(^{-1}\),+13.9%, vs PL: −1.1±1.5 kN s\(^{-1}\); p < 0.05). From these data, it was concluded that 4 weeks of BA supplementation significantly improved isometric endurance and impulse of the knee extensors at 45% MVIC force. The improvements seen were attributed to both increased intramuscular
carnosine levels, as well as improved pH management resultant from the BA supplementation (46). Therefore, it is clear that BA supplementation can have a positive role in improving sprint/power, endurance, and strength performance. As such, its use should be considered to aid the improvement of these measures in special populations outside the typically studied groups of athletes and trained individuals.

In addition, BA supplementation has been shown to have a significant ergogenic effect in different sport populations with varying physical demands (12, 24–26). Using college football players, Hoffman et al. (2008) measured anaerobic performance after 3 weeks of BA supplementation. While there was a non-significant trend (P = .07) for reduced fatigue during anaerobic performance exercises, a modified Wingate anaerobic power test (WAnT) and a repeated line drill in the BA group; both an increased training volume and decreased subjective feelings of fatigue after continued supplementation made the effectiveness of BA apparent (28). Similarly, Kern and Robinson (2011) studied the effects of BA supplementation on performance and body composition in male collegiate wrestlers and football players. The athletes consumed 4g/day of either BA supplement or PL for 8 weeks. While not statistically significant, the BA football group improved measures on the performance tests: 300-m shuttle run time (s) (BA: -1.1 ± 0.94; PL: -0.4 ± 2.2; p > 0.05) and 90° flexed arm hang time (s) (BA: 3.0 ± 5.4; PL: 0.39 ± 6.5; p > 0.05) to a greater degree than the PL group. The BA football group averaged a ~1.0 kg gain in lean body mass, while the PL football group gained only 0.5 kg (p > 0.05). The wrestlers did not have as many improvements as the football players, although some differences (non-significant) were observed between the BA and PL wrestler groups. Although not statistically significant, total time for the 300-meter shuttle run decreased to a greater degree in the BA group (BA: -1.6 ± 2.2; PL: -1.3 ± 1.7) than did the PL. Hold time for the 90° flexed-arm hang also increased more in
BA (BA: +6.5 ± 7.3 seconds; PL: 5.0 ± 3.9 seconds; p > 0.05) than PL. The BA wrestler group also increased their lean mass (kg) while the PL group had a decrease, although neither was statistically significant (BA: +0.5 ± 1.9 kg; PL: -0.45 ± 1.3 kg; Evidence of even minor improvements from BA supplementation, although not statistically significant, could still translate to tangible improvements in daily physical functioning for special populations.

Conclusions about the efficacy of BA have been further complicated by findings like those of Sweeney et al. (2010), which found no significant improvements from BA supplementation on power performance in young, college-age males during repeated treadmill sprint activity. The 5 week study used an increasing amount (4.0-6.0 g/day) of BA or PL (rice flour) over its duration. Testing consisted of two sets of 5 sprints (5 second duration) at a resistance equal to 15% of the participant’s bodyweight. The study found no significant differences between or among groups. However, it was concluded that the depletion of phosphocreatine (PCr) stores, rather than acidosis from proton accumulation, was responsible for muscle fatigue. The extremely short duration of the sprints meant that the participants were liking relying on their PCr system, not the anaerobic system typically aided by BA supplementation (31). With such a range of findings the support for supplementation, particularly in terms of body composition, with BA is inconsistent in the literature. This makes the need for additional research in this area more apparent and urgent. Studies focusing specifically on its effects in individuals of different ages, particularly older adults, and physical status, like PD patients with diminished physical capacity, are also warranted.
Dosage

Recommendations for an absolute dose of BA during the loading phase range from 1.6-6.4g/day for 4 to 12 weeks and result in muscle carnosine increases of 15-85% above baseline concentrations (9, 14, 19, 25, 53). Without a maintenance dose of BA, muscle carnosine levels can return to their pre-supplementation amounts in 6 to 20 weeks (2, 53). To improve function in clinical populations, maintenance of muscle carnosine at least 50% above unsupplemented levels is recommended (52).

Recently, Stegen et al. (2014) examined the dose of BA needed to maintain elevated intramuscular carnosine levels in both young men and women. Different loading protocols were used, but all participants consumed a total of 3.2g BA/day for 46 days. Nineteen of the participants continued supplementing with BA at a reduced dose (0.4g, 0.8g, or 1.2g BA/day) for 6 weeks after the loading phase to maintain their elevated carnosine levels. The absolute increase of muscle carnosine (1.5-2.0 mM) was not significantly impacted by gender, bodyweight (BW) or baseline carnosine concentrations, suggesting that 3.2g BA/day was sufficient to raise carnosine levels in all individuals regardless of those factors. The relative changes seen in muscle carnosine were found to be greater in women that was attributed to their lower body mass and lower muscle carnosine content prior to supplementation. In addition, a dose of 1.2g BA/day was found to maintain the same intramuscular carnosine levels as were found after the loading phase. A linear relationship was found to exist after correcting for bodyweight, between BA dosage and muscle carnosine levels. This lead the researchers to postulate that the ideal dose of BA should be calculated relative to the individual’s BW, approximately 18 mg/kg BW/day (52). These findings are important for supporting a BA supplementation regimen of 4.8 g/day.
Aerobic Endurance & VO$_2$

BA supplementation may also improve physical endurance capacity. The alterations in physical endurance capacity may be due to increased VO$_2$ and/or reduced muscular fatigue as a result of BA supplementation. Ghiasvand et al. reported improvements in VO$_2$ and time to exhaustion in active males following 6 weeks of BA supplementation (2g/day) compared to the PL (dextrose) group. Post intervention VO$_2$ (L/min$^{-1}$) increased, albeit not statistically increased, to a greater degree in the BA group (pre, 2.62 ± 0.82 vs. post, 2.79± 0.73; p < 0.05) than the PL group (pre, 2.85± 0.67 vs. post, 2.81± 0.79 (22). These data suggest that aerobic capacity to perform daily functions may be improved or sustained for a greater duration in PD patients after BA supplementation, particularly when combined with an exercise intervention. Similarly, Stout et al. (2007) used a double-blind, randomized, placebo-controlled, parallel design to examine the effects of 4 weeks of BA supplementation on PWC$_{FT}$, ventilatory threshold (VT), VO$_2$, and TTE in young women. Participants were randomly assigned to either the BA (CarnoSyn ®) or PL group whereby they consumed 3.2g/day (4 x 800mg) for the first week and 6.4g/day (4 x 1600mg) for the remaining 3 weeks. Before and after supplementation, participants performed a continuous, incremental test on a cycle ergometer to determine the VT, PWC$_{FT}$, VT, and TTE. BA significantly delayed the onset of both the PWC$_{FT}$ and the ventilatory threshold (VT = +13.9%, PWC$_{FT}$ = + 12.6, TTE = +2.5%; p<0.05) at submaximal workloads, while no changes were seen in PL (p>0.05). These results indicate that BA supplementation can delay the onset of neuromuscular fatigue at the fatigue threshold and the VT at submaximal workloads, and increase in TTE during maximal performance on a cycle ergometer.. It was concluded that the results were perhaps due to an increased buffering capacity resulting from elevated muscle carnosine levels after BA supplementation (54). These results, while observed in a young healthy population,
provide theoretical support that improvements in fatigue/endurance from BA supplementation could occur in special populations.

Water et al. (2010) conducted a study on young adult women where BA was supplemented during a 6-week high-intensity training (HIIT) protocol on a cycle ergometer. During the first half of the study, participants consumed 6.0g/day (4 x 1.5g) of a BA-containing drink powder or a PL (dextrose) powder; followed by 3.0g/day (2 x 1.5g) during the second half to maintain muscle carnosine. No differences were seen between the BA and PL groups on measures of VO$_2$peak after 6 weeks of HIIT. Thus, it was concluded that BA did not seem to have any effect on measures of aerobic exercise (67). This may have been due to combining BA supplementation with HIIT, especially since the combination had not previously been studied in the study population. Despite this, the action of exercise training alone has been shown to increase muscle carnosine content and it is plausible that the training alone may have raised the participants’ carnosine levels. If intramuscular carnosine content were raised to a high enough level from exercise alone, the addition of BA would not cause any further increases. A contributing mechanism may have also been the content of the participants’ diets, which may have contained higher than normal carnosine. The young age and engagement in structured HIIT by the participants of the study are reasons why we would not expect to see this occur in PD patients. Based on these findings it is also important to note that BA supplementation was not associated with negative changes in aerobic performance either.

*Creatine + BA*

There are numerous published studies on the effect of BA supplementation (alone or in conjunction with creatine supplementation) that show greater anaerobic performance
improvements in comparison to creatine alone or a PL in athletes (27). One study on a creatine multi-ingredient supplement (containing both BA and creatine) showed not only a significant improvement ($p < 0.05$) in measures of lower body muscular endurance by maintaining power (leg press), but also increased perceived level of energy and decreased fatigue (51). Improvements in both objective and subjective measures of strength/fatigue are important for individuals who experience chronic physical fatigue, like PD patients.

In another study of a multi-ingredient performance supplement (MIPS) containing both creatine and BA, Ormsbee et al. recruited 24 healthy, resistance-trained males to consume the MIPS or an isocaloric PL (maltodextrin) during 6 weeks of resistance training. Participants consumed 21g of MIPS (~73 kilocalories) immediately pre- and post-resistance training in addition to 1-21g serving on non-training days. The exact BA/creatine content of the MIPS was unknown due to proprietary formulation. Measures of strength, power, and body composition were measured before and after the 6 weeks of supplementation. A significant ($p = 0.017$) group x time interaction was observed for the MIPS group, but not the PL group in terms of lean body mass (MIPS: pre, $62.9 \pm 8.8$ kg vs. post, $65.7 \pm 8.8$ kg, +4.7%; $p < 0.001$; PL: pre, $63.5 \pm 5.2$ kg vs. post, $64.7 \pm 5.9$ kg, $p = 0.63$). Total body fat percent also significantly ($p = 0.004$) decreased in the MIPS (pre, $21.6 \pm 1.4\%$, vs. post, $20.5 \pm 1.3\%$), but not PL. In measures of anaerobic power (Wingate test) the MIPS group significantly increased: peak anaerobic power (W) (pre, $932.7 \pm 172.5$, vs. post, $1119.2 \pm 183.8$, +16.2%, $p = 0.002$), anaerobic power relative to bodyweight (W·kg$^{-1}$) (pre, $11.1 \pm 1.7$, vs. post, $13.1 \pm 1.8$, +9.4%, $p = 0.003$), mean anaerobic power (W) (pre, $676.4 \pm 145.3$, vs. post, $751.1 \pm 1.8$, +9.9%, $p = 0.02$), and mean anaerobic power relative to bodyweight (W·kg$^{-1}$) (pre, $7.9 \pm 1.0$, vs. post, $8.8 \pm 1.1$, +8.2%, $p = 0.03$), while PL did not have any changes. The results of this study show that a BA + creatine containing supplement in
combination with resistance training was sufficient to increase lean body mass and anaerobic power in trained males (36). In conjunction with the findings of other studies it is plausible that the supplementation of a BA+ creatine-containing supplement may contribute to favorable changes in body composition and anaerobic power.

Another study suggested that supplementation with creatine + BA may enhance an individual’s potential for submaximal endurance performance as measured by the lactate and ventilatory thresholds (69). Creatine supplementation in older adults has been shown to have many of the same beneficial effects as in younger populations such as increased skeletal muscle phosphocreatine content (12, 23, 61, 69). Its use as a therapeutic agent in PD may also be beneficial. Improvements in body composition, strength, power, and endurance through the use of these supplements provide plausible basis for their use in PD patients; for whom even minor improvement in these factors could significantly impact their physical functioning and quality of life.

**Special Populations**

While the overwhelming majority of BA supplement studies are useful for the sport performance community, little is known about BA’s potential for use in special populations, especially clinical groups like PD patients. However, it has been suggested that the same buffering improvement seen in healthy populations could be used to enhance function and improve symptoms in clinical populations (27). In this instance, the frequently reported symptoms of increased muscular fatigue and decreased muscular strength/power in PD patients could potentially be reduced or eliminated through BA supplementation.
Despite an overall lack of special population research with BA, studies conducted with older adults will most likely provide useful information on the plausible effects and outcomes of BA supplementation in PD patients.

**Older Adults**

It is important to mention that intramuscular carnosine content can also be affected by gender and age, with older individuals and older women in particular having disproportionately low concentrations of carnosine (17, 60). This has been attributed to less overall muscle mass, lower levels of circulating free testosterone (38), decreased physical activity, less meat consumption, or the action of progressive denervation (24). Despite many theories, the specific physiologic reasons for the age-related difference has not been fully determined (17, 38, 60). There have been very few studies which have examined the effects of BA supplementation in older adults.

