

Caitlin Brown, DPT

Department of Physical Therapy,
University of Florida, Gainesville,
Florida, 32610

Correspondence:

caitcbrown@gmail.com

Combination of Physical Therapist Guided Interventions and Baclofen for Treating an Undiagnosed White Matter Brain Disorder: A Case Report

Purpose: Deep and periventricular white matter lesions in the parietal lobe have a negative impact on balance, gait and cognition. Guided physical therapy interventions have been shown to be effective in the treatment of neurological conditions by targeting the brain's neuroplasticity. Baclofen is a commonly prescribed medication to treat spasticity in the neurological population. The purpose of this case report is to observe the changes in body impairment and functional abilities of a patient with an undiagnosed cerebral white matter disorder treated with baclofen and physical therapy interventions. **Case Description:** The patient was a 54-year-old female who was referred to an outpatient physical therapy clinic by her neurologist for an unknown white matter disorder. Scores on the SF-36, DGI, Purdue Peg Board, Fugl-Meyer, and Modified Ashworth Scale indicated initial disability. The patient was seen for 10 visits over 6 weeks and was provided functionally targeted physical therapy interventions as well as oral baclofen by her neurologist. **Outcomes:** Patient scores on the SF-36 and DGI showed clinically important improvements in function and general health. **Clinical Relevance:** This case observed positive functional outcomes with the combination of physical therapy interventions and oral baclofen. Further research is necessary to determine long-term outcomes as well as appropriate physical therapy dosage and specific exercises.

Key Words: *white matter lesion, spasticity, baclofen*

INTRODUCTION

Diagnosing and treating damage to the central nervous system is complex and requires extensive knowledge of Neuroanatomy, as well as diverse functional presentations. White matter lesions, revealed as hyperintensities on T2 weighted MRIs, have been shown to have a negative impact on cognition, gait, and balance. Periventricular lesions can be observed around the cerebral ventricles while deep white matter lesions are located in the subcortical cerebral white matter. The functional impacts of periventricular and deep white matter lesions have been studied extensively and these lesions have been associated with changes in cognition, depression, gait, and balance¹. According to Murray et al, however, the most prominent correlations with functional outcomes may not be seen with periventricular versus deep white matter lesions as a whole, but with their general location in the lobes of the brain. This study identified that white matter hyperintensities in the parietal lobe most closely correlated with impaired gait and postural instability when compared to the other brain lobes².

A prominent feature of many neurological conditions, including white matter lesions, is the presence of spasticity. Symptoms associated with spasticity include muscle fatigue and spasm, hypertonicity, clonus, and hyperreflexia, which further compound issues related to a neurological insult. Baclofen is one of the leading drugs utilized to treat spasticity in Multiple Sclerosis, stroke, and traumatic brain injury. Placebo-controlled trials indicate that baclofen produces statistically significant improvements in spasticity³. However, adverse side effects must be taken into consideration as they can cause a negative impact on the patient and their functional presentation. Adverse effects include sedation, somnolence, weakness, vertigo and psychological disturbances. Patients must be monitored closely by their physician for any presentation of these symptoms.

In addition to medical management with baclofen, interventions provided by a physical therapist can play a role in treatment of these symptoms. The incorporation of physical therapy into treatment of white matter disorders has been shown to target the

brain's neuroplasticity, which allows for neurons and neural networks to form new connections by passing areas of damage to complete activities in a new ways. Physical exercise is known to promote cellular responses that enhance neuroplasticity. Neurotrophins are activity-dependent supporters of neuroplasticity that signal growth and differentiation of neurons⁴. The specific neurotrophic factor of interest, brain-derived neurotrophic factor (BDNF), is enhanced by activity levels and plays a role in dendritic growth and remodeling⁴. However, the BDNF produced by acute exercise bouts is only temporary. By performing acute aerobic exercise at the beginning of treatment sessions, physical therapists are able to augment the neuroplastic effects of treatment.

