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The Effects of Cognitive Load on Gait in Individuals with Parkinson Disease

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THE EFFECTS OF COGNITIVE ENHANCING MEDICATION ON GAIT IN INDIVIDUALS WITH PARKINSON DISEASE

By

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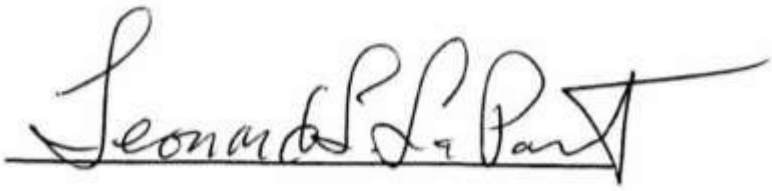

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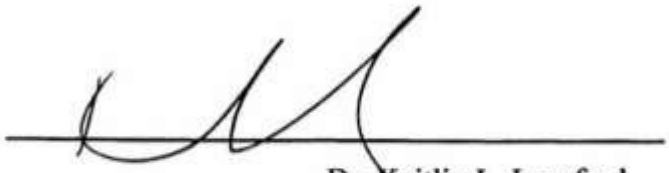

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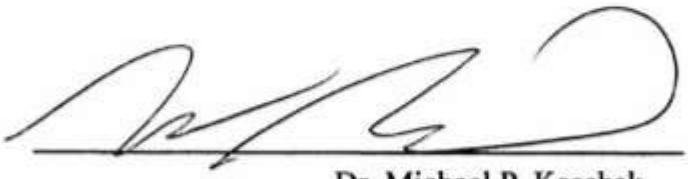

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INTRODUCTION

Injurious falls are, as the name would suggest, a fall in which an injury of some kind is sustained. Although such falls are not typically problematic for young people they can be disastrous for the elderly. According to the CDC one-third of Americans aged 65 and older fall each year. This translates to more than 2.4 million injuries in emergency departments resulting in over 772,000 hospitalizations and over 21,700 deaths annually. The cost related to falls in 2012 alone was over $36 billion and is projected to be over $59 billion annually by 2020. The average hospital cost of injuries sustained in just one fall is $35,000. The monetary cost does not reflect the significant personal cost of injury, hospitalization, and frequently a loss of independence. With one out of five falls causing serious injury ("Costs of Falls among Older Adults," 2015). It is evident that there is a need to further study the factors that contribute to falls. Injurious falls are a major medical concern and a huge drain on resources in our healthcare system, both in terms of monetary and personal costs.

The Effects of Aging

Changes in skeletal structure and reduced muscle mass from aging affects gait patterns likely contributing to an increased risk of falling ("Important Facts about Falls," 2016). Another, less considered, contributing factor is the influence of multitasking while walking in the elderly. One investigation, conducted at the University of Iowa examined the susceptibility of distraction in older drivers. The study included 203 participants, 120 of them over the age of 65, and 83 middle-aged drivers aged 40 to 64. Before completing an on the road driving test the participants completed a series of visual, motor and cognitive tests. They were then asked to participate in an on-road test in which they were tasked with identifying different landmarks and traffic signs along a mile and a half stretch of road. The car in which they were driving captured the mean

speed, lateral and longitudinal acceleration and steering wheel position for each participant. In addition to these parameters being captured the driving test was also captured on camera and was later analyzed by a certified driving instructor to identify driving errors as defined by the Iowa Department of Transportation. It was found that the older drivers performance was worse in all domains tested (visual, motor cognitive), it was stated that the pervasive effects of aging could account for these differences. In addition to poorer performance on the cognitive tests it was also found that the older drivers more frequently made safety errors and were unable to identify landmarks as accurately (Aksan et al., 2013). These findings would suggest that individuals who are aging have a harder time dividing their attention among tasks that are cognitively demanding, compared to those who are younger.

Falls in Parkinson Disease

This declined ability for task sharing could be one contributing factor to injurious falls in older individuals. However, as individuals age, there is also an increase in the number of individuals suffering from neuropathology and cognitive decline (LaPointe, Murdoch, & Stierwalt, 2010). One group of researchers investigated the impact of cortical cholinergic and midbrain dopamine loss on striatal function and the impact on injurious falls in persons with Parkinson disease (PD). They discovered that in typically aging adults there are structural abnormalities exhibited in the cholinergic axons in the cortex. For individuals with PD the extent of loss of neurons in the basal forebrain and related cortical innervation is much greater when compared with typically aging adults (Sarter, Albin, Kucinski & Lustig, 2014). Individuals with PD exhibit deficits in balance and postural control. These deficits become more exaggerated when attention is divided away from walking or when they are presented with

navigating a complex surface such as stairs (Cole et al., 2010, 2011; Marchese et al., 2003; Paul et al., 2013).