Del Favero et al. recruited 18 sedentary but otherwise healthy elderly adults, age 60-80 years for a 12 week study. Twelve participants were grouped into the BA group and the remaining 6 were placed in a PL group. Exercise capacity, muscular function, muscle carnosine content, and quality of life were measured before and after 12 weeks of supplementation (3.2 g/day) using sustained-release BA (SRCarnoSyn®) or PL (maltodextrin). The participants’ physical capacity was measured using two different treadmill tests. The first test was an incremental load test used to determine ventilatory anaerobic threshold (VAT) and VO₂ peak. It began at 1.5 miles-per-hour (mph) and was increased by 0.5 mph every min up to 3.5 mph; after which slope increments (+2% per min) were made until exhaustion. Second was a constant load test, which was a single repetition square-wave transition going from rest to an exercise intensity based on 75% of (VAT-
VO2 peak). This intensity was maintained to the limit of tolerance. Significant improvements were seen in the BA group compared to PL or muscle carnosine concentration (BA group: + 85.4%, PL group: +7.2%; p = 0.004) and TTE in both the constant load (BA: pre, 5.2 ± 1.9 vs. post, 6.6 ± 1.7 min, +36.5%; PL: pre, 4.4 ± 1.1 vs. post, 4.7 ± 1.2 min, +8.6%; p <0.05) and incremental load tests (BA: pre, 11.0 ± 2.1 vs post, 12.1 ± 2.1 min, 12.2%; PL group: pre, 12.6 ± 1.7 vs. post, 12.5 ± 1.5 min, 0.1%; p = 0.04). The increase in carnosine content was positively correlated to the improvements in TTE for the constant (r = 0.62; p = 0.01) and incremental tests (r = 0.48; p = 0.02). Most importantly, the study showed that it is possible to increase muscle carnosine levels in older adults. This is a promising finding if age alone negatively affects muscle carnosine without supplementation (17, 19). Strong evidence was presented that the increase in muscle carnosine was connected to improved exercise tolerance with no reports or evidence of adverse side effects (19).

The only other known study on the topic examined the effects of BA supplementation on the “physical working capacity at the fatigue threshold” (PWCFT) of elderly adults. Twenty-six men (n=9) and women (n=17) were assigned to either a BA (n=12) or PL group (n=14). Participants consumed 2.4g/day (3x800mg/day) of BA (CarnoSyn ®) or PL (microcrystalline cellulose) for 3 months (90 days). PWCFT was determined through electromyographic (EMG) measurements of the vastus lateralis during a cycle ergometer test, using EMG fatigue curves. A significant treatment x time interaction (p = 0.007) was observed for the PWCFT. An increase in PWCFT after supplementation was seen with BA (+28.6%; p < 0.05), but not PL. Additionally, BA improved to a greater degree after supplementation than did PL (BA: +67%; PL: +21.5%). These findings are important because BA was shown to improve physical capacity in older adults and had no reported side effects (55).

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Conclusions

The complicated pathology and other etiological aspects of PD make its diagnosis and subsequent treatment difficult. It is clear that PD is brought about by decreased levels of dopamine, resulting from the loss of dopaminergic neurons within the SNPC. The exact cause(s) of the dopaminergic neuronal death have not been fully elucidated. Since no clinical diagnostic test currently exists, the presence of the primary PD motor symptoms (bradykinesia, hypertonia, resting tremor, and postural instability) and their subsequent improvement with L-DOPA therapy is often the only means of making a PD diagnosis. The current treatment strategies of PD can only aim to delay and/or manage the patients’ most debilitating symptoms. A major contributing, but often overlooked, symptom to the loss of physical functioning in PD patients is muscle fatigue. Some novel treatment approaches to PD have been examined, but none have specifically addressed improving muscle fatigue. The sport supplement, BA, is well-known as an anti-muscular fatigue ergogenic aid with extensive research conducted in healthy populations. Based on research of the action of the dipeptide carnosine, which is synthesized in part by BA, in both healthy and elderly populations it is plausible that it may have anti-fatigue effects in PD patients. Carnosine is, among other things, a major intracellular proton (H⁺) buffer. By preventing a rapid decline in intramuscular pH carnosine slows the onset of muscular fatigue. The attenuation of muscle acidity during muscular activity may improve physical functioning in PD, based on studies in other populations. Based on the review of current literature, research is warranted to study the effects of BA supplementation in PD patients particularly in regard to improvements in muscle fatigue and physical function.
RESEARCH DESIGN & METHODOLOGY

Participants

Nineteen patients, thirteen men and six women, previously diagnosed with Parkinson’s Disease (PD) were recruited to participate in this study from Tallahassee, Florida and the surrounding areas. Participants were not taking any ergogenic supplement(s) or compounds. An assent letter was sent to their primary care doctor and all participants were cleared by a physician for physical activity/exercise. Participants had no unresolved, uncontrolled, or recent major medical issues, as well as musculoskeletal injuries. All participants were independently ambulatory without the use of an assistive device (cane, walker, etc.). Participants continued to take their normal medication regimen throughout the study with no changes other than the addition of the BA supplement or PL (maltodextrin). As compensation for travel expenses, participants were paid fifty dollars ($50.00) after completion of their return testing visit. This study was approved by the FSU Human Subjects Review board. A written informed consent was received from each participant before participating in the study. At their initial visit, participants had a copy of the Informed Consent (Appendix A) read and explained to them by one of the researchers before any paperwork or data was collected. Upon their voluntary agreement to participate, both the participant and the explaining researcher signed and dated the Informed Consent.

Treatment

The study was a stratified, placebo-controlled, double blind study with two groups: BA (SRCarnoSyn ®; NAI, San Marcos, CA) and PL (maltodextrin). Groups were matched based on relative maximal isometric strength during voluntary knee extension on a dynamometer (Biodex
Medical Systems, Shirley, New York), as well as gender. Both groups consumed 2-800 mg pills, 3 times per day for the 28 day supplementation period (±2 days). Participants were given the dosing instructions both verbally and in writing (Appendix B). Sufficient supplement was provided to the participant for the 28 day period (±2 days). Participants were instructed to bring all supplement bottles and remaining pills to their return testing visit to verify compliance; which was determined by >80% of supplement consumption. Participants who did not meet the supplementation threshold were eliminated from the study.

**Measures**

Participants visited the Human Performance & Sports Nutrition Laboratory at Florida State University twice: once for the initial baseline testing session and again for a post-supplementation testing session after 28 days (±2 days). Participants were tested at the same time of day (morning, afternoon, evening) for both their baseline and post-supplementation sessions. The time chosen was based upon their medication schedule which allowed for patients to test during their most functional time frame, commonly referred to as the “on” phase. Both baseline and post-supplementation testing took place at the same time of day during the participants “on” phase to ensure that they were at their highest level of physical functioning for all testing. Participants followed their usual BA/PL supplementation schedule on the re-testing day as well. After completion of the informed consent, laboratory measurements were collected as described below.

**Health History Questionnaire**

A complete health history (Appendix C) from each participant was collected and reviewed before testing began. Their list of current medications and supplements was analyzed to determine
that a BA-containing compound was not being consumed. Participants were asked to clarify or expound on any information that could affect their health and/or safety while participating.

**Dietary Analysis**

Dietary analysis was measured using a 3-day food record (Appendix D) before baseline testing and during the last week of supplementation. Participants were asked to maintain their normal eating patterns and habits, and record them for two weekdays and one weekend day. Instructions and a food record were provided one week prior to initial testing so that participants could bring the record with them to their first session. A second food log was sent home after initial testing for the participant to complete in the week prior to their final visit. FoodWise dietary analysis software (McGraw- Hill, New York, NY) was used for analysis by the same research technician to minimize error. Each participant was also asked to mimic their pre-baseline day of eating prior to post-testing to the best of their ability based off of their dietary food logs.

**Physical Activity Questionnaire**

Participants were asked to list and describe all of their typical physical daily activities, exercise, and physical therapy, in regard to the previous month, at both testing sessions. The questionnaire asked about the frequency, intensity, type, and time of all physical activity, exercise, and therapy sessions (Appendix E).
**Anthropometric Measures**

Height and weight were measured using a physician’s scale (SECA; Hamburg, Germany) and recorded on data collection sheets at each visit (Appendix F). Participants were measured without shoes, in a workout outfit of their choosing.

**Cardiovascular Measures**

All cardiovascular measures were taken before exercise testing begins, after sitting quietly with both feet on the floor for at least five minutes. Systolic and diastolic blood pressures were taken using a standard sphygmomanometer (American Diagnostic Corp., Hauppauge, NY) and stethoscope. Pulse rate were measured manually at the radial artery for 30 seconds and then multiplied by two to obtain a beats-per-minute (bpm) value.

**Body Composition**

Body composition was measured using dual-energy X-ray absorptiometry (DXA; Lunar iDXA, General Electric Company, Fairfield, CT) operated by a certified technician. Participants were asked to refrain from eating at least two hours before the scan. Participants were asked to remove their shoes, all jewelry, and any metal-containing objects, including clothing with zippers, buttons, metal hooks, etc. prior to the scan. Metal-free clothing was provided to the participants for the scan, if necessary. Metal joint replacements were not affected by the scan. Participants then laid supine on the padded DXA table and were instructed move as little as possible until the scan was complete. Scans typically lasted seven to ten minutes, depending on participant body mass.
Maximal Muscular Power (Wingate Test)

Anaerobic capacity was measured using a Wingate test (4) on a plate-loaded and friction-braked Monark Ergomedic 874-E (Monark Exercise AB, Vansbro, Sweden) cycle ergometer. Participants were fitted to the cycle ergometer using the greater trochanter of the femur as a means of measuring proper seat height. They began with an unweighted warmup, pedaling at a self-selected rate for up to 2 minutes. This was done to allow for a necessary warm-up and brief acclimatization to the cycle, without inducing fatigue. Once the participant felt sufficiently warmed up, a weight equivalent to 7.5% of the individual’s total bodyweight (kg) was loaded onto the cycle ergometer’s weight basket. Before the initiation of the test participants were advised that they were to pedal as hard and fast as they could for 30 seconds while remaining seated on the cycle. The participants began to pedal as fast as they could, 3 seconds prior to the test initiation. The 30 second test began when the weight basket was released, applying resistance to the cycle ergometer’s flywheel. Verbal encouragement and time-status were provided to participants throughout the duration of the test. The right pedal of the ergometer was filmed during the test, from the ankle down, to allow for post-testing analysis. Immediately following the 30 second mark, the weight basket was raised and participants were allowed to “cool down” while pedaling. If at any time during the test the participant could no longer continue pedaling, the test ended immediately and was considered incomplete. Testing on moderate or high-risk individuals was not conducted unless a physician was present.

Submaximal VO\textsubscript{2} (YMCA Protocol)

Submaximal VO\textsubscript{2} was determined using the standard YMCA protocol (5) (Appendix G) for a cycle ergometer (Monark Exercise AB, Vansbro, Sweden). Age-predicted max heart rate
(220- age in years) was used to calculate the 85% max heart rate threshold for each participant. Meeting or exceeding the threshold, or any relative or absolute contraindications, resulted in the immediate termination of the test for reasons of both safety and validity (Appendix G). Heart rate was measured each minute using a wireless heart rate monitor (Polar, Kempele, Finland). Blood pressure was measured in the second minute of each stage using a standard sphygmomanometer and stethoscope. After the test was terminated, participants pedaled at a self-selected rate to cool down. Testing on moderate or high-risk individuals was not conducted unless a physician was present.

**Six-Minute Walk Test**

The six-minute walk test was conducted using standard protocol and procedures (41) (Appendix G). Participants were informed that they were to walk as fast as they could for the entire six-minute period without resorting to a “trot” or run. However, they could stop or sit down if needed, although the timer did not stop. A 100-foot straight walking course was set up in an indoor hallway; which allowed for maximum distance coverage with minimal turns. Turning options included: a “tap and pivot” where the participant crossed the 100 ft mark and immediately pivoted; or a “gentle turn” where they crossed the 100ft mark while making a wide turn. These options were provided given the unique gait and balance difficulties of each individual; with the turning option remaining the same for all laps in both testing sessions.

**Muscular Strength, Power, and Fatigue (Biodex)**

The order of performance testing was kept the same for each participant during both laboratory visits. Participants were placed in the upright seated position on a Biodex System 3 (Biodex Medical Systems, Shirley, New York). The seat height and position were adjusted in
order to align the instrument’s axis of rotation with that of the participant’s dominant knee. Isokinetic 60°sec\(^{-1}\) and 180°sec\(^{-1}\) unilateral knee extension/flexion tests were conducted first. Five repetitions of consecutive maximal extension and flexion were performed during each test, with a one minute rest interval between tests. Following the isokinetic tests, a 60° isometric knee extension/flexion test was performed. The test required three maximal extension and flexion exertions against an immovable arm, with 10 second rest periods between attempts. Finally, a 50-repetition unilateral knee extension/flexion fatigue test, with no gravity correction, was performed at an isokinetic speed of 180°sec\(^{-1}\). Continuous verbal encouragement was provided by the research team throughout the duration of all tests. Criterion measures were peak and average torque for each repetition.

**Compliance**

Compliance to the supplement was checked by counting the participants’ remaining pills at their return testing visit. Reminders were sent to participants before the end of the study to make sure they completed their final three-day food logs and physical activity questionnaires. Participants were asked to contact the researchers if they experienced any side effects before their return testing visit. Additionally, they were asked in-person about side effects during their return testing visit.