Along with enhancing neuroplasticity, physical exercise has also been shown to promote improvements in quality of life. A randomized control trial by Studenski et al. examined the effect of therapeutic exercise on quality of life in subacute stroke patients and showed that while both the control and intervention groups demonstrated recovery of function over the course of the study, gains in the intervention group were significantly greater for quality of life⁵. It is unclear if a singular component of the exercise program or if exercise as a whole leads to improved quality of life measures, but this does provide grounds for inclusion into physical therapy intervention.

A major limitation identified in literature in this area is that there is little research linking specific areas of damage to their functional outcomes in the adult population. Most literature has targeted the elderly population and the aging process rather than injury in the study of periventricular white matter lesions. Also, while there is extensive evidence supporting the use of both physical therapy and baclofen for specific neurological diagnosis such as multiple sclerosis and stroke, there is limited evidence supporting their use in a patient without a formal diagnosis.

The purpose of this case report is to observe the changes in body impairment and functional abilities of a patient with an undiagnosed cerebral white matter disorder treated with oral baclofen and physical therapy interventions.

CASE DESCRIPTION

The patient was a 54-year-old female who was initially referred to an outpatient physical therapy clinic by her neurologist for vertigo and post-concussion syndrome after a car accident. The patient presented with severe positionally provoked vertigo, lightheadedness, nausea, headaches, whiplash

symptoms, upper and lower extremity spasticity, difficulty walking and decreased coordination and dexterity. She required the assistance of a rolling walker and right ankle brace to ambulate immediately following the accident but was no longer using her walker at the beginning of this case report. The patient was initially treated in outpatient physical therapy to address these symptoms for 6 months before updated MRI results altered her medical diagnosis. The case report begins at this transition. While the whiplash symptoms, headache, and vertigo symptoms had resolved, the patient continued to present with difficulty walking, upper and lower extremity spasticity, and decreased coordination and dexterity.

The patient's MRI results revealed bilateral periventricular and subcortical white matter signal alteration throughout the centrum semiovale. The neurologist had not provided a specific diagnosis, but ruled out multiple sclerosis and a stroke, despite similarities in symptoms. Her neurologist hypothesized that the lesions had been dormant in her brain prior to the motor vehicle accident, which then triggered their arousal.

Patient goals for physical therapy treatment included ambulation without the feeling of falling or tripping, returning to driving, and being able to maintain her balance while on a cruise ship.

Examination

During the physical therapy initial examination, the patient completed an SF-36, Dynamic Gait Index (DGI), Purdue Peg Board Test, Fugl-Meyer, and Modified Ashworth. The patient had not yet begun Baclofen treatment at initial completion of these tests and measures but had been on other medications since onset of symptoms (Table 1).

Table 1: Daily Medication List and Dosage

Medication	Dosage
Baclofen	10 MG tablet, 3x per day
Buspirone	15MG tablet, 3x per day
Gabapentin	600 MG tablet, 2x per day
Trazodone	50 MG tablet, 1x per day
Venlafaxine	75 MG capsule, 2x per day

The SF-36 was used as a general report of overall patient self-report quality of life and was administered at the initial and final visits. The patient was instructed to take the exam home and to answer

the questions as honestly and accurately as possible. The SF-36 has been tested and validated in a wide range of populations including neurological conditions and has adequate to excellent test-retest reliability, as well as adequate to excellent criterion validity when compared to similar outcome measures ⁶. The patient's initial

scores in each of the subdomains can be found in Table 2. Higher scores indicate higher levels of health. The patient chose to diverge from standard protocol when answering the "pain" category by replacing the word pain with tremor, as she had no pain but was limited by her tremors.

Table 2. SF 36 Subscale Scores

SF-36 Scale	Initial	Final	Change	MDC
Physical Function	10	75	65	28
Role Limitations Due to Physical Health	0	0	0	45
Role Limitations Due to Emotional Problems	100	100	0	45
Energy/Fatigue	40	80	40	19
Emotional Well Being	68	84	16	19
Social Functioning	87.5	87.5	0	29
Tremor (Pain)	32.5	45	12.5	25
General Health	50	80	30	28