In another examination of a group with PD, a prospective study investigated over 100 individuals with PD in which 68.3% of the sample had experienced a fall. A self-report follow up of the same sample a year later found that 50% of those who initially reported falling had experienced additional falls (Wood et al., 2002). This literature indicates that the process of aging can have detrimental effects on cognition and on the likelihood of developing a neuropathology. In addition, people with PD are even more vulnerable to the effects of multitasking which may increase the likelihood of them experiencing an injurious fall. These factors indicate a need to study the effects of cognitive demands on ambulation in those suffering from neuropathology in the hopes of better understanding the risk for falls as well as developing compensatory strategies to aid in the prevention of falls.

Cognitive Load

In an effort to study the range of cognitive demands on individuals during ambulation, the concept of cognitive loading while walking has been examined in the Communication Neuroscience Laboratory at Florida State University and is continued in the present study. In these studies cognitive loading was comprised of a series of cognitive tasks that are increasingly difficult (low and high) during simultaneous walking. The low cognitive load consisted of walking while simultaneously counting aloud by ones (1,2,3…), while the high cognitive load involves walking while completing an alpha-numeric sequence (D-7, E-8, F-9…), a measure found to be highly demanding of working memory. A series of studies at Florida State University's Communication Neuroscience Laboratory have investigated the effects of simultaneous cognitive load on gait and ambulation. In these studies, the researchers utilized the

GAITRite© walkway system. This system is a 14' portable carpet with over 16,128 embedded sensors that instantly capture footfalls including temporal and spatial parameters that are recorded, quantified, and prepared for analysis.

One of these studies compared a group of 26 participants who had Parkinson disease with a mean age of 67.4 to a group of 13 healthy elderly adults with a mean age of 68.1. Each participant was asked to complete three gait conditions (Stierwalt, LaPointe, Maitland, & Toole, 2008). The three gait conditions consisted of, a baseline measure the participants walked across the GAITRite© system with no simultaneous talking; a low cognitive load; and a third condition where subjects were asked to complete a trial with a high cognitive load. In this study, the effects on gait during these conditions of cognitive load were examined according to changes in the dependent measures of velocity (cm/s), stride length (cm), and double support time, which is the percentage of time per ambulation cycle with both feet on the ground. This study found that while both groups demonstrated effects of cognitive load, the impact was greater in the group with Parkinson disease. In addition, the healthy adult group significantly increased double support time during the high cognitive load, while the group with Parkinson disease did not, indicating an increased risk of falling. The implications of this finding are that in situations of high cognitive load, the control group compensated for the effect by increasing double support (a compensatory measure of stability), thereby permitting extra time for the participant to regain balance. Conversely, the individuals with Parkinson disease, did not increase double support time or institute compensatory measures to stabilize their walk during the cognitively demanding task. The authors concluded that this finding likely accounts for the increased risk of falling (Stierwalt, LaPointe, Maitland, & Toole, 2008).

In the study just reviewed, the group with Parkinson disease completed the experiment during the peak effects of their medication cycle, when their motor system was operating at its best. The same group of researchers retested a number of the participants to complete the study once again, this time at the low end of their medication cycle. Twenty of the subjects from the first study agreed to enroll in the second study. The researchers hypothesized that the effects of cognitive load would be even greater when the participants were completing tasks when their medication state was low. Interestingly, no differences were discovered in the effects of cognitive load when performance was compared across the two medication states (Oh, Stierwalt, LaPointe, & Maitland, 2015).

Statement of the Problem

With injurious falls being a huge medical concern and drain on finances it is evident that there is a need to study them further. By understanding the factors contributing to them, researchers can further develop strategies to prevent them. In addition to possible avenues of fall prevention, this may predict factors in some people who are at greater fall risk. This has implications for all aging individuals as it has been shown that cognitive decline and neuropathology is a natural part of aging, putting these individuals at risk for falls. However, for people with PD the need is intensified since persons with movement disorders are at an even greater risk, than those with typical cognitive decline. Persons with PD are at an increased risk for falls and one report reports 70 percent of people in their study reported an incident of injurious fall in the previous six months regardless of their medication state (Wood et al., 2002). This indicates the need for the development of medication that will aid with their cognitive function or promoting additional compensatory strategies to decrease the likelihood of them experiencing an injurious fall. This study is currently underway at Florida State University in

collaboration with Tallahassee Memorial HealthCare and the practice of Dr. Charles Gerald Maitland, MD.