**Statistical Analysis**

An *a priori* power analysis was performed which revealed a need for approximately 10 participants per group with a power of 0.80, \(\alpha = 0.05\), standard deviation = 10, difference = 20, based off of data from Stout et al. (55). Data was first analyzed using a one-way analysis of variance (ANOVA) to examine possible group differences at baseline. A 2 x 2 repeated
measures ANOVA (RMANOVA) was used to analyze changes in dependent variables over time ([BA x PL]) x ([pre x post]). Post-hoc analysis using a student’s t-test was conducted when a significant value was observed for time x group interaction. Significance was set at (p < 0.05) and all data are reported as means ±SD unless otherwise noted. SPSS Version 21 software (SPSS IBM, New York, U.S.A) was used for all analyses.
RESULTS

Participant Demographics

A total of 25 individuals with PD were recruited to participate, with 24 of them undergoing baseline testing. A total of 20 individuals completed the supplementation and return testing, however only 19 were used in the statistical analysis. Of the five individuals who were dropped after baseline testing: two individuals were dropped after missing a significant number of supplement doses; one individual declined to be re-tested; one individual dropped after baseline testing due to unrelated health complications; and one was excluded from analysis after completing the study because of physical limitations that lead to incomplete physical testing. There were no statistical differences between groups at baseline (Table 1).

Body Composition

Significant group x time differences were observed for body fat percent (BA: pre, 35.2 ± 6.3% vs. post, 35.5 ± 6.4%, +0.3%; PL: pre, 30.2 ± 7.8% vs. 29.3 ± 7.9%, -0.9%; p=0.013) (Figure1), lean mass (BA: pre, 48.9 ± 9.1 kg vs. post, 48.4 ± 9.4 kg, -0.5 kg; PL: pre, 50.2 ± 8.3 kg vs. post, 51.1 ± 8.8 kg, +0.9 kg; p=0.004) (Figure 6), and android fat percent (BA: pre, 39.5 ± 11.1 % vs. post, 40.5 ± 10.9 %, +1.0%; PL: pre, 34.3 ± 11.4 % vs. post, 32.4 ± 12.5 %, -2.1 %; p=0.008) (Figure 7). A significant time effect (p=0.039) as well as a trend (p=0.064) toward group x time significance was observed for fat mass (BA: pre, 26.4 ± 5.5 kg vs. post, 26.4 ± 5.4 kg, 0 kg; PL: pre, 21.8 ± 6.9 kg vs. post, 21.1 ± 6.9 kg, -0.7 kg). No other significant differences were observed (Table 1).
**Dietary Analysis**

A total of seventeen food logs were analyzed (BA: n=8; PL: n=9). The remaining two participants, one from each group, did not return their 3-day food records for analysis. Total kilocalorie (kcal) and macronutrient (carbohydrate, fat, protein) content (g) were analyzed for each day of the food logs. The average intake for each measurement was calculated for the first 3-day food log (Pre) and second 3-day food log (Post) of each participant. A significant group x time difference was observed for total protein intake (BA: pre, 89.1 ± 23.9 g vs. post, 99.6 ± 28.4 g, +10.5 g; PL: pre, 89.8 ± 22.6 g vs. post, 80.0 ± 24.2 g, -9.8 g; p=0.045)(Table 2). No other significant differences were observed (Table 2).

**Physical Activity**

Based upon the participants answers from the Physical Activity Questionnaire, participants were categorized as: sedentary, with no reported exercise, additional physical activity, or physical therapy (BA: n=3, 3 men; PL: n= 3, 2 men, 1 woman); or physically active, with reported regular exercise and/or additional physical activity (BA: n=6, 2 men, 4 women; PL: n=7, 6 men, 1 woman). There were no participants who reported participation in physical therapy alone. This classification was done both to control for individual physical activity and also allowed for sedentary vs. physically active participant comparison. Participants did not change their physical activity or exercise habits from baseline during supplementation, according to self-reported answers. Post-supplementation analysis did not result in a reclassification of any participants from sedentary to physically active or vice versa. Following data analyses, no significant differences were observed between sedentary vs. physically active participants in the supplement group.
Cardiovascular Measurements

No significant effects were observed for resting heart rate (BA: pre, 69 ± 6.2 bpm vs. post, 73 ± 8.8 bpm, + 4 bpm; PL: pre, 74 ± 13.0 bpm vs. post, 76 ± 10.6 bpm, + 2 bpm). Significant time effects were observed for systolic blood pressure (BA: pre, 132 ± 12 mmHg vs. post, 127 ± 10 mmHg, -5 mmHg; PL: pre, 130 ± 10 mmHg vs. post, 124 ± 12 mmHg, -6 mmHg; p=0.05) and diastolic blood pressure (BA: pre, 82 ± 9 mmHg vs. post, 78 ± 8 mmHg, -4 mmHg; PL: pre, 80 ± 6 mmHg vs. post, 75 ± 9 mmHg, -5 mmHg; p=0.036). However, significant group x time differences were not observed.

Maximal Muscular Power (Wingate Test)

Of the 19 participants, only 13 were able to complete the 30-second maximal power test (BA: n=6, 3 men, 3 women; PL: n=7, 6 men, 1 woman) during both testing sessions. No significant time or group x time differences were observed for any measures including: resistance force (kg), total number of pedal revolutions, peak power output (Watts), relative peak power output (Watts/kg), anaerobic fatigue (%), anaerobic capacity (Watts).

Submaximal VO\textsubscript{2} (YMCA Protocol)

Of the 19 participants, only 6 participants (BA: n=3, 2 men, 1 woman; PL: n=3, 3 men) met the protocol requirements necessary to determine submaximal VO\textsubscript{2} (Table 3). However, these groups were too small to conduct any meaningful statistical tests. Two participants from each group were excluded for not completing two full stages of the test (BA: n=2, 1 man, 1 woman; PL: n=2, 1 man, 1 woman) while the remaining 9 were excluded due to self-reported usage of blood pressure medications (BA: n=4, 2 men, 2 women; PL: n=5, 4 men, 1 woman) (5).
Six-Minute Walk Test

All 19 participants were able to successfully complete the six-minute walk test (BA: pre, 436.8 ± 98.4 m vs. post, 473.0 ± 86.8 m, +36.2 m; PL: pre, 461.1 ± 100.1 m vs. post, 499.9 ± 94.2 m, +38.8 m). A significant time effect (p=0.001) was observed, however a group x time effect was not (p=0.892) (Figure5).

Muscular Strength, Power, and Fatigue

Isokinetic 60º/second test

Significant time effects were observed for peak torque during flexion (BA: Δ +3.8 N-M; PL: Δ +5.7 N-M; p=0.023); average peak torque during flexion (BA: Δ +5.4 N-M; PL: Δ +6.0 N-M; p=0.007); relative peak torque during flexion (BA: Δ +5.4%; PL: Δ +8.2%; p=0.028); total work during flexion (BA: Δ +31.1 J; PL: Δ +37.7 J; p=0.014); average power during both extension (BA: Δ +5.5 Watts; PL: Δ +8.6 Watts; p=0.023) and flexion (BA: Δ +8.4 Watts; PL: Δ +7.5 Watts; p=0.000); as well as deceleration time during extension (BA: Δ -44.5 msec; PL: Δ -78.0 sec; p=0.008). Time effects approached significance for peak torque during extension (p=0.072) and average peak torque during extension (p=0.062). No significant group x time effects were observed (Table 3).

Isokinetic 180º/second test

Significant time effects were observed for: peak torque during extension (BA: Δ + 6.5 N-M; PL: Δ +4.3 N-M; p=0.024); average peak torque during extension (BA: Δ +6.0 N-M; PL: Δ +6.0 N-M ;p=0.021); relative peak torque during extension (BA: Δ +7.5% ; PL: Δ + 6.1%; :p=0.034); total work during both extension (BA: Δ +23.5 J; PL: Δ +26.0 J ;p=0.016) and flexion
(BA: Δ +22.1 J; PL: Δ +26.8 J :p=0.001); average power during both extension (BA: Δ +12.8 Watts; PL: Δ +12.0 Watts :p=0.007) and flexion (BA: Δ +12.5 Watts; PL: Δ +11.7 Watts :p=0.001); acceleration time during both extension (BA: Δ -7.8 msec; PL: Δ -14.0 msec :p=0.028) and flexion (BA: Δ -16.7 msec; PL: Δ -24.0 msec :p=0.037); as well as deceleration time during extension (BA: Δ -20.0 msec; PL: Δ -22.0 msec; p=0.037). No significant group x time effects were observed (Table 4).

**Isometric 60° test**

Significant time effects were observed for peak torque (BA: Δ +6.5 N-M; PL: Δ +4.3 N-M;p=0.017) and relative average peak torque (BA: Δ +7.5 %; PL: Δ +6.1%;p=0.045), both during the away phase. The time effect for average peak torque during the away phase approached significance (p=0.063). No significant group x time effects were observed (Table 5).

**Fatigue test - Isokinetic 180°/second**

Significant time effects were observed for: peak torque during extension (BA: Δ +3.9 N-M ; PL: Δ +10.0 ;p=0.006); relative peak torque during extension (BA: Δ +4.7% ; PL: Δ +13.9% ;p=0.007); relative total work during extension (BA: Δ + 3.2%; PL: Δ + 8.6% ;p=0.026); and acceleration time during extension (BA: Δ +4.4 msec ; PL: Δ -13.0 msec; p=0.043). The time effect approached significance for relative peak torque during flexion (p=0.058) and average peak torque during extension (p=0.063). Significant group x time effects were observed for relative total work during flexion (BA: Δ -2.4 % ; PL: Δ +9.1 % ;p=0.018)(Figure 10) and acceleration time during extension (p=0.000) (Figure7). The relative peak torque during flexion
approached a significant group x time effect (p=0.052). No other significant effects were observed (Table 6).

**Reported Side Effects**

There were no reported side effects from any participants in either group, including paresthesia.

### Table 1. Participant demographics at baseline and after 4 weeks of supplementation (N=19)

<table>
<thead>
<tr>
<th></th>
<th>BA n = 9; 5 men, 4 women</th>
<th>PL n = 10; 8 men, 2 women</th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>68.1 ± 9.2</td>
<td>68.0±8.9</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169.1 ± 8.3</td>
<td>171.0 ± 1.1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Body Weight, kg</td>
<td>78.4 ± 11.7</td>
<td>75.3 ± 10.4</td>
<td>0.34</td>
<td>0.16</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.4 ± 3.1</td>
<td>25.9 ± 3.8</td>
<td>0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>Body Fat,%</td>
<td>35.2 ± 6.3</td>
<td>30.2 ± 7.8</td>
<td>0.15</td>
<td>0.013</td>
</tr>
<tr>
<td>FM, kg</td>
<td>26.4 ± 5.5</td>
<td>21.8 ± 6.9</td>
<td>0.039</td>
<td>0.064</td>
</tr>
<tr>
<td>LM, kg</td>
<td>48.9 ± 9.1</td>
<td>50.2 ± 8.3</td>
<td>0.46</td>
<td>0.004</td>
</tr>
<tr>
<td>ASMI, kg/m²</td>
<td>11.7 ± 1.2</td>
<td>11.5 ± 2.0</td>
<td>0.20</td>
<td>0.55</td>
</tr>
<tr>
<td>Android Fat, %</td>
<td>39.5 ± 11.1</td>
<td>34.3 ± 11.4</td>
<td>0.37</td>
<td>0.008</td>
</tr>
<tr>
<td>Gynoid Fat, %</td>
<td>34.9 ± 6.6</td>
<td>31.2 ± 8.4</td>
<td>0.88</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; BMI = body mass index; FM = fat mass, LM = lean mass, ASMI = appendicular skeletal muscle mass index, *a*, post-hoc analysis indicating p<0.05 from pre within the same group

### Table 2. Dietary analysis pre- and post-supplementation (N=17)

<table>
<thead>
<tr>
<th></th>
<th>BA n = 8</th>
<th>PL n = 9</th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total kilocalories</td>
<td>2598 ± 580</td>
<td>2325 ± 639</td>
<td>0.99</td>
<td>0.32</td>
</tr>
<tr>
<td>Total CHO, g</td>
<td>313.6 ± 58.3</td>
<td>292.6 ± 68.6</td>
<td>0.92</td>
<td>0.45</td>
</tr>
</tbody>
</table>
**Table 2 continued.**

<table>
<thead>
<tr>
<th></th>
<th>BA</th>
<th>PL</th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre n=8</td>
<td>Post n=9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total PRO, g</td>
<td>89.1±23.9</td>
<td>99.6±28.4</td>
<td>+10.5</td>
<td>89.8±22.6</td>
</tr>
<tr>
<td>Total Fat, g</td>
<td>109.4±43.4</td>
<td>117.0±45.0</td>
<td>+7.6</td>
<td>93.3±38.2</td>
</tr>
<tr>
<td>CHO, %</td>
<td>49.6±9.6</td>
<td>46.3±9.3</td>
<td>-3.3</td>
<td>50.8±4.8</td>
</tr>
<tr>
<td>PRO, %</td>
<td>13.8±2.6</td>
<td>14.9±3.1</td>
<td>+1.1</td>
<td>15.8±3.4</td>
</tr>
<tr>
<td>Fat, %</td>
<td>36.8±7.9</td>
<td>38.1±7.5</td>
<td>+1.3</td>
<td>35.3±5.0</td>
</tr>
<tr>
<td>Rel PRO, g/kg BW</td>
<td>1.13±0.27</td>
<td>1.29±0.40</td>
<td>+0.16</td>
<td>1.22±0.29</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; CHO = carbohydrate, PRO = protein, *, post-hoc analysis indicating p<0.05 from pre within the same group