The DGI is validated for use in brain injury, multiple sclerosis, stroke and vestibular disorders. Although the patient does not specifically fit into one of these categories, the presenting symptoms are similar enough to allow for consideration. For the purpose of consistency, the excellent test-retest reliability and excellent criterion and content validity has been assessed based off of use in the stroke population ^{7,8}. The initial DGI resulted in a score of 11/24, which is indicative of a fall risk based off of the cutoff score of 19/24. The patient demonstrated toe drag of the right foot when completing all tasks on the DGI. She was most limited in her dynamic reactive balance with the "gait and pivot turn" score of 0 due to requiring assistance to safely turn and stop. Anticipatory balance was also limited as evidenced by scores of 1 in both the "step over obstacle" and "steps" categories. The patient's approach to the obstacle was fluid until two steps prior when she became slightly off balance and had to take several short steps. She required increased time to step over and completed the motion with a slow and hesitant step once reaching the obstacle.

The Purdue Peg Board was chosen to assess upper extremity coordination and dexterity changes. The patient was given 30 seconds to place as many cylindrical pegs as possible in a line of holes while using only the right hand. This test was then repeated using the left hand. Initial scores for this test are as follows: 13 pegs in 30 seconds with the right hand, 11 pegs in 30

seconds with the left hand. This test has a test-retest reliability coefficient from 0.85-0.90 ⁹.

The patient completed a lower extremity Fugl-Meyer assessment to measure motor impairment. Other sections of this assessment were not included for this patient due to the time commitment involved and lack of relevance to this patient. This test was selected due to the observation of movement within and outside of typical synergy patterns as well as hyper reflexivity across all joints. While this measure is typically used to assess post-stroke hemiplegia, it was included in this report due to its comprehensiveness in assessment of the patient's impairments. The volitional movement subscale assessment of bilateral lower extremities was performed with an initial score of 12 out of a possible 34. The patient scored the lowest in movement combining synergies, movement out of synergy and coordination/speed in sitting. Marked tremor and pronounced dysmetria were observed with bilateral heel to shin movements. The patient had difficulty with initiation of the movement, fluidity of the movement and inability to discontinue the movement. This measure has excellent test-retest reliability (ICC > 0.8), and excellent inter-rater/intra-rater reliability across all domains. The Fugl-Meyer has been assessed for criterion, construct and content validity in the stroke population and has been shown to be good to excellent in this population ^{10,11}.

The Modified Ashworth scale is often used to measure degree of spasticity in patients with central

nervous system dysfunction. The scale is from 0 to 4, with 0 meaning no increase in muscle tone with a quick stretch and 4 meaning affected joint is rigid in flexion or extension. The joints tested included bilateral elbow extension and knee flexion. Left elbow extension and knee flexion rated at 1 out of 4, and right elbow extension and knee flexion was a 1+ out of 4. This measurement has adequate intra-rater test-retest reliability across the chosen joints. However, evaluation of content validity suggests that resistance to passive movement is not exclusive to the assessment of spasticity¹².

Evaluation

Upon completion of this examination it was determined that the patient was appropriate for physical activity directed by a physical therapist in conjunction with medicinal treatments by her neurologist. She presented with upper motor neuron dysfunction as evidenced by hypertonicity, spasticity, positive babinski and clonus signs, however the patient did not demonstrating any gross muscular weakness. The patient also demonstrated minimal spasticity and moderate to severe dysfunction of movement based off of the Modified Ashworth and Fugl-Meyer scores respectively. The patient's functional impairments included severe dynamic balance impairments based upon observation of movement as well as completion of the DGI. Overall, based on patient observation and outcome measures, this patient is at an increased risk for falls due to decreased control of the upper and lower extremities. Additionally, when the patient fatigued after a mentally challenging task or prolonged concentration, her frequency and intensity of spasticity and tremors increased. This was taken into account when prescribing exercise interventions, but required trial and error with clinical judgment to meet the appropriate level of difficulty for the patient.

INTERVENTION

The patient was seen for a total of 10 visits over 6 weeks with approximate treatment time of 60-70 minutes. The patient did not wear her ankle brace during these treatment sessions. The patient was instructed to take her dose of oral baclofen within a sufficient time frame so it would be most effective during treatment. All treatment sessions began with a 10-minute aerobic warm up on the recumbent cycle at a self-selected speed.