The purpose of this study therefore, was to conduct a preliminary examination of the effects of two medications (Azilect & placebo) on the gait performance of individuals with Parkinson disease. The active medication, Azilect is designed to reduce dopamine depletion, thus, have advantageous cognitive and motor effects. Our hypothesis is that those participants who receive Azilect will demonstrate improvement on measures of gait. Specifically, we will utilize the GAITRite© system to examine whether these two conditions result in changes in the gait parameters of:

- Functional Ambulation Profile (FAP),
- Velocity,
- Double Support, and
- Step Count

METHODS

Participants

Twenty-four participants with PD originally consented to participate in this study. There were 17 men and 7 women. During the course of data collection, there was a hardware malfunction that resulted in the loss of data from three participants. Another five participants withdrew from the study because of medication side-effects. Finally there was one participant who did not complete their final data collection session. Though there was considerable attrition in the recruitment of participants, the group who completed all data collection opportunities

consisted of a total of 15 people. This group included eleven men and four women with a mean age of 78.21 (see Table 1).

Table 1. Demographic information for study participants.

	Men	**Women**	**Total**
	N = 11	N = 4	N = 15
Age			
Mean (SD)	68.12 (11.92)	71.75 (14.00)	78.21 (10.72)
Education			
Mean (SD)	13.25 (3.40)	16.69 (2.85)	15.30 (4.57)
Ethnicity		Caucasian	
UPDRS			
Mean (SD)	16.69 (2.85)	13.25 (3.40	14.84 (4.67)

Instrumentation

The data in this study was gathered utilizing the GAITRite© walkway system. This system is a 14' portable carpet with over 16,128 embedded sensors that instantly capture footfalls including temporal and spatial parameters that are recorded, quantified, and prepared for analysis. The dependent measures selected for this study included functional ambulation profile

(FAP), velocity, double support time and step count. The operational definitions for these measures are as follows:

- Functional Ambulation Profile (FAP): an algorithm-based score resulting from several critical gait parameters found to be highly related to fall risk. Normal scores range from 90-100, scores below 90 indicate a strong correlation for falls.
- Velocity: gait speed for ambulation cycle measured in centimeters per second (cm/s).
- Double Support: the percentage of time per ambulation cycle with both feet on the ground before taking the next step.
- Step Count: this is a measure of the number of steps used to complete an ambulation cycle across the GAITRite© walkway system.

Procedures

This study was a double blind randomized control study where participants were randomly assigned an active drug (Azilect) or placebo tablets. Assignment was determined using a random number generator algorithm. Random numbers were generated based on a total subject population of 50 subjects, with equal assignment to each treatment condition. The double blind nature of the study required that neither the participants, nor the researchers were aware of the treatment condition assignment. A pre-treatment measure was taken where each individual was asked to complete three trials of ambulation on the GAITRite© walkway: a baseline measure (walking across the mat without talking), a low cognitive load (walking while counting by ones) and a high cognitive load (walking while completing an alpha-numeric sequence). Each participant was then randomly assigned either the active drug or a placebo. The individuals were administered the drug for 30 days and then their dosage was increased. Those receiving the active drug got a higher dosage and those receiving placebo were given additional tablets. After

60 days of treatment the final post-treatment data was collected where the participants were again asked to complete the three conditions (baseline, low and high) on the GAITRite© mat.

Treatment

There were two pharmacologic conditions in this study. One group received Azilect and one group received placebo pills at the schedule reviewed above. Azilect has been used to treat the symptoms of PD by inhibiting monoamine oxidase B (MAO-B). This is an enzyme that breaks down serotonin, dopamine, norepinephrine and other neurotransmitters in the brain. By inhibiting the breakdown of these chemicals the result is an increased level of dopamine in the brain thus affecting some of the signs and symptoms of PD ("Azilect").

RESULTS

Descriptive Statistics

This thesis is a part of a larger ongoing study and consists of a preliminary examination of data from a few participants.

To examine the performance of each treatment group (active drug & placebo) descriptive statistics were calculated and are visually displayed in Figures 1-4.