**Table 3. Biodex Isokinetic 60º/sec test measures pre- and post-supplementation (N=19)**

<table>
<thead>
<tr>
<th></th>
<th>BA</th>
<th>PL</th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre n=9</td>
<td>Post n=10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Trq. Ex., N-M</td>
<td>96.1±38.7</td>
<td>103.3±50.8</td>
<td>+7.2</td>
<td>93.1±29.7</td>
</tr>
<tr>
<td>Peak Trq Flx, N-M</td>
<td>47.9±15.4</td>
<td>51.7±20.7</td>
<td>+3.8</td>
<td>51.1±15.7</td>
</tr>
<tr>
<td>Avg Peak Trq Ex, N-M</td>
<td>85.4±36.6</td>
<td>93.3±47.2</td>
<td>+6.9</td>
<td>83.3±28.4</td>
</tr>
<tr>
<td>Avg Peak Trq Flx, N-M</td>
<td>41.4±13.8</td>
<td>47.0±19.1</td>
<td>+5.4</td>
<td>44.9±16.3</td>
</tr>
<tr>
<td>Rel Peak Trq Ex, %</td>
<td>119.6±35.3</td>
<td>128.5±51.6</td>
<td>+8.4</td>
<td>124.5±36.2</td>
</tr>
<tr>
<td>Rel Peak Trq Flx, %</td>
<td>60.2±14.5</td>
<td>65.6±24.0</td>
<td>+5.4</td>
<td>67.7±17.4</td>
</tr>
<tr>
<td>Total Work Ex, J</td>
<td>356.4±156.3</td>
<td>376.1±197</td>
<td>+19.7</td>
<td>344.5±108.6</td>
</tr>
<tr>
<td>Total Work Flx, J</td>
<td>178.2±77.0</td>
<td>209.3±90.2</td>
<td>+31.1</td>
<td>188.0±89.3</td>
</tr>
<tr>
<td>Work Fatigue Ex, %</td>
<td>2.3±41.1</td>
<td>-7.9±76.3</td>
<td>-10.2</td>
<td>7.0±17.4</td>
</tr>
<tr>
<td>Work Fatigue Flx, %</td>
<td>-17.7±210.4</td>
<td>33.6±22.6</td>
<td>+51.3</td>
<td>45.6±27.1</td>
</tr>
<tr>
<td>Avg Power Ex, Watts</td>
<td>53.6±21.5</td>
<td>59.1±29.1</td>
<td>+5.5</td>
<td>54.1±20.1</td>
</tr>
<tr>
<td>Avg Power Flx, Watts</td>
<td>21.3±8.7</td>
<td>29.7±12.9</td>
<td>+8.4</td>
<td>24.1±11.8</td>
</tr>
<tr>
<td>Accel. Ex, msec</td>
<td>56.7±24.5</td>
<td>67.8±46.6</td>
<td>+11.1</td>
<td>57.0±19.5</td>
</tr>
</tbody>
</table>
### Table 3 continued.

<table>
<thead>
<tr>
<th></th>
<th>BA n = 9</th>
<th></th>
<th></th>
<th>PL n = 10</th>
<th></th>
<th></th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>∆</td>
<td>Pre</td>
<td>Post</td>
<td>∆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accel. Flx, msec</td>
<td>87.8 ± 26.4</td>
<td>74.4 ± 26.5</td>
<td>-13.4</td>
<td>85.0 ± 29.5</td>
<td>74.0 ± 31.3</td>
<td>-11.0</td>
<td>0.081</td>
<td>0.86</td>
</tr>
<tr>
<td>Decel. Ex, msec</td>
<td>218.9 ± 104.5</td>
<td>174.4 ± 87.3</td>
<td>-44.5</td>
<td>199.0 ± 62.1</td>
<td>121.0 ± 59.2</td>
<td>-78.0</td>
<td>0.008</td>
<td>0.42</td>
</tr>
<tr>
<td>Decel. Flx, msec</td>
<td>313.3 ± 58.3</td>
<td>242.2 ± 67.6</td>
<td>-71.1</td>
<td>645.0 ± 831.1</td>
<td>231.0 ± 73.4</td>
<td>-414.0</td>
<td>0.10</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; Ex = extension, Flx = flexion; Trq = torque, Avg = average, Rel = relative, Accel = acceleration time, Decel = deceleration time.

### Table 4. Biodex Isokinetic 180º/sec test measures pre- and post-supplementation (N=19)

<table>
<thead>
<tr>
<th></th>
<th>BA n = 9</th>
<th></th>
<th></th>
<th>PL n = 10</th>
<th></th>
<th></th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>∆</td>
<td>Pre</td>
<td>Post</td>
<td>∆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Trq Ex., N-M</td>
<td>67.5 ± 29.8</td>
<td>74.0 ± 33.7</td>
<td>+6.5</td>
<td>64.3 ± 22.4</td>
<td>68.6 ± 24.0</td>
<td>+4.3</td>
<td>0.024</td>
<td>0.62</td>
</tr>
<tr>
<td>Peak Trq Fx, N-M</td>
<td>49.4 ± 18.9</td>
<td>50.1 ± 16.3</td>
<td>+0.7</td>
<td>48.5 ± 13.6</td>
<td>48.7 ± 13.5</td>
<td>+0.2</td>
<td>0.85</td>
<td>0.91</td>
</tr>
<tr>
<td>Avg Peak Trq Ex, N-M</td>
<td>61.4 ± 28.3</td>
<td>67.4 ± 30.6</td>
<td>+6.0</td>
<td>56.6 ± 20.2</td>
<td>62.6 ± 22.9</td>
<td>+6.0</td>
<td>0.021</td>
<td>1.00</td>
</tr>
<tr>
<td>Avg Peak Trq Fx, N-M</td>
<td>42.4 ± 15.1</td>
<td>43.1 ± 14.0</td>
<td>+0.7</td>
<td>42.9 ± 12.1</td>
<td>44.0 ± 11.9</td>
<td>+1.1</td>
<td>0.56</td>
<td>0.90</td>
</tr>
<tr>
<td>Rel Peak Trq Ex, %</td>
<td>83.9 ± 26.9</td>
<td>91.4 ± 30.5</td>
<td>+7.5</td>
<td>86.3 ± 29.2</td>
<td>92.4 ± 34.8</td>
<td>+6.1</td>
<td>0.034</td>
<td>0.81</td>
</tr>
<tr>
<td>Rel Peak Trq Fx, %</td>
<td>61.6 ±16.8</td>
<td>63.1 ± 15.3</td>
<td>+1.5</td>
<td>64.4 ± 17.0</td>
<td>65.0 ± 18.5</td>
<td>+0.6</td>
<td>0.70</td>
<td>0.87</td>
</tr>
<tr>
<td>Total Work Ex, J</td>
<td>267.1 ± 132.9</td>
<td>290.6 ± 144.8</td>
<td>+23.5</td>
<td>234.4 ± 88.0</td>
<td>260.4 ± 87.2</td>
<td>+26.0</td>
<td>0.016</td>
<td>0.90</td>
</tr>
<tr>
<td>Total Work Fx, J</td>
<td>133.2 ± 63.7</td>
<td>155.3 ± 58.7</td>
<td>+22.1</td>
<td>118.2 ± 81.9</td>
<td>145.0 ± 74.5</td>
<td>+26.8</td>
<td>0.001</td>
<td>0.72</td>
</tr>
<tr>
<td>Work Fatigue Ex, %</td>
<td>10.0 ± 13.6</td>
<td>10.4 ± 18.4</td>
<td>+0.4</td>
<td>7.8 ± 14.5</td>
<td>10.3 ± 15.3</td>
<td>+2.5</td>
<td>0.73</td>
<td>0.81</td>
</tr>
<tr>
<td>Work Fatigue Fx, %</td>
<td>4.0 ± 81.4</td>
<td>11.5 ± 17.0</td>
<td>+7.5</td>
<td>-8.0 ± 78.4</td>
<td>-3.1 ± 38.5</td>
<td>+4.9</td>
<td>0.73</td>
<td>0.94</td>
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<tr>
<td>Avg Power Ex, Watts</td>
<td>97.8 ± 47.4</td>
<td>110.6 ± 52.9</td>
<td>+12.8</td>
<td>87.4 ± 38.9</td>
<td>99.4 ± 39.7</td>
<td>+12.0</td>
<td>0.007</td>
<td>0.92</td>
</tr>
<tr>
<td>Avg Power Fx, Watts</td>
<td>42.1 ± 21.5</td>
<td>54.6 ± 21.1</td>
<td>+12.5</td>
<td>38.5 ± 21.8</td>
<td>50.2 ± 26.9</td>
<td>+11.7</td>
<td>0.001</td>
<td>0.89</td>
</tr>
<tr>
<td>Accel. Ex, msec</td>
<td>81.1 ± 27.6</td>
<td>73.3 ± 25.0</td>
<td>-7.8</td>
<td>98.0 ± 39.4</td>
<td>84.0 ± 32.0</td>
<td>-14.0</td>
<td>0.028</td>
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Table 4 continued.

<table>
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<tr>
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<th>BA</th>
<th>PL</th>
<th>Time</th>
<th>Time x Group</th>
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<tr>
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<td>n=9</td>
<td>n=10</td>
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<td>Accel. Flx, msec</td>
<td></td>
<td></td>
<td>0.037</td>
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</tr>
<tr>
<td>Values are mean ± SD. BA, beta alanine; PL, placebo; Ex = extension, Flx = flexion; Trq = torque, Avg = average, Rel = relative, Accel = acceleration time, Decel = deceleration time</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>

Table 5. Biodex Isometric 60° test measures pre- and post-supplementation (N=19)

<table>
<thead>
<tr>
<th></th>
<th>BA</th>
<th>PL</th>
<th>Time</th>
<th>Time x Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=9</td>
<td>n=10</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Peak Trq Away, N-M</td>
<td>67.5 ± 29.8</td>
<td>74.0 ± 33.7</td>
<td>+6.5</td>
<td>0.024</td>
</tr>
<tr>
<td>Peak Trq Twd, N-M</td>
<td>49.4 ± 18.9</td>
<td>50.1 ± 16.3</td>
<td>+0.7</td>
<td>0.85</td>
</tr>
<tr>
<td>Avg Peak Trq Away,N-M</td>
<td>61.4 ± 28.3</td>
<td>67.4 ± 30.6</td>
<td>+6.0</td>
<td>0.021</td>
</tr>
<tr>
<td>Avg Peak Trq Twd, N-M</td>
<td>42.4 ± 15.1</td>
<td>43.1 ± 14.0</td>
<td>+0.7</td>
<td>0.56</td>
</tr>
<tr>
<td>Rel Peak Trq Away, %</td>
<td>83.9 ± 26.9</td>
<td>91.4 ± 30.5</td>
<td>+7.5</td>
<td>0.034</td>
</tr>
<tr>
<td>Rel Peak Trq Twd, %</td>
<td>61.6 ± 16.8</td>
<td>63.1 ± 15.3</td>
<td>+1.5</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; Ex = extension, Flx = flexion; Trq = torque, Avg = average, Rel = relative,

Table 6. Biodex Fatigue (Isokinetic 180°/sec) test measures pre- and post-supplementation (N=19)

<table>
<thead>
<tr>
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<th>BA</th>
<th>PL</th>
<th>Time</th>
<th>Time x Group</th>
</tr>
</thead>
<tbody>
<tr>
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<td>n=9</td>
<td>n=10</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Peak Trq Ex., N-M</td>
<td>58.9 ± 27.6</td>
<td>62.8 ± 28.0</td>
<td>+3.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Peak Trq Flx, N-M</td>
<td>51.8 ± 14.7</td>
<td>51.6 ± 15.6</td>
<td>-0.2</td>
<td>0.15</td>
</tr>
<tr>
<td>Avg Peak Trq Ex, N-M</td>
<td>37.9 ± 16.6</td>
<td>40.2 ± 19.2</td>
<td>+2.3</td>
<td>0.063</td>
</tr>
<tr>
<td>Avg Peak Trq Flx, N-M</td>
<td>35.9 ± 9.7</td>
<td>36.7 ± 11.0</td>
<td>+0.8</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; Ex = extension, Flx = flexion; Trq = torque, Avg = average, Rel = relative,
Table 6 continued.