Visit 1 of the intervention included patient examination and evaluation. Visits 2 to 3 consisted of synergy movement impairments as identified by the

Fugl-Meyer, upper and lower extremity targeting and upper extremity coordination utilizing the peg board. Visits 4 to 7 included components of previous visits as well as initiation of reactive dynamic balance via ball toss exercises. Visits 8 to 10 also included components of previous visits as well as the addition of anticipatory dynamic balance exercises such as stepping over obstacles and step-ups.

Specific visit exercises can be found in Table 3, and descriptions of exercises can be found in Appendix 1. Appropriateness of progression was determined by subjective observation of spasticity and tremor as well as patient self-report of time to recover between visits. The patient's home exercise program consisted of memory games with a deck of cards as well as hand dexterity exercises performed by turning cards and buttons over.

OUTCOMES

The patient's SF-36 scale sub scores can be found in Table 2. The accepted standard deviation of the SF-36 is 10 points, so differences greater than this suggests changes are due to more than chance. While this scale has been studied across many populations there is no established minimal clinically important difference (MCID), however the minimal detectable change has been established in the Parkinsonism population⁶ and is also displayed in Table 2. Using this MDC, the patient demonstrated improvement in the categories of physical function, energy/fatigue, and general health. It is unknown what impact exchanging the "pain" category for "tremor" had on the use of the outcome measure and MDC, but answering the questions in the correct manner would have also produced a skewed result as the patient did not experience any pain.

As established in the tests and measures section, the cutoff score for the DGI is 19/24 as indicative for an increased fall risk. The established MCID for community dwelling older adults with an initial score <21/24 is 1.8 points¹³. This patient's DGI scores improved significantly from 11/24 at initial assessment to 23/24 at final assessment indicating that she is no longer at an increased fall risk. Observation of the patients gait on the final assessment revealed a decreased toe drag of the right foot and improved ability to step over an obstacle in a fluid manner.

The Purdue Peg Board and Fugl-Meyer outcome measures were taken at initial, eighth, and final visits (Table 4). There is no established MDC or MCID for the Purdue Peg Board based on research. For this patient, MDC at 95% confidence was calculated to be 1, which

indicates the patient did experience a change from initial to final examination. The established MDC for the lower extremity motor category of the Fugl-Meyer assessment is 4 points¹⁴. The patient demonstrated greater than the 4-point change from initial to final assessment on both the right and left leg. The patient improved most in the Fugl-Meyer categories of movement combining synergies, and coordination/speed on the right lower extremity.

The patient did not demonstrate any change in spasticity at the elbow or knee joint from initial to final

assessment with the Modified Ashworth Scale. MDC for this scale is established as a 1-point decrease¹⁵. While no difference can be seen on the scale, based on observation and self-report, the patient experienced less frequent and less intense episodes of spasticity after beginning her baclofen treatment.

The patient achieved two of her initially established goals including the reported ability to ambulate without falling and the potential to stand on an unstable surface such as a cruise ship. However, she continues to be unable to drive.

Table 5. Outcomes for DGI, Purdue Peg board, FMA, and MAS

Time	DGI	PPB Right	PPB Left	FMA Right	FMA Left	MAS L elbow	MAS R elbow	MAS L knee	MAS R Knee
Initial	11	13	11	11	11	1	1+	1	1+
Visit 8	19	17	15	-	-	-	-	-	-
Final	23	16	15	19	17	1	1+	1	1+

PPB= Purdue Peg Board, FMA = Fugl-Meyer Assessment, MAS= Modified Ashworth Scale

DISCUSSION

The purpose of this case report was to describe outcomes for a patient with the aforementioned diagnosis and neurological deficits who was treated with physical therapy exercise intervention in combination with prescribed baclofen medication. While outcome measures are an excellent resource to track patient improvement across treatment, it is important to also consider direct patient report of improvements. This patient noted that she was improving from baseline to the end of this case report but also verbalized that she had a tremendous distance to go before she would be happy with her progress. Her independence and ability to return to her normal daily routine are very important, and while she has made improvements, she is not at the point she would like to be.