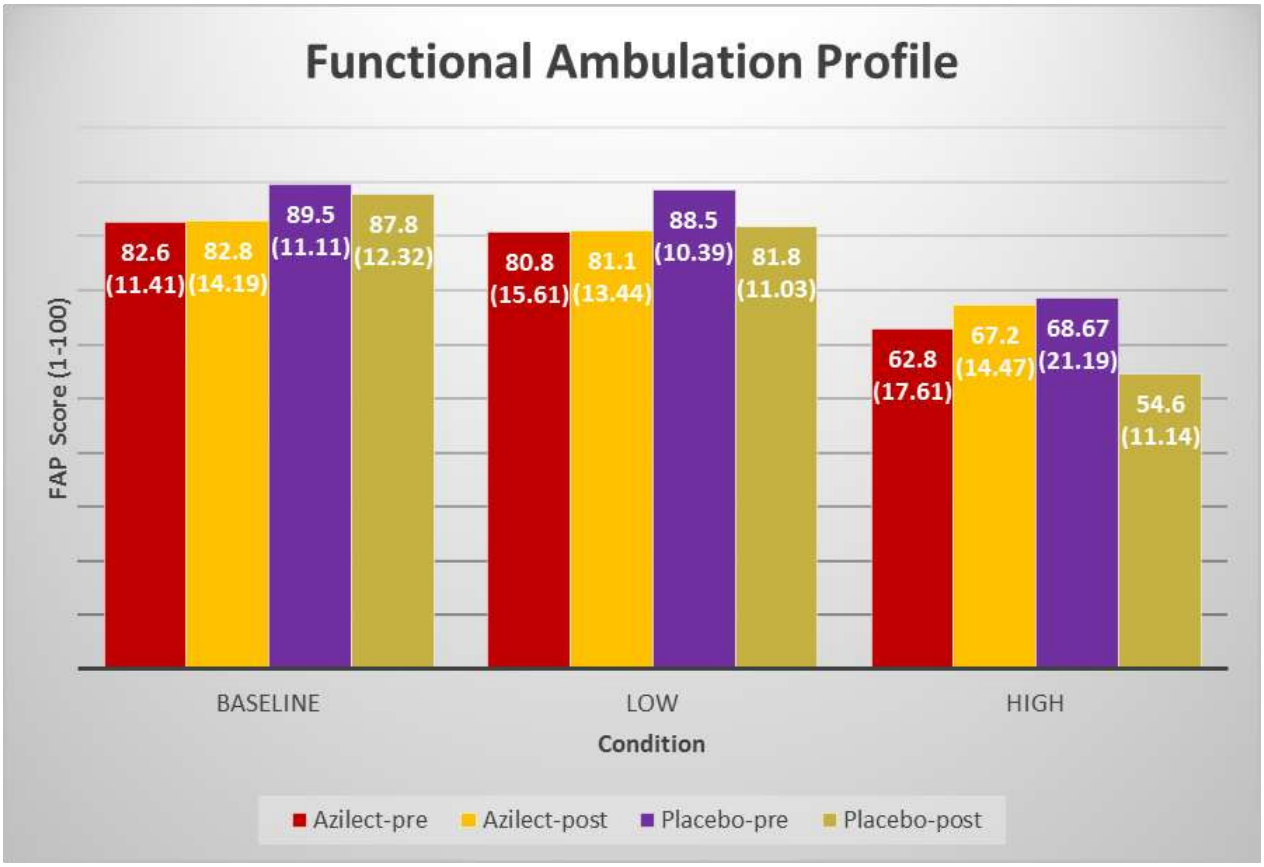

Figure 1. Means (Standard Deviation) on the measure of FAP for each group across conditions of cognitive load.