<table>
<thead>
<tr>
<th></th>
<th>BA</th>
<th></th>
<th>PL</th>
<th></th>
<th>Time p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 9</td>
<td></td>
<td>n = 10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rel Peak Trq Ex, %</td>
<td>73.1 ± 26.0</td>
<td>77.8 ± 25.7</td>
<td>+4.7</td>
<td>69.6 ± 32.5</td>
<td>83.5 ± 36.1</td>
<td>+13.9</td>
</tr>
<tr>
<td>Rel Peak Trq Flx, %</td>
<td>65.7 ± 13.4</td>
<td>65.6 ± 16.4</td>
<td>-0.1</td>
<td>66.6 ± 19.7</td>
<td>76.6 ± 24.7</td>
<td>+10.0</td>
</tr>
<tr>
<td>Rel Total Work Ex, %</td>
<td>52.8 ±22.6</td>
<td>56.0 ± 21.5</td>
<td>+3.2</td>
<td>50.6 ± 25.6</td>
<td>59.2 ± 27.5</td>
<td>+8.6</td>
</tr>
<tr>
<td>Rel Total Work Flx, %</td>
<td>57.6 ± 15.4</td>
<td>55.2 ± 13.6</td>
<td>-2.4</td>
<td>52.9 ±22.4</td>
<td>62.0 ± 21.6</td>
<td>+9.1</td>
</tr>
<tr>
<td>Total Work Ex, J</td>
<td>1314.5 ± 652.1</td>
<td>1355.0 ± 743.6</td>
<td>+40.5</td>
<td>1239.7 ± 636.9</td>
<td>1381.0 ± 621.8</td>
<td>+141.3</td>
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<tr>
<td>Total Work Flx, J</td>
<td>1452.9 ± 471.5</td>
<td>1432.8 ± 450.6</td>
<td>-19.9</td>
<td>1290.1 ± 539.9</td>
<td>1450.7 ± 446.7</td>
<td>+160.6</td>
</tr>
<tr>
<td>Work Fatigue Ex, %</td>
<td>48.4 ± 15.4</td>
<td>50.7 ± 10.5</td>
<td>+2.3</td>
<td>37.5 ± 27.9</td>
<td>44.5 ± 13.9</td>
<td>+7.0</td>
</tr>
<tr>
<td>Work Fatigue Flx, %</td>
<td>46.9 ± 8.8</td>
<td>41.6 ± 6.2</td>
<td>-5.3</td>
<td>32.3 ± 32.7</td>
<td>38.6 ± 18.8</td>
<td>+6.3</td>
</tr>
<tr>
<td>Avg Power Ex, Watts</td>
<td>49.6 ± 24.7</td>
<td>52.6 ± 28.3</td>
<td>+3.0</td>
<td>47.5 ± 25.9</td>
<td>52.6 ± 25.6</td>
<td>+5.1</td>
</tr>
<tr>
<td>Avg Power Flx, Watts</td>
<td>50.0 ± 16.0</td>
<td>51.3 ± 17.4</td>
<td>+1.3</td>
<td>46.6 ± 19.7</td>
<td>52.0 ± 17.8</td>
<td>+5.4</td>
</tr>
<tr>
<td>Accel. Ex, msec</td>
<td>67.8 ± 19.9</td>
<td>72.2 ± 23.9</td>
<td>+4.4</td>
<td>85.0 ± 22.2</td>
<td>72.0 ± 20.4</td>
<td>-13.0</td>
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<tr>
<td>Accel. Flx, msec</td>
<td>110.0 ± 47.7</td>
<td>122.2 ± 46.3</td>
<td>+12.2</td>
<td>112.0 ± 46.6</td>
<td>96.0 ± 29.5</td>
<td>-16.0</td>
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<tr>
<td>Decel. Ex, msec</td>
<td>124.4 ± 15.9</td>
<td>128.9 ± 23.7</td>
<td>+4.5</td>
<td>127.0 ± 23.6</td>
<td>119.0 ± 24.7</td>
<td>-8.0</td>
</tr>
<tr>
<td>Decel. Flx, msec</td>
<td>153.3 ± 39.4</td>
<td>151.1 ± 42.6</td>
<td>-2.2</td>
<td>136.0 ± 15.8</td>
<td>128.0 ± 23.9</td>
<td>-8.0</td>
</tr>
</tbody>
</table>

Values are mean ± SD. BA, beta alanine; PL, placebo; Ex = extension, Flx = flexion; Trq = torque, Avg = average, Rel = relative, Accel = acceleration time, Decel = deceleration time, * post-hoc analysis indicating p<0.05 from pre within the same group.
Figure 5. A) Total body fat at baseline (pre) and after 4 weeks of supplementation (post) with BA or PL. Data are individual participants. B) Change in total body fat after 4 weeks of supplementation with BA or PL. Data are individual participants.
Figure 6. A) Total lean body mass (LBM) for at baseline (pre) and after 4 weeks of supplementation (post) with BA or PL. Data are individual participants. B) Change in lean body mass (LBM) after 4 weeks of supplementation with BA or PL. Data are individual participants.
Figure 7. A) Total android fat at baseline (pre) and after 4 weeks of supplementation (post) with BA or PL. Data are individual participants. B) Change in android fat after 4 weeks of supplementation with BA or PL. Data are individual participants.
Figure 8. Distance covered during six-minute walk test at baseline (pre) and after 4 weeks of supplementation (post). Data are individual participants.

A)

Figure 9. A) Work performed relative to bodyweight during flexion in the fatigue test at baseline (pre) and after 4 weeks of supplementation (post). Data are individual participants. B) Change in work performed relative to bodyweight during flexion in the fatigue test after 4 weeks of supplementation. Data are individual participants.
Figure 9 continued.

Figure 10. A) Acceleration time during extension in the fatigue test at baseline (pre) and after 4 weeks of supplementation (post). Data are individual participants. B) Change in acceleration time during extension during the fatigue test after 4 weeks of supplementation. Data are individual participants.
Figure 10 continued.
DISCUSSION

The main findings of this pilot study were that 4 weeks of BA supplementation was not sufficient to improve body composition, submaximal VO2, and muscular performance more than PL in older adults diagnosed with PD. These findings do not support the hypotheses that BA would improve such measures of physical performance and body composition, while PL would have no change. The complex and still relatively-unknown nature of PD, as well as the absence of a physical activity intervention were likely contributing factors to the lack of significant findings.

Body Composition

BA was not shown to improve any measures of body composition to a greater degree than PL in the present study. This finding is supported by some research (28, 58) but is ultimately in contrast to the majority of studies (31, 33, 36, 67), including those of elderly adults(19, 55). In fact, total body fat percent, lean mass, and android fat percent, statistically significant favorable changes were seen in PL but not BA. Examination of the individual results and changes for these measures (Figures 1, 2 and 3) reveals that the response amongst individuals in both groups varied widely greatly. This may also be the result of some participants being a “responder” vs. “non-responder” to BA, which is seen with other nutritional supplements such as creatine (59). However, the lack of an exercise intervention in conjunction with supplementation in the study is most likely the reason significant improvements were not observed. Despite the statistical significance of these findings, the “real-world” magnitude of these changes does not seem to be of major concern. DXA has been repeatedly validated as a reliable measurement of body composition (6, 40, 56) even in the elderly (44). Use of DXA rather than the gold-standard
hydrostatic weighing method however, can still result in an error percentage of 3.8% for body fat alone (40). The changes observed for body fat (BA: +0.3%; PL: -0.9%) easily fall within this error range. Additionally, the hydration status of an individual can greatly affect the analysis made by DXA. Insufficient hydration can result in an overestimation of fat mass and an underestimation of lean mass, with the opposite being true for hyperhydration. The small changes seen in total fat and android fat percent as well as lean mass (Table 1) may easily fall within the inherent variability in body composition measurements made using DXA. More research on the possible effects of BA supplementation on body composition is warranted before conclusions can be made, especially in a PD patient population. The most applicable research conducted in the elderly reported favorable changes in body composition, however both instances incorporated an exercise protocol with BA supplementation which this study did not do.

**Dietary Analysis**

The significant difference between the group’s protein consumption was interesting, as it was counter to the significant changes seen in body composition and physical performance. It is well known that an increase in protein consumption is associated with improvements in lean mass, however the results of this study do not agree. The BA group had a significant decrease in lean mass despite a significant increase in protein consumption while PL had a significant increase in lean mass despite no change in protein consumption. These results are contrary to the established relationship between protein consumption and lean mass and their cause be fully determined. Evaluation of individual protein consumption showed relatively minimal change in most participants intake. However, there were three participants in both groups who had an average increase or decrease in protein consumption of ≥30 g. Surprisingly, when normalized to
bodyweight, nearly all of the participants were consuming more relative protein (BA: pre, 1.13 ± 0.27 g/kg vs. post, 1.29 ± 0.40 g/kg, +0.16 g/kg; PL: pre, 1.22 ± 0.29 g/kg vs. post, 1.10 ± 0.31, -0.12 g/kg) than the recommended 0.8 g per kg of bodyweight both pre- and post-supplementation (63, 72). A recent review suggested a range of 1.2-1.5 g/kg for healthy elderly adults (37), however the necessary amount for elderly PD patients may be even greater and further research is warranted. The group average intake values are less than the 1.6-2.0 g/kg recommended for athletes to maintain and build lean mass during training (39), however the lack of physical activity intervention in this study leads us to conclude that the loss in lean mass is likely a variation in DXA analysis than any true change.

**Maximal Muscular Power (Wingate Test)**

The lack of significant findings from the Wingate 30-second maximal anaerobic power test may be due in part to the physical requirements of the test (a true, all-out maximal physical effort) and the diminished physical functioning of the research participants, which may be due to their age, PD diagnosis, or a combination thereof. Previous research using the Wingate test in elderly sedentary, but otherwise healthy adults did not report issues with administration of the test (18). We have found no precedent in the literature for exercise performance testing being performed in a PD patient population, so the usefulness of the Wingate test in this group cannot be unequivocally determined. Measures of physical functioning have previously been shown to be directly related to Wingate performance in elderly adults (50). As such it is most likely that the decrease in physical functioning associated with PD, aging, and perhaps physical activity are why our participants struggled with this test. The results of the present study suggest that the standard requirements of the Wingate test may be too physically demanding for this particular population (4, 30). Again, the lack of previous research in PD patients looking at these
parameters made it difficult to determine which tests would be feasible prior to actually attempting them. While the standard resistance applied during a Wingate test is 7.5% of the participant’s weight (kg), it is possible that a scaled down resistance may be needed for a special population like PD patients. It may be ideal to determine resistance based on lean mass, rather than bodyweight. However, the ideal resistance for the elderly, sedentary, obese, or a combination thereof have yet to be decisively concluded (64). It is likely that 7.5% of total bodyweight is too great of a resistance, given that so many of our participants were unable to cycle for the entire 30 second duration. Many of the participants who did complete the test struggled to continue pedaling the entire duration, with some getting as few as 1 or 2 full revolutions in a 5-second time period of the test. The upright design of the standard cycle ergometer also seemed to pose some difficulty for the participants. It is possible that there was a sacrifice in power output because of the potentially unstable nature of the ergometer’s design, despite researchers being on either side of the ergometer during testing for safety. It was suggested by several participants that the use of a (modified) recumbent cycle ergometer should be considered for future research studies.

Submaximal VO\textsubscript{2} (YMCA Protocol)

The insufficient number of valid results available to make an analysis of submaximal oxygen consumption in this study was unfortunate. As with the Wingate test, use of a cycle ergometer for this test proved to be more difficult than expected for our participants. With most of the tests lasting 6-9 minutes, it may be advisable to use alternate testing measures like peak VO\textsubscript{2} or substitute a ramp-style protocol on a treadmill in future studies (20).
Six-Minute Walk Test

The absence of changes from pre- to post-supplementation suggests that the six-minute walk test may have too great a variability to measure any possible changes in the participants’ functional endurance. Nearly all participants increased the total distance covered from pre to post (Figure 8), which suggests that unique individual factors like intrinsic motivation and/or external influence (e.g. participating in the study) may be important for improving physical capacity in PD patients regardless of supplementation. Recent work suggests the use of a predetermined distance in combination with the Borg Rate of Perceived Exertion (RPE) scale rather than predetermined time, like the six minute walk test, alone. Their results showed the combination accurately represented changes in the fatigability of healthy older adults (49). Similarly, a study of healthy older men found that the six minute walk test alone was not able to detect improvements in cardiorespiratory fitness after 24 weeks of training (47). This is important because cardiorespiratory fitness, as it relates to physical functioning and fatigue in this study, ought to still be detectable by a functional test. The growing evidence that the six minute walk test may not be the best measure of functional endurance in older adults likely means that its usefulness for PD patients is less than previously thought, especially since it was not combined with an exercise intervention in this study. Future studies should consider the use of an absolute distance for time to measure functional changes in fatigue for PD patients.

Muscular Strength, Power, and Fatigue (Biodex)

With numerous time effects observed throughout the four Biodex tests, a learning effect was likely the source- given the “unusual” manner of the tests and lack of participant familiarity with performing the tests prior to the immediate pre-testing instructions. Use of a pre-testing
familiarity sessions would be ideal to ameliorate learning effects in future studies. The significant group x time effects observed for relative total work during flexion and acceleration during extension of the fatigue test however, cannot be fully explained. The individual participant results and changes from both tests (Figures 5 & 6) better illustrate the findings of this study than group results (Table 6), but do not give clear answers as to why the changes occurred. The change seen in relative total work during flexion appears to follow the group results (Figure 9), but it is unclear why these improvements were seen in PL and not BA. The significance observed for acceleration during extension may be the result of three individuals in both groups who had favorable decreases ≥30 msec (Figure 10). In tests of muscle function in the elderly, no improvements were seen in either test (30 second timed-stands and timed-up-and-go) after 12 weeks of BA supplementation with exercise (19). While these tests were purely measures of function, and not as specific as those conducted on the dynamometer, they do support the idea that the impact of BA supplementation is not likely to be determined through the absolute measurement of one specific factor in one specific instance. Rather, it is more likely a combination of slight improvements in many areas like fatigue/endurance, muscular function (power, strength, neuromuscular control), and other factors which will collectively yield improvements in physical functioning and quality of life for PD patients. So while the exact cause(s) for this cannot be fully elucidated, these findings do emphasize the importance of more research in this area to explore these findings and determine the true mechanism at work.