In similar neurologic populations, the earlier the intervention the greater the return to higher-level functional abilities¹⁶, so it was appropriate to begin treatment in this patient without a definitive diagnosis. The literature on this topic as well as results from this case report demonstrate the possible benefits of providing similar patients with targeted physical therapy interventions in conjunction with oral baclofen. Because of the lack of evidence for exercise programs in this population, clinical judgment based on the patient's impairments and response guided intervention. The dosage and progression for this patient was able to affect change without overwhelming the patient, but it

cannot be generalized to other patients with unknown cerebral white matter conditions, as they will have their own thresholds for exercise tolerance.

There is a multitude of research on the benefits of physical therapy in multiple sclerosis and post stroke, but there is little to no evidence for best physical therapy practice when a patient has yet to be formally diagnosed. In a Cochrane review by Rietberg on exercise therapy for multiple sclerosis, no randomized control trial was able to provide a definitive answer on the specific dose of exercise necessary to effect changes¹⁷. Also, across all exercise programs, no program has been shown to be more successful in improving a patient's activity and participation than another exercise program¹⁷.

The research, as well as results from this case report, impacted future clinical practice in a way that despite a lack of formal diagnosis, a patient can be treated in physical therapy to target specific functional limitations with success. Unique patient characteristics must be taken into consideration when designing a physical therapy intervention, and the program should incorporate aspects of interprofessional interventions to produce the most effective result. In this case report, the combination of baclofen and physical therapy produced this result. Additionally, outcome measures will be utilized on all patients to track progress, but stock will also be placed on patient perception of progress.

Due to the nature of the case report, it is impossible to distinguish whether the observed outcomes were due to either physical therapy interventions or oral baclofen individually or the combination of the two. Therefore, further research is needed in the area of undiagnosed neurological patients and the benefits of participation in individualized physical therapy programs. Although this patient was able to attain functional improvement over this short period of time, the long-term benefit and outcomes of her combined physical therapy interventions and baclofen treatment is unknown. Future research should

explore what dosage of physical therapy guided exercises and baclofen intervention is necessary to evoke long-term functional changes in a patient with an undiagnosed white matter disorder and what specific exercises are most beneficial. A randomized control trial of patients with undiagnosed neurological conditions should be completed with half of the population receiving combination of physical therapy guided interventions and baclofen and half with baclofen treatment alone, with a long-term follow up of 6 months to observe efficacy of treatments on long-term functional outcomes.

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APPENDIX 1

Description of Exercise Interventions and Progressions

Exercise	Description	Progression
Standing Extension Synergy	The patient was in standing with the left foot on a carpet slider. The patient moved the left foot from a neutral position in an arc including hip abduction, external rotation and extension. This was then repeated with the right foot on the carpet slider.	
Peg Board	The patient placed cylindrical pegs into holes on the Purdue peg board and then placed washers on top of the pegs with bilateral hands.	
LE/UE Targeting	Patient began in sitting. Sticky notes numbered 1-5 were placed in front of the patient (on the ground for LE and on the wall for UE). Numbers were then called out and the patient placed corresponding extremity on the identified number.	1) Patient transitioned from sitting to standing. 2) Sticky notes were of varying colors to increase cognitive demand.
Driving Simulation	The patient completed this exercise in sitting. A blood pressure cuff was placed on the floor with a prostretch positioned overtop. The patient was instructed to increase pressure of the blood pressure cuff by altering ankle dorsiflexion and plantar flexion sustained positioning.	Addition of fluctuating "speeds" based off of cuff pressure when called out by therapist at varying time frames.
Proprioceptive Neuromuscular Facilitation	Patient was positioned in supine on mat table. Movement began with PROM of the lower extremity into hip flexion, internal rotation, abduction, knee flexion and ankle dorsiflexion. The movement was progressed to AAROM and to AROM as tolerated by the patient.	
Step Over	Five single point canes were placed parallel to each other in a line on the floor of a hallway equidistant apart. The patient was instructed to begin walking down the hallway and step over each cane with no pause.	Each cane was replaced with a semicircular foam roller to increase height of obstacle.