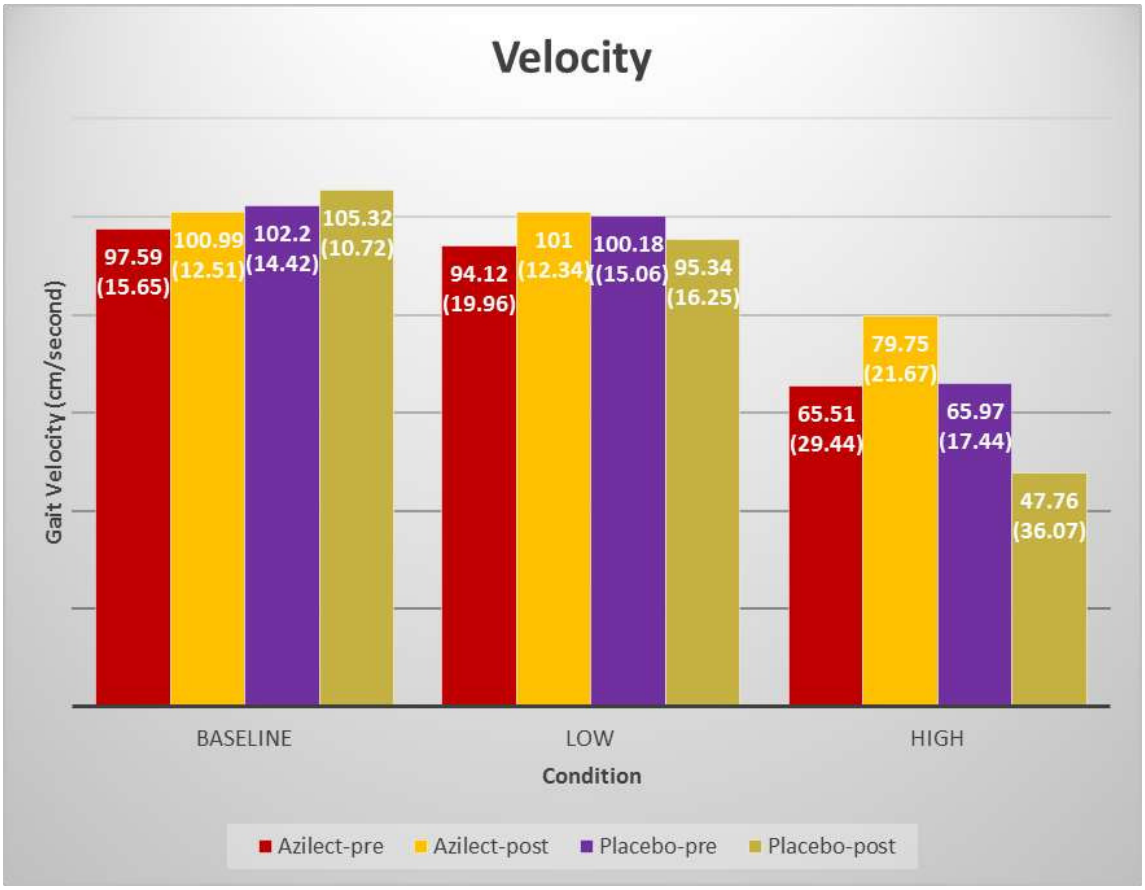

Figure 2. Means (Standard Deviation) on the measure of gait velocity for each group across conditions of cognitive load.