Side Effects

There were no side effects reported in either group in the present study. With PD patients already experiencing numerous serious side effects from both the disease and the medications used to control its most debilitating symptoms; not contributing to this burden was just as
important as attempting to improve physical measures. The use of a sustained-release BA supplement appears to prevent the paresthesia commonly associated with its use (9). This is an important contribution for future research with this population and potentially for other similar neurodegenerative-type conditions. The lack of reported side effects when using a sustained-release BA supplement is confirmed by several studies, including those with elderly populations (19, 55).

Limitations

As a pilot study, this research was subject to several limitations. No familiarization session prior to baseline testing was a limitation to this study. Given the frequency of significant time effects throughout the results, future studies need to allow for a longer data collection period, with a minimum of three laboratory visits (familiarization, baseline, and post-intervention). The use of an absolute BA dose (4.8 g/day) may have been a limitation. Recent research has suggested that BA dosing should be based on an individual’s lean or total bodyweight with the threshold set at a minimum of 0.018 g/kg BW/day of BA (52). Supplementation with an absolute, rather than relative to bodyweight or lean mass dose may result in individuals with a larger body mass having lower intramuscular carnosine content than smaller individuals. However, in our study the BA group had an average BA consumption of 0.0625 ± 0.0091 g/kg BW/day vs. PL 0.0651 ± 0.0107 g/kg BW/day, with a range of 0.0497-0.0719 g/kg BW/day (BA) vs. 0.0547-0.0915 g/kg BW/day (PL). These values are well above the minimum recommendation of 18 mg/kg BW/day (52) as mentioned above. Thus it is likely that our participants, regardless of bodyweight received a sufficient daily dose of BA for efficacious results to occur. Without prior research using both a PD population (or similar) and physical testing protocols to draw upon, assumptions and approximations about the participants’ physical abilities had to be made. Even
with the help of an experienced neurologist, the participants’ ability to perform all of the study measures was unknown until testing commenced. Use of cycle ergometers for physical testing in the future with this population would not be considered ideal; based on the difficulty our participants experienced in both the maximal 30-second anaerobic and submaximal 6-9 minute aerobic tests. Rapid fatigue of the legs while cycling and difficulty with the fixed path of pedal rotation were commonly cited as the cause of difficulty or physical failure by participants during both tests. Future studies should examine whether treadmill protocols are more easily tolerated by this population, with the possible use of a weight-bearing harness for safety. This study also did not examine biological markers like blood or intramuscular chemistry, which would be useful for analyzing proton production in PD individuals and their buffering capacity. The inclusion of individuals diagnosed with and/or taking medication for high blood pressure, diabetes, and obesity was another limitation, but almost unavoidable given the highly specific nature of our target population and relatively small geographic pool to draw from. With consideration of the typical PD population, it may be advisable to still include these individuals in the future since they may be a representative cross-section of the PD population as a whole. However, consideration should be given to how these conditions/medications could affect test participation and results. Finally, incorporation of a physical activity/exercise intervention with BA supplementation is paramount for any future research in this area. Nearly all of the available literature on BA supplementation incorporated regular training or a new exercise protocol as part of the study. Time and again, the benefits of BA supplementation are seen only, or to a greater degree, in BA + exercise groups than BA or exercise alone.
**Conclusions**

In conclusion, this study was the first to evaluate the effects of BA in the clinical population of PD patients. Moreover, our evaluation of physical functioning and capacity through exercise testing in PD patients is novel. It was concluded that our hypotheses were not supported because four weeks of BA supplementation alone were not sufficient to significantly improve strength, power, and fatigue in older adults diagnosed with PD more than PL. However the magnitude of change in the BA group for the six minute walk test, acceleration during fatigue test extension, and peak/average peak torque generated during isometric and isokinetic knee extension/flexion, still suggests that there may be potential for BA to help PD patients; however, more work is required before a definitive statement can be made. In particular, the combination of supplementation + exercise or physical training for a longer duration would be recommended for future research into the efficacy of BA use in PD patients.
APPENDIX A

IRB APPROVAL LETTER

Office of the Vice President For Research
Human Subjects Committee
Tallahassee, Florida 32306-2742
(850) 644-8673 · FAX (850) 644-4392

APPROVAL MEMORANDUM

Date: 01/11/2014

To:

Address:

Dept.:

From:

Re: Use of Human Subjects in Research
A Double-Blind Placebo-Controlled Study of the Effect of Beta-Alanine, a Non-essential Amino Acid on Neurologic Motoric Function and Quality of Life in Parkinson’s Disease

The application that you submitted to this office in regard to the use of human subjects in the research proposal referenced above has been reviewed by the Human Subjects Committee at its meeting on 03/13/2013. Your project was approved by the Committee.

The Human Subjects Committee has not evaluated your proposal for scientific merit, except to weigh the risk to the human participants and the aspects of the proposal related to potential risk and benefit. This approval does not replace any departmental or other approvals which may be required.

If you submitted a proposed consent form with your application, the approved stamped consent form is attached to this approval notice. Only the stamped version of the consent form may be used in recruiting research subjects.

If the project has not been completed by 03/12/2014 you must request a renewal of approval for continuation of the project. As a courtesy, a renewal notice will be sent to you prior to your expiration date; however, it is your responsibility as the Principal Investigator to timely request renewal of your approval from the Committee.

You are advised that any change in protocol for this project must be reviewed and approved by the Committee prior to implementation of the proposed change in the protocol. A protocol change/amendment form is required to be submitted for approval by the Committee. In addition, federal regulations require that the Principal Investigator promptly report, in writing, any unanticipated problems or adverse events involving risks to research subjects or others.

By copy of this memorandum, the chairman of your department and/or your major professor is reminded that he/she is responsible for being informed concerning research projects involving human subjects in the department, and should review protocols as often as needed to insure that the project is being conducted in compliance with our institution and with DHHS regulations.

This institution has an Assurance on file with the Office for Human Research Protection. The Assurance Number is IRB00000446.

CC:

HSC No. 2U15-10144
APPENDIX B

FSU HUMAN SUBJECTS COMMITTEE APPROVED INFORMED CONSENT

Consent for Research

Title of Project: A Double-Blind Placebo-Controlled Study of the Effect of Beta-Alanine, a Non-essential Amino Acid on Neurologic Motoric Function and Quality of Life in Parkinson's Disease

Principal Investigator: John Gianinni M.D
Co-Principal Investigator: Michael Ormsbee PhD.

Other Investigators: Charles G. Malland M.D, Elizabeth Coughlin, Brittany DiFabio, Arielle Bivin, Donya Salmasinia M.S

Participant's Printed Name: ____________________________

This is a research study. Research studies include only people who want to take part. This form gives you information about this research, which will be discussed with you. It may contain words or procedures that you do not understand. Please ask questions about anything that is unclear to you. Discuss it with your family and friends and take your time to make your decision.

1. Purpose of the Research
You are being offered the opportunity to take part in this research because you have been diagnosed with Parkinson’s Disease. This research is being undertaken to determine if dietary supplementation with amino acid, Beta-alanine will increase your strength and muscle performance. Beta-alanine (BA) is a non-essential amino acid that has been already studied in athletes and healthy elderly individuals. Non-essential amino acid is one that is made both by the body and can be ingested. Beta-alanine demonstrates a positive effect on motor and exercise performance and endurance in both trained and non-trained individuals by substantially increasing muscle carnosine levels that are otherwise produced in low concentrations in the human body. Carnosine probably works by improving the force of the contraction of your muscles by several different mechanisms. To date, we are aware of no significant side effects from this drug. Muscle carnosine levels are lower in women, decline with age, and is probably lower in vegetarians. Potentially administration of this compound may contribute to the reduction of fatigue by enhancing strength in disorders such as Parkinson’s Disease.

The purpose of this research may benefit you and others by providing information on its effect on muscle performance. We anticipate 20 participants will be involved in the study at the Balance Disorders Clinic and the Florida State University Human Performance Laboratory.

2. Procedures to Be Followed
The following tests will be administered followed by obtained permission from your private doctor.

- You will answer a questionnaire concerning some of your activities of daily living, your overall mood and the degree to which you feel fatigued.
- You will be examined using a standard examination for patients with suspected or proven Parkinson’s Disease.
- We will give you a series of questionnaires as listed below. These will be administered at the beginning and the end of the study.
  a. Schwab and England Activities of Daily Living

b. Short Form 36 Health Survey
   a. Modified Fatigue Impact Scale (assesses the level of fatigue impacting your life)
   d. Beck’s Depression Inventory to assess any degree of depression
   - Next, objective motor performance will be evaluated at the Human Performance Laboratory, Florida State University.
   - Your height and weight will be measured.
   - You will be asked to change into clothing that is free of metal and/or hard plastic
     (buttons, zippers, snaps, etc.) and asked to remove all metal from the body (jewelry, eyeglasses, hair accessories, etc). All variables will be placed in a secure location.
   - The composition of your total body composition of the total body will be measured
     non-invasively via the use of a scanner called DXA. (This is the same system that
     your doctors use routinely to measure degrees of osteoporosis). The scan will take
     approximately 10 minutes to complete. From the scan, lean mass (kg), fat free mass
     (kg), percent fat and bone density will be determined.
   - Next, Muscle Performance Testing-After completing the 5 minute warm up cycle, I
     will have my lower body muscle performance measured by the Wingate anaerobic
     power test and strength determined using the Biodex System 3 (Biodex Medical
     Systems, Shirley, New York) exercise dynamometer performing an isokinetic and
     isometric strength.
   - Submaximal Aerobic Fitness Treadmill Test (VO2)-Your aerobic fitness will then be
     assessed using a motorized treadmill (WOODWAY USA, Inc., Waukesha, WI,
     USA) with an affixed safety harness (PneuThera Technologies, Sandpoint, ID.
     USA). Prior to beginning exercise, the testing protocol will be described to you in
     detail. Your maximal aerobic capacity (VO2max) will be calculated based on the
     results of a submaximal walking test following the American College of Sports
     Medicine (ACSM) guidelines (2010). The difficulty of the test will increase
     progressively, dependent upon your heart rate response.
   - If you are unable to perform testing on the treadmill, your aerobic capacity may be
     analyzed through Submaximal Aerobic Fitness Bicycle Ergometer Test (VO2). Prior to
     beginning exercise, the testing protocol will be described to you in detail. Your
     submaximal aerobic capacity will be measured using a cycle ergometer following the
     multi-stage YMCA protocol (Glyngring 1989). You will begin exercising at a low
     resistance, which will increase after three minutes by an amount dependent upon your
     heart rate. Additional three-minute stages of cycling at a higher resistance may be
     required dependent upon your heart rate response. You will maintain a cycling
     cadence of 50 RPM. During the test you will wear a heart rate monitor around your
     chest. This will be done to measure your heart rate.
   - Prior to administration of the supplements, you will be asked to keep a record of your
     food intake for two weekdays and one weekend day prior to both testing (before and
     after supplementation). You will be asked to maintain normal eating patterns and
habits. It is important to note that you will be asked to replicate pre-baseline day of eating prior to visiting the laboratory at Florida State University to the best of your ability based on dietary food logs.

- Following these examinations, you will be administered either BA or an identical placebo and will be asked to consume 4.8 grams daily split in 3 doses per day (3 doses of 1600 mg) for 4-weeks.
- Half way through the investigational period, you will be contacted by a research investigator to verify supplement compliance. You will also be asked to turn in your supplement containers at the end of 4-weeks so the investigators can count any remaining pills to determine compliance.
- After one month, you will be asked to return to the laboratory and the tests performed at baseline will be repeated.
- Initial and final clinical testing will be performed either at the Human Performance Laboratory or at the Balance Disorder Clinic.
- Throughout the study, one or more co-investigators will be available should any inquiries arise via phone or in person contact.

3. **Discomforts and Risks**

Please understand there is minimal risk involved with any test procedure. Beta alanine is a nutritional supplement and is known to be a safe amino acid that is normally made in the human body and has shown to improve muscle strength and reduce fatigue in athletes and the elderly. There is very minimal risk in doing this study.

The only known side effect of this nutritional supplement may be temporary paresthesia (tingling of the extremities). The severity of paresthesia episodes is dose-dependent, but generally lasts 60 minutes after ingestion (Curuso, et al. 2012). There have been no reports of sustained or chronic paresthesia as a result of beta alanine supplementation/consumption. Please note that over-the-counter supplement products as well as research study dosages have generally ranged from 3.2-6.4g/day of beta alanine supplement. This study intends to supplement with 3-1600mg dosages spread throughout the day, totaling 4800mg well within the normal dose range.

The neurologic examination Dr. Mainland and his colleagues will administer is no different from the standard examination you receive each time you visit a neurologist’s clinic. The tests of power administered are tests routinely administered to this age group, a co-investigator will be in immediate proximity to the individual while being tested. The composition of the total body will be measured via the use of a scanner called DXA. Very low doses of radiation are used in this procedure; however, this test is non-invasive. Testing will be completed according to the manufacturer’s instructions and specifications by a certified X-ray technician. During these tests there is a minimum risk of falling and/or muscle strain. Before testing permission will be obtained by your private medical doctor asserting that you are capable of participating.