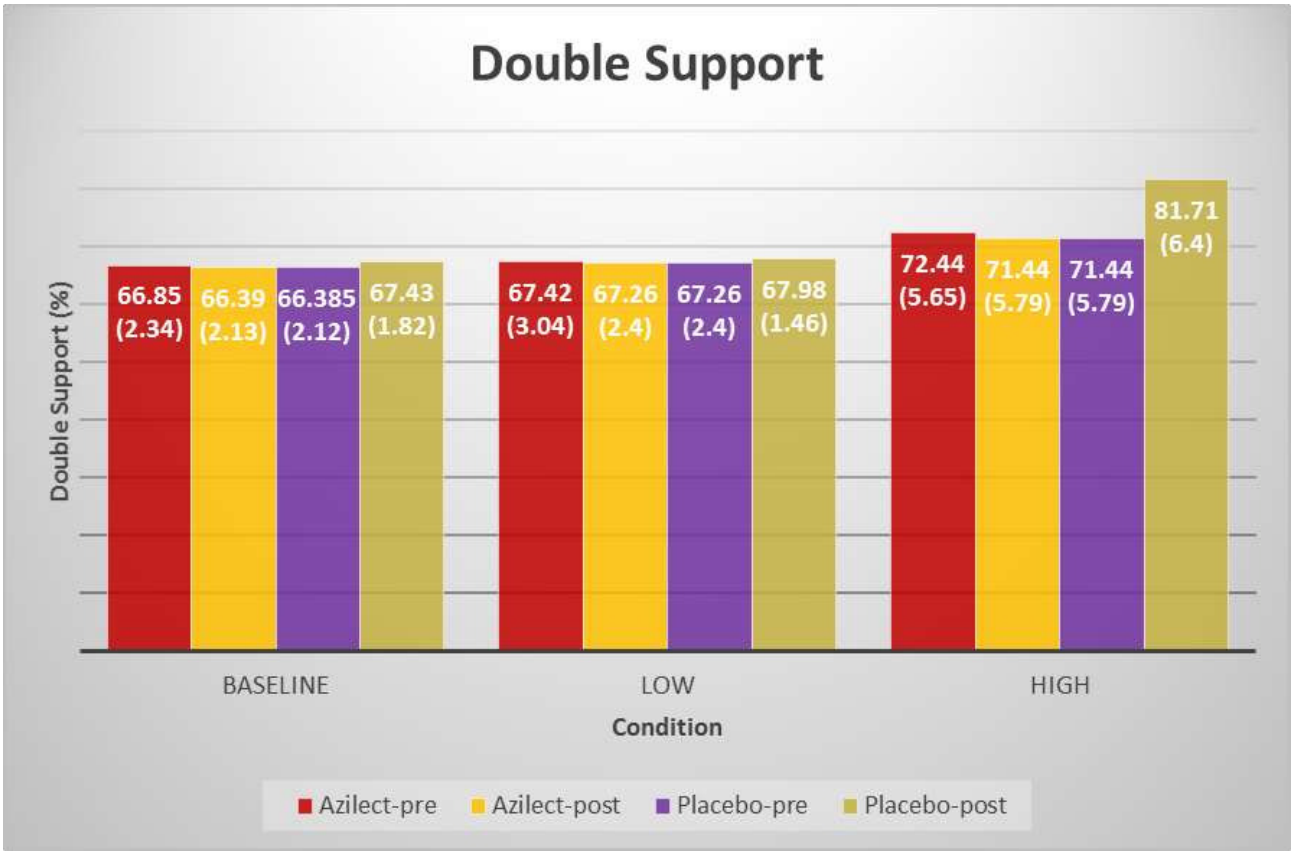

Figure 3. Means (Standard Deviation) on the measure of percent double support for each group across conditions of cognitive load.

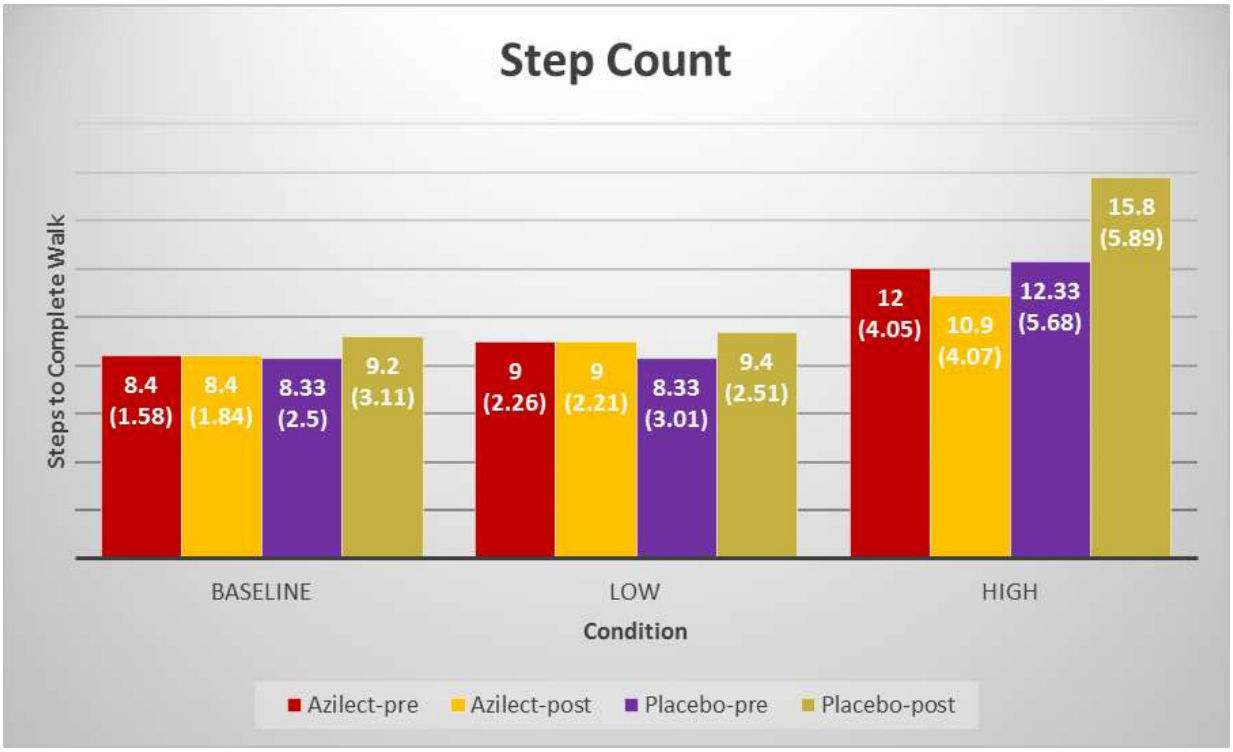

Figure 4. Means (Standard Deviation) on the measure of FAP for each group across conditions of cognitive load.

The purpose of this study was to conduct a preliminary examination of the effects of two pharmacologic agents (Azilect & placebo) on the gait performance of individuals with Parkinson disease. Attrition of the participant pool secondary to data loss and participant withdrawal, resulted in small and unequal groups (Azilect, N=10; Placebo, N=5). Consequently, we chose to report Delta values. A report of delta is the overall change in a value, for the purposes of our study we calculated the delta for performance on dependent measures pre and post-treatment across the measures of cognitive load and compared those between the group who received Azilect, and the group who received a Placebo.

Delta values

FAP

For the dependent measure of FAP, delta values for the group who received Azilect between pre and post treatment were $\Delta = 0.2$ for the Baseline condition, $\Delta = 0.3$ for the Low condition and $\Delta = 4.4$ for the High cognitive load condition. To summarize, the FAP scores went up slightly from pre-treatment to post-treatment for the Baseline and Low measures (0.2 and 0.3 respectively) but went up almost 4 and a half points in the high cognitive load condition from pre to post treatment.

For the group who received a Placebo, Delta values indicated a decrease in FAP scores across conditions. The decrease was $\Delta = 1.7$ in the Baseline condition, $\Delta = 6.7$ for the Low condition and a decreased $\Delta = 14.07$ for the High cognitive load condition. A comparison of the two groups indicated a divergent pattern. Those who received the active drug had minimal change in FAP scores in the Baseline to Low load conditions from pre-treatment to post-treatment. However, there was an increase in FAP between pre and post treatment. In contrast, the individuals who received the placebo exhibited a decrease in FAP scores across all measures, regardless of treatment, with the largest decrease of 14.07 points in the high cognitive load measure.

Velocity

For the dependent measure of velocity, the delta values for the group who received Azilect between pre and post conditions were $\Delta = 3.4$ in the Baseline condition, $\Delta = 6.88$ in the Low condition and $\Delta = 14.24$ in the High condition. In summary the velocity of the participant's

ambulation cycle increased across conditions from pre-treatment to post-treatment with a large increase of 14.24 cm/s in the High condition.

In the group who received placebo there was an increase of Δ= 3.12 for the baseline condition from pre-treatment to post-treatment while the delta values indicated a decrease in velocity for the Low and High conditions. With a decrease of Δ= 4.84 for the Low condition and a large reduction of Δ= 18.21 in the High condition. In comparing the two groups, those who received Azilect increased their velocity across conditions from pre to post treatment with a large increase of 14.24 cm/s in the high cognitive load task. However, those who received the placebo had a decrease in velocity in both the cognitive loading tasks with an even larger decrease of 18.21 cm/s in the high condition.

Double Support

For the dependent measure of double support the delta values for the group who received Azilect between pre-treatment and post-treatment there was a decrease in double support time across conditions, with a decrease of Δ= 0.46 for Baseline, a decrease of Δ= 0.46 for the Low condition and a minimal decrease of Δ= 0.16 in the High condition.

The group who received placebo had an increase in double support time across the conditions with a score of Δ= 1.05 in the Baseline condition, Δ= 0.72 in the Low condition and a noticeable increase of Δ= 10.27 for the High condition. When looking at the two groups together there was a small decrease in the percentage of double support time across all conditions. The smallest decrease being seen in the High load at .16%. The participants receiving the placebo increased their double support time across all conditions especially in the high load condition with an increase of 10.27%

Step Count

For the dependent measure of step count there was no change in steps taken from pre to post treatment, for those who received Azilect, in the Baseline and Low conditions but a decrease of Δ= 1 in the High condition. In those individuals who received placebo there was an increase in step count across the conditions with a Δ= 1 in the Baseline and Low conditions and a slightly larger increase of Δ= 3 in the High condition. In comparing the two groups there was only a change in steps taken per cycle in the high condition with a decrease of 1 step, in those receiving the Azilect. For the placebo group, the step count was increased across conditions with an increase of 1 step seen in the baseline and low conditions and a slightly greater increase in the High condition of 3 steps.

DISCUSSION

The purpose for this study was to examine whether there were effects on measures of gait across conditions of cognitive load and across drug conditions (Azilect vs. Placebo). Specifically, are there differences across conditions of cognitive load and conditions of drug administration?

Conclusions

Any definite conclusions are hard to be made in this study because of the impact of attrition resulting in a small sample size. However, because this analysis is part of a larger ongoing study, the data analyzed from this sample will provide a foundation for the continuing research being done, at Florida State University's Communication Neuroscience Laboratory, examining the effects of Azilect on gait performance in patients with PD.

Although there was a small sample size analyzed in this study, there were trends seen across measures. Those receiving the Azilect exhibited improved performance from pre-treatment to post-treatment in all measures except double support time. Even though they did not increase their double support time across conditions there was only a minimal decrease of .15% in the high condition. This was the anticipated direction of performance for those receiving Azilect with the exception of double support time.