4. **Possible Benefits:**

a. Possible benefits to the participant:
You may benefit in taking part in this research study in that you will have a chance to learn about their body composition (fat mass, bone mass, and lean mass), and emotional state. There will be no cost to the tests administered to you and all tests will be available to your attending physician if they so desire, at no cost.

b. Possible benefits to others: This research could potentially provide methods to improve motor functions and fatigue reduction in patients suffering from motor diseases such as Parkinson’s Disease. It will provide grounds for further research, which could lead to implementation of treatment methods that may improve functional and quality of life in patients with Parkinson’s Disease.

You may decline to participate in this research, if you so choose. If you do, your routine care at neurology clinic will be maintained as always. If you choose to participate, you may stop at any time during the test sequence. We anticipate the testing will take approximately 1 hour. During that time you may choose to take rest periods and/or ask questions of the examiners as you would like.

5. Other Options that Could be Used Instead of this Research: You do not have to take part in this research study. Participation in this study is not an alternative to medical care. Participation in this study would be in addition to your normal medical care. To our knowledge, there is no other institutional study examining the effect of Beta-alanine supplements in Parkinson’s Disease.

6. Time Duration of the Procedures and Study: Participation in this study requires two visits of approximately an hour each prior to and after a 4-week supplementation period.

7. Statement of Confidentiality:
   a. Privacy and confidentiality measures

Any information during this study regarding your performance or anything that could identify you will be kept strictly confidential to the extent allowed by law. The data will be encrypted and kept in a password-protected computer within the Balance Disorders Clinic that is only accessible to the principle investigator and co-investigators. There will be no identifiable information released or made available to anyone other than the principle or co-investigators. The de-identified information obtained in this study may be published in professional journals or presented at professional meetings, but your name will not be used, nor will any personally identifiable information be used. You are free to withdraw permission for the use of sharing of health information at any time. If you so choose to do so, you must do this in writing and you will write Dr. Charles G. Maitland at the Balance Disorders Clinic at 1401 Centerdale Road, Suite 510, Tallahassee, FL 32308 to let us know you are withdrawing from the research study. The aforementioned investigators, along with the FSU Institutional Review Board (IRB), a group of people who review the research study and protect your rights, and Office for Human Research Protections (OHRP), a group which reviews research to ensure research is being done safely and correctly, have the right to
inspect all records. Material gathered in the investigation will be destroyed after publication of the study results or within five (5) years of the end of the study. In the event of any publication or presentation resulting from the research, no identifiable information will be shared.

7b. The use of private health information:

Health information about you will be collected if you choose to be part of this research study. Health information is protected by law as explained in the Balance Disorders Clinic Privacy Notice. If you have not received this notice, please request a copy from the researcher. At the Balance Disorders Clinic your information will only be used or shared as explained and authorized in this consent form or when required by law. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information and may share it without your permission. To participate in this research you must allow the research team to use your health information. If you do not want us to use your protected health information, you may not participate in this research. Your permission for the use, retention, and sharing of your identifiable health information will expire after publication of the study results or within five years of the end of the study. Any research information in your medical record will be kept indefinitely. If you choose to participate, you are free to withdraw your permission for the use and sharing of your health information at any time. You must do this in writing. Write to Dr. CG Mailleard, and let him know that you are withdrawing from the research study. The mailing address is 1401 Centerville Road, Suite 510, Tallahassee, FL 32308. If you withdraw your permission:

- We will no longer use or share medical information about you for this research study, except when the law allows us to do so.
- We are unable to take back anything we have already done or any information we have already shared with your permission.
- We may continue using and sharing the information obtained prior to your withdrawal if it is necessary for the soundness of the overall research.
- We will keep our records of the care that we provided to you as long as the law requires.

The research team may use the following sources of health information.

- Your neuromotor, emotional, and functional status.

Medical information collected from or about the participant in connection with this research study includes:

- Unified Parkinson's Disease Rating Scale (UPDRS)
- Beck's Depression Inventory
- Fatigue Status Scale
- Short Form-36 Health Survey

- Body composition evaluation that will quantify your bone mass, fat, and lean mass.
- Maximal lower body power on a stationary cycle ergometer that tests your lower extremity power.
- Isometric and isokinetic strength tests your overall muscle strength.

FSU Human Subjects Committee Approved on 6/06/2013. Valid after 5/12/2014. HSC#2013:10724 Page 6 of 8
- submaximal aerobic capacity and fatigue which will examine how fast you experience fatigue.

Representatives of the following people/groups within the Balance Disorders Clinic may use your health information and share it with other specific groups in connection with this research study.

- The Principal Investigator
- The Institutional Review Board at Florida State University
- The co-investigators.

The above people/groups may share your health information with the following people/groups outside the Balance Disorders Clinic for their use in connection with this research study. These groups, while monitoring the research study, may also review and/or copy your original Balance Disorders Clinic records.

- The Office of Human Research Protections in the U.S. Department of Health and Human Services

We will do our best to make sure that the personal information in your medical record will be kept private. However, because of the need to release information to the above parties, absolute confidentiality cannot be guaranteed. Once your personal health information is released, it may be redisclosed and no longer protected by federal privacy regulations. Your personal information may also be given out if required by law and in rare circumstances may be subpoenaed by a court.

8. Costs for Participation:
   a. Costs: There are no costs to you for either the examination or the testing.
   b. Treatment and compensation for injury:
      Every effort to prevent injury as a result of your participation will be taken. It is possible, however, that you could develop complications or injuries as a result of participating in this research study. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. It is the policy of this institution to provide neither financial compensation nor free medical treatment for research-related injury. In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. You or your insurance company will be charged for continuing medical care and/or hospitalization if needed.

      No funds have been set aside to compensate you in the event of an injury.

      You do not waive any of your legal rights by signing this form.

9. Compensation for Participation:
   You will receive reimbursements of $25 per visit at the time of the testing to account for travel expenses. You will receive reimbursement for travel expenses regardless of completion of the study or if deemed ineligible within 7-10 working days.
10. Research Funding:
   Funding disclosure: This study is funded through the Tallahassee Memorial HealthCare Foundation.

11. Voluntary Participation:
   Taking part in this research study is voluntary. You do not have to participate in this research. If you decide not to participate, there will be no penalty or loss of benefits to which you are entitled.

12. Contact Information for Questions or Concerns:
   You agree that you have been given the right to ask any questions regarding the study and that all of your questions have been answered to your satisfaction. You will also be asked questions to confirm your understanding of your participation in the study. You understand you may contact Dr. CG Mainland at the Balance Disorders Clinic in the Professional Office Building at Tallahassee Memorial Hospital at (850) 878-3592, or at Florida State University College of Medicine Department of Clinical Sciences at (850) 645-3844, or a representative from the Human Subjects Committee (644-8836), for answers to questions about the research or my rights. Group results will be sent to you at my request upon completion of the study.

   If you have questions regarding your rights as a research participant or you have concerns or general questions about the research, contact the research protection advocate the Balance Disorders Clinic and Cynthia Blair, Administrative Liaison IRB, Tallahassee Memorial HealthCare, (850) 431-5676. You may also call this number if you cannot reach the research team or wish to talk to someone else. Also, you may contact the FSU IRB office at (850) 644-7900.

Signature and Consent/Permission to be in the Research
Before making the decision regarding enrollment in this research you should have:
   - Discussed this study with an investigator,
   - Reviewed the information in this form, and
   - Had the opportunity to ask any questions you may have.

You certify that you have read the preceding or that it has been read to you and that you understand its contents. You agree to participate in this experimental study: _____ YES _____ NO

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Participant: By signing this consent form, you indicate that you are voluntarily choosing to take part in this research.

Signature of Participant ___________________ Date _______________ Time _______________ Printed Name ___________________
Person Explaining the Research: Your signature below means that you have explained the research to the participant/participant representative and have answered any questions he/she has about the research.

<table>
<thead>
<tr>
<th>Signature of person who explained this research</th>
<th>Date</th>
<th>Time</th>
<th>Printed</th>
</tr>
</thead>
</table>

Name
(Only approved investigators/research coordinators and those trained in obtaining research informed consent and familiar with this research may explain the research and obtain informed consent.)

A witness or witness/translator is required when the participant cannot read the consent document; so it was read or translated.
Greetings!

Thank you for taking part in this study on behalf of

You have been given two (2) bottles of Beta-Alanine supplement or an identical placebo to take for the duration of this study. This study is “double-blind” meaning that neither you nor the researchers will know if you have been given Beta-Alanine or an identical placebo until the conclusion of the study. This method is the “gold standard” in research; eliminating potential bias that could affect the outcome of the study. You will need to return to this laboratory for your final testing session in 28 days (±2 days).

Directions: Take two (2) capsules, 3 times per day

Example: Two (2) capsules at breakfast

Two (2) capsules at lunch

Two (2) capsules at dinner

Total: Six (6) capsules per day

After this initial testing session, you will need to begin taking the capsules you have been given. Continue to take your assigned capsules until you have returned and completed your final testing session. Please bring both bottles back to the laboratory during your final testing session, whether they are empty or not.

Each bottle contains 120 capsules; however you will not use the full amount of pills you have been given. Do not take more or less capsules than directed. If you accidentally lose or damage some of the capsules, please make a note and tell the researchers during your final testing session.

If you have any questions or concerns regarding your assigned capsules or participation in this research study, please contact: (Your Contact Information)

Initial Testing Date: ________________ Scheduled Final Testing Date: ________________

Please contact the researchers as soon as possible if you need to re-schedule your final testing date.
APPENDIX D

HEALTH HISTORY QUESTIONNAIRE

Human Performance Laboratory
Florida State University
Nutrition, Food, and Exercise Sciences

HEALTH AND FITNESS HISTORY QUESTIONNAIRE

The following questions are designed to obtain a thorough preliminary medical history. The information you provide will help us to make the best determination about your eligibility for a particular study or other studies. Please answer all questions and provide as much information as you possibly can. This questionnaire, as well as any other medical information you provide will be kept confidential and will not be shared with any unauthorized person or organization unless you specifically request us to do so.

Name: ______________________________
Street Address: ______________________________
City, State, Zip code: ______________________________
Telephone Number: H ( ) W ( )
Email address: ______________________________
Date of Birth: ____________ Age: ________
       (mm/dd/yy)
Sex:      M       F
Personal Physician’s Name: ______________________________ Phone: ( )
       Address: ______________________________
Height _______ in. ________ cm
Weight _______ lb. ________ kg
Social Security Number: ______________________________
Signature: ___________________________________________
Date: ___________            ID #: ___________

**Occupation**
Current occupation:
__________________________

**Race** ________________

**Personal Health History**

Have you ever been hospitalized or had surgery? Yes____ No____
Please list all hospitalizations and surgeries to the best of your recollection.

<table>
<thead>
<tr>
<th>Disease/Operation</th>
<th>Duration</th>
<th>Age when hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

List any disease or illness you have had not listed above (e.g., mumps, measles, broken bones, etc.)

Are you allergic, sensitive or intolerant of any foods or medications? Yes____ No____
If yes, please describe:

Food ________________________________________________________________
Medication ________________________________
Other ______________________________________

Are you currently seeing a doctor or other health care provider for any reason?
Yes____ No____
If yes, please explain:

______________________________

______________________________

______________________________

______________________________
1. Have you ever been diagnosed as having any of the following and if yes, how are you currently treating the condition?

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Y</strong></td>
<td><strong>N</strong></td>
<td><strong>High Blood Pressure</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Please indicate last known reading:</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Blood pressure:</strong></td>
</tr>
<tr>
<td><strong>Y</strong></td>
<td><strong>N</strong></td>
<td><strong>High Cholesterol or High Triglycerides</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Please indicate last known reading:</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Cholesterol:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Triglycerides:</strong></td>
</tr>
<tr>
<td><strong>Y</strong></td>
<td><strong>N</strong></td>
<td><strong>Diabetes (Circle: Type 1 or Type 2)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note: Type 1 diabetes is insulin-dependent diabetes mellitus. It is typically diagnosed at an early age and requires insulin shots or an insulin pump immediately upon diagnosis. Type 2 diabetes is often diagnosed at an older age (post age 40) and is usually initially treated with changes in diet and/or medication (pills).</td>
</tr>
<tr>
<td><strong>Y</strong></td>
<td><strong>N</strong></td>
<td><strong>Hypoglycemia (low blood sugar)</strong></td>
</tr>
<tr>
<td><strong>Y</strong></td>
<td><strong>N</strong></td>
<td><strong>Asthma</strong></td>
</tr>
</tbody>
</table>

2. Have you ever had a glucose tolerance test?  **Y**  **N**

If yes, what were the results?

3. Have you ever had a fasting blood sugar test?  **Y**  **N**

If yes, what were the results?

4. Does anyone in your family (immediate family including your grandparents) have a history of cardiovascular disease (heart attacks, stroke, etc.)? Please explain:

5. Do you have any neurological problems including fainting, dizziness, headaches, or seizures?

6. Do you have any orthopedic or other health problems that may affect your ability to perform exercise? If yes, please explain.

7. Do you smoke or use smokeless tobacco?  **Y**  **N**

If yes, how many cigarettes per day? ______

8. Do you drink coffee or other caffeinated beverages?  **Y**  **N**

If yes, what kind, how much, and how often?
Date: ___________________________   ID #: ___________________________

9. Please list all vitamins, minerals and herbs and other nutritional (performance) supplements as well as medications you are currently taking. How long have you been taking them and how frequently?

Are you willing to stop taking all other nutritional supplements you are currently on for the duration of this research study? (Y/N) __________________________

10. Do you have any food allergies or intolerances (e.g., allergic to dairy or lactose intolerance)? Please describe:

11. How would you describe the type of diet you currently eat? Have you recently been on any special diets? What kinds of diets have you used to lose weight or lower cholesterol? Please list and describe:

12. What changes have you made in your diet in the last 6 months?

13. Do you exercise regularly?   Y   N   What kinds of exercise?

How often? Please be detailed in a description of your average week of training

14. How does your current exercise and physical activity compare to 6 months ago? 1 year ago?

15. Have you had a physical exam in the past 2 years?   Y   N

Please describe your assessment of your overall health:
APPENDIX E
THREE DAY FOOD RECORD

3 Day Food Record

Directions for 3-Day Food and Activity Record

1. Keep your 3-day food record on three consecutive days.
2. Please record each food you eat immediately after you eat it.
3. Record only one food item per line.
4. Be as specific as possible when describing a food eaten: how it was cooked and the amount you ate. Don’t forget to include all beverages you drink. For example: Coffee with 1 tsp. Cream, 12 oz. Regular Coke, or 8 oz. Sweetened Tea.
5. Include brand names or labels from food items whenever possible.
6. Record amounts eaten in household measures. For example: one cup nonfat milk, 3 ounces grilled chicken, 2 tablespoons ranch dressing, 1 medium fruit, 2 slices cheese.
7. Include the method used to prepare the food item. For example: fresh, frozen, stewed, fried, baked, canned, broiled, raw, braised.
8. For canned foods, include the liquid in which it was canned. For example: Sliced peaches in heavy syrup or Fruit cocktail in light syrup.
9. If you eat at a restaurant, do your best to estimate portion size and list the restaurant you ate at. List any visible fat, oil, or sauces added to your food.
10. List amount and type of oil or butter you use in the preparation of your food.
11. Do not alter your diet while you are keeping a food record.
12. Please indicate the activities you participated in during each of the days that you record your diet along with the duration of activity.
# 3 Day Food Record

**Date**: October 2, 2010  
**Participant ID**: # 035

**Day of the Week**: Wednesday

<table>
<thead>
<tr>
<th>Time of day</th>
<th>Serving Size</th>
<th>Food Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 am</td>
<td>1 cup</td>
<td>Cheerios</td>
</tr>
<tr>
<td></td>
<td>½ cup</td>
<td>2% milk</td>
</tr>
<tr>
<td></td>
<td>1 cup</td>
<td>Apple juice</td>
</tr>
<tr>
<td>10:00 am</td>
<td>1 medium</td>
<td>Banana</td>
</tr>
<tr>
<td></td>
<td>1 cup</td>
<td>water</td>
</tr>
<tr>
<td>12:00 pm</td>
<td>2 slices</td>
<td>Bread – hamburger bun</td>
</tr>
<tr>
<td></td>
<td>1 slice</td>
<td>Cheddar cheese</td>
</tr>
<tr>
<td></td>
<td>1 patty</td>
<td>Hamburger</td>
</tr>
<tr>
<td></td>
<td>1 supersized</td>
<td>French fries</td>
</tr>
<tr>
<td></td>
<td>1 16 ounce</td>
<td>Regular coke</td>
</tr>
<tr>
<td>3:30 pm</td>
<td>15</td>
<td>Crackers - Sociables</td>
</tr>
<tr>
<td></td>
<td>2 Tbsp</td>
<td>Peanut butter</td>
</tr>
<tr>
<td></td>
<td>1 8 ounce</td>
<td>Juice box</td>
</tr>
<tr>
<td>6:30 pm</td>
<td>5 ounces</td>
<td>Chicken – thigh - baked</td>
</tr>
<tr>
<td></td>
<td>1 ½ cups</td>
<td>rice</td>
</tr>
<tr>
<td></td>
<td>½ cup</td>
<td>Broccoli</td>
</tr>
<tr>
<td></td>
<td>1 cup</td>
<td>2% milk</td>
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<tr>
<td></td>
<td>½ cup</td>
<td>Mixed fruit – fruit cocktail with sauce</td>
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<tr>
<td>7:45 pm</td>
<td>1 ½ cups</td>
<td>Vanilla ice cream</td>
</tr>
<tr>
<td></td>
<td>3 Tbsp</td>
<td>Chocolate sauce</td>
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</table>

**Did you consume your supplement?** (Y/N) ___________

**Was this a typical day’s intake?** (Y/N. If no, please explain).

No. This was not a typical day’s intake because I had a doctor’s appointment and we went to McDonald’s afterwards for lunch.
3 Day Food Record

Date _______________  Participant ID # ____________

Day of the Week

<table>
<thead>
<tr>
<th>Time of day</th>
<th>Serving Size</th>
<th>Food Item</th>
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<tbody>
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Did you consume your supplement? (Y/N)

Was this a typical day's intake? (Y/N. If no, please explain).

______________________________________________________________

______________________________________________________________
# 3 Day Food Record

**Date**

**Participant ID**

**Day of the Week**

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<tr>
<th>Time of day</th>
<th>Serving Size</th>
<th>Food Item</th>
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**Did you consume your supplement?** (Y/N) __________

**Was this a typical day’s intake?** (Y/N, If no, please explain).

________________________

________________________

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80
3 Day Food Record

Date ___________________ Participant ID # __________

Day of the Week __________

<table>
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Did you consume your supplement? (Y/N) __________

Was this a typical day’s intake? (Y/N. If no, please explain).

__________________________________________________________________________________
APPENDIX F

PHYSICAL ACTIVITY QUESTIONNAIRE

ID: __________

Physical Activity Questionnaire  Date: __________

Do you exercise regularly?  Y   N   How many times per week? __________

What kinds of exercise? (be specific)

How long does each exercise session typically last? (minutes, hours)

Do you attend physical therapy?  Y   N   How many times per week? __________

What type of PT activities do you perform?

How long does each PT session last?

Other:
APPENDIX G
DATA COLLECTION SHEETS

ID: ___________

Beta-Alanine Data Sheet    Date: ___________

☐ Informed Consent

☐ 3-Day Diet Log/ PA Questionnaire

☐ Supplement & Directions

DOB: ___________    Gender: M / F    Med: Y / N

Height: __________ cm    Weight: __________ kg    BMI: __________(kg/m²)

☐ Polar HR monitor

☐ Resting HR/BP

Anaerobic Power:    Seat Height: _______

Resistance: __________ kg

Rev/5 sec: __________    Total Rev/30 sec: __________

Submax VO₂ Test:

☐ YMCA Cycle Ergometer

☐ 6-minute Walk    Distance: __________

☐ Return Polar HR monitor/ DEXA

Muscular Strength/Fatigue:    Leg: R    L

Entire Chair (front/back): _______    Seat (front/back): _______

Attachment Length: _______    ________________________________

☐ Collect Parking Pass
Return Visit Beta-Alanine Data Sheet

Date: ____________

☐ 3-Day Diet Log

☐ PA Questionnaire

☐ Supplement Bottle[s] Count: ____________ Days since Baseline: ____________

DOB: ____________ Age: ____________ Gender: M / F / MND: Y / N

Height: ____________ cm Weight: ____________ kg BMI: ____________ (kg/m²)

☐ Resting BP and Resting HR

Anaerobic Power:

Resistance: ____________ kg

0-5 ______ 5-10 ______ 10-15 ______

Total Rev./30 sec: ____________

15-20 ______ 20-25 ______ 25-30 ______

☐ Polar HR monitor

Submax VO₂ Test:

☐ YMCA Cycle Ergometer

6 minute Walk Distancet: ____________

☐ Return Polar HR monitor

☐ DEXA

☐ Muscular Strength/Fatigue: Leg: R L

☐ Collect Parking Pass
APPENDIX H

YMCA SUBMAXIMAL VO2 PROTOCOL FOR CYCLE ERGOMETER

ID: ________________

YMCA Cycle Ergometer- Data Collection Sheet

Date: ________________

- Pedal @ 50 rpm
- Before moving to next stage: need 2nd & 3rd minute HRs within ±5 bpm of each other
  - if not, extend Stage by 1 min until ±5 bpm
  - Ask for RPE @ end of each Stage
- End test: Two measurements of HR between 110-150 bpm @ two separate workloads
  - Ask for final RPE

Resting HR: __________  Resting BP: __________  Age-predicted Max HR: __________

Warm-up: 50 rpm at 0 Kp for 1 minute

Begin time

Stage 1: 0.5 Kp
01:00 HR: _________  01:30 BP: _________  02:00 HR: _________  03:00 HR: _________  RPE: _______

Additional:

Stage 2: ______ Kp
04:00 HR: _________  04:30 BP: _________  05:00 HR: _________  06:00 HR: _________  RPE: _______

Additional:

Stage 3: ______ Kp
07:00 HR: _________  07:30 BP: _________  08:00 HR: _________  09:00 HR: _________  RPE: _______

Additional:
Before testing:
At rest: SBP > 200 mmHg and/or DBP > 110 mmHg

While exercising:
From resting value: drop in SBP > 10 mmHg, despite increase in workload (from one stage to the next)
- Absolute: accompanied by other evidence of ischemia/Relative: absence of ischemic evidence

Excessive pressure: SBP > 250 mmHg or DBP > 115 mmHg
- Hypertensive Individuals: Keep SBP ≤ 220 mmHg and/or DBP ≤ 105 mmHg

Shortness of breath, wheezing, leg cramps or claudication (pain in legs)
Angina or angina-like symptoms

Signs of poor perfusion: light-headedness, confusion, ataxia, pallor, cyanosis, nausea, or cold and clammy skin

Failure of heart rate to increase with increased exercise intensity
Subject requests to stop and/or manifestations of severe fatigue (RPE: > 15)

During Testing:
Increase in HR by 10±2 bpm per MET (for inactive subjects, not on β blockers)
Increase in SBP of 10±2 mmHg per MET (normal)
- SBP that fails to rise or decreases may signify myocardial ischemia and/or LV dysfunction
- Vasodilators, Ca²⁺ channel blockers, ACE inhibitors, and α- and β-blockers will attenuate BP

No change or decrease in DBP (normal)

Recovery:
Decrease in HR during recovery of ≤12 bpm @1 min (walking) or ≤22 bpm @ 2 min (supine)

Hypertensive Individuals: vasodilators, Ca²⁺ channel blockers, and α-blockers may cause sudden decrease in recovery BP
- Extend recovery and monitor BP
APPENDIX I

SIX MINUTE WALK TEST PROTOCOL

6 Minute Walk Test Instructions

General Information:
- individual walks without physical assistance for 6 minutes and the distance is measured
  - start timing when the individual is instructed to “Go”
  - stop timing at 6 minutes
  - assistive devices can be used but should be kept consistent and documented from test to test
  - if physical assistance is required to walk, this should not be performed
  - a measuring wheel is helpful to determine distance walked
- should be performed at the fastest speed possible

Set-up and equipment:
- ensure the hallway free of obstacles
- stopwatch
- measuring wheel recommended to calculate distance

Patient Instructions (derived from references below):
“Cover as much ground as possible over 6 minutes. Walk continuously if possible, but do not be concerned if you need to slow down or stop to rest. The goal is to feel at the end of the test that more ground could not have been covered in the 6 minutes.”
REFERENCES


22. **Ghiasvand R, Askari G, Malekzadeh J, Hajishafiee M, Daneshvar P, Akbari F, Bahreynian M.** Effects of Six Weeks of β-alanine Administration on VO(2) max, Time to


BIOGRAPHICAL SKETCH

Arielle L. Biwer received her Bachelor of Science degree in Kinesiology from Arizona State University in the spring of 2012. While at Arizona State, she successfully defended her undergraduate honors thesis entitled, “Alpha and Beta EEG frequencies in persons with Down syndrome.” She then began her graduate studies at Florida State University where she is currently a Master of Science degree candidate in Exercise Science with a concentration in Exercise Physiology under the supervision of her major professor, Dr. Michael J. Ormsbee, in the College of Human Sciences’ Department of Nutrition, Food and Exercise Science. She is also an adjunct instructor at Tallahassee Community College, where she has taught since Fall 2012. Arielle received her certification as a sports nutritionist (CISSN) from the International Society of Sports Nutrition in November 2012. During her time at Florida State, she has conducted research in both typical and clinical populations, including Parkinson’s disease and multiple sclerosis patients. For her research work with Parkinson’s patients, Arielle was a Top 8 Finalist for the Master’s Student Research Creativity Award from the Southeast chapter of the American College of Sports Medicine (SEACSM). She will also present a poster on her work with Parkinson’s patients at the annual meeting of the American College of Sports Medicine in May 2014. Findings from her work with multiple sclerosis patients will be also presented at the American Academy of Neurology’s annual meeting in April 2014. In her free time Arielle enjoys weightlifting and participating in CrossFit, as well as cooking and spending time with her loved ones.