In regards to double support time, the group receiving placebo increased their double support time across all conditions. There was a noticeable increase 10.27% in the high condition. This finding is something that has not been seen before, in previous research, it was found that as the cognitive load increased there was no change found on the double support time in patients with PD. However, owing to the small sample size of placebo recipients it is hard to determine if these findings are valid or are can be accounted for by normal variability.

Although it is hard to make specific determinations because of the small data set analyzed in this sample size, there is one thing that was seen across all measures and conditions. All participants, regardless of their drug condition (Azilect or Placebo) performed worse in the high cognitive load condition in comparison with baseline. This supports previous research that has been done examining the effects of cognitive linguistic load in people with PD. This seems to

indicate a positive relationship between complexity of cognitive linguistic tasks and risk for injurious falls.

It is evident that there is a need to further study the effects of Azilect on gait in patients with PD. These dependent measures will continue to be examined as part of the larger ongoing study in an effort to examine a larger sample size. This needs to be done to determine if there is a significant change seen in those receiving Azilect. In addition to determining statistical significance, it will determine if the findings of this study will translate to the larger clinical population.

Clinical Implications

The findings of this study contribute to what has been previously found concerning the effects of cognitive linguistic load in the elderly population and people suffering with neuropathology, more specifically, persons with PD. It was shown across conditions and measures that as the cognitive load increased the participants' performance decreased. Although interpretations are difficult to draw from this analysis due to the small sample size, as stated above it was seen that as the cognitive load increased so did the risk for suffering an injurious fall. By educating care providers and individuals with PD on the effects of cognitive-linguistic loading while walking and its contribution to injurious falls, compensatory strategies can be further developed in an attempt to reduce the occurrence of these falls.

These findings are something for healthcare providers to consider when setting expectations for their clients. The effects that cognitive-linguistic loading have on gait is important to keep in mind when working with individuals with PD. In doing this providers can monitor the cognitive-linguistic demands placed on individuals while walking and particularly

during increased risk conditions, such as low light descending stairs or in environments with obstructions on the floor, or even the presence of household pets.

As seen in the results the clients who received Azilect saw an increase in their FAP scores across the cognitive loading conditions. The opposite was seen for those receiving placebo with a noticeable decrease of 14.07 points in the high load condition. Since the Functional Ambulation Profile (FAP) has been found to be a valid and consistent predictor of future injurious falls, these findings would indicate a decreased risk of falling in those who received Azilect. To strengthen this conclusion those who received placebo were at an increased risk for injurious falls if these findings hold true for a larger sample. As previously stated, the ongoing investigation needs to be completed in order to determine if Azilect has a positive effect on FAP scores in comparison with those who have received no treatment.

Although it is hard to make concrete determinations from this small sample set the participants who received Azilect performed better across all measures, with the exception of double support time, than those who received placebo. This indicates a need for further research to be done to see if Azilect has a significant impact on cognitive function in individuals with PD. If a positive correlation can be found between Azilect and cognitive performance, the clinical implications for that could be far reaching. With people receiving Azilect, an increase in cognitive performance has widespread implications. We must be adequately cautious about extracting conclusions until this research rises to the level of adequate statistical power and effect size, but at least these preliminary trends are encouraging.

Theoretical Implications

The theoretical implications of this study are overshadowed by the clear clinical implications but they might relate to learning generally about advancing our knowledge of brain and behavior. Three obvious areas of potential include:

- Learning more about brain and behavior and the effects of pharmacology and cognition
- A better understanding of dopamine and other neurotransmitters on cognitive function
- A better understanding of models of cognitive resource allocation and its association with models of attention

Future Research

As it has been presented, injurious falls are a significant problem for the elderly population in terms of overall health, monetary cost and personal independence. Injurious falls are not just a concern for typically aging adults, but those suffering from movement disorders and neuropathology. These clinical populations are at an even greater risk for injurious falls. The research being done at Florida State University's Communication Neuroscience Laboratory, has shown promising findings in understanding the contributing factors to these falls, as well as the contributing factors that put people at increased risks for suffering from an injurious fall. However, further research is needed to determine and extend the significance of these findings. In addition to studying individuals with PD, there is a need to study other clinical populations suffering from neuropathology or cognitive decline including those having experienced traumatic brain injury, stroke, or other neurodegenerative conditions. Examination of common trends across groups of clinical populations, may lead us to a better appreciation of dual tasks, multi-tasking, and the effects or risks of individuals who have diminished capacities in these areas.

Also, we would hope that this better understanding would lead to efficient means of treatment or compensation for these conditions.

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