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Module 5 Part A

**PICO: For individuals recently diagnosed with Multiple Sclerosis (0-3 years) or who have an Expanded Disability Status Scale (EDSS) ≤3.5 (no impairment to walking), does an early intervention of gait training delay or decrease development of gait abnormalities compared to no early intervention?**

**Introduction:**

 Multiple Sclerosis (MS) is a chronic and unpredictable immune mediated disease that leads to demyelination in the central nervous system. Symptoms include weakness or paralysis, changes in vision, numbness and tingling, pain, spasticity, fatigue, bowel and bladder dysfunction, cognitive and emotional changes. Some recent evidence is focused on evaluating disease activity related to these symptoms in individuals who are newly diagnosed.

The results of several studies indicate subtle gait changes can be detected in early MS, even in the absence of clinical disability.1-4,6 Martin et al compared minimally impaired subjects with MS(EDSS 0-2.5), grouped by mild pyramidal signs or no pyramidal signs, to control subjects.1 Both MS groups demonstrated reduced speed and stride length, and prolonged double limb support compared to controls.1 Similar findings were also seen in individuals without functional limitations (EDSS ≤2).2 Subjects with clinically isolated syndrome (1-3 months from first demyelinating event, mild neurological signs, and no functional limitations) demonstrated prolonged double limb support time, differences in step-length, extended step time, and wider base of support compared to controls.3 Sosnoff et al also found persons with MS (EDSS ≤3.5) walk slower, with shorter and wider steps, and spend increased time in double limb support compared to controls.4 Individuals with mean EDSS 1.8±1.2 demonstrated similar changes when jogging including slower self-selected velocity, shorter step length, longer stance phase, and prolonged double limb support.5 Many of these parameters are associated with decreased walking stability.1

Subjects with MS demonstrated altered ankle muscle activation and decreased ankle motion at all gait speeds.1 In subjects with no clinical disability (EDSS ≤1.5), the ankle angle at heel contact was significant different from controls matched by physical activity level.6 Those with clinically isolated syndrome demonstrated reduced knee flexor torque, increased muscle fatigue, and greater asymmetry between plantar flexor and dorsiflexor muscle torque.3 Benedetti et al found altered muscle recruitment, most consistently with sustained tibialis anterior activation and early onset of gastrocnemius activity during stance phase.2 Difficulty with functional reach suggested balance impairment also can begin early in the disease course.1 Early gait and balance changes may be detected without clinical signs of pyramidal dysfunction or clinical impairment.1-3,6

 75% of patients with MS experience mobility impairments.6 This is significant because studies have shown gait changes are associated with disease progression as well as negative impact on QOL.6,7 Studies indicate that self-perceived health status is not related to disease duration or disease course.8 Even subjects with no clinical impairment (EDSS ≤1.5) perceived higher impact on walking, decreased balance and increased fatigue compared to healthy controls.6 These findings support interventions targeting individuals with minimal disability in early disease stages.8 Physical limitations, specifically gait abnormalities, may greatly impact activity, participation, and quality of life.

 This goal of this review is to determine if early intervention of gait training for individuals who are newly diagnosed with MS (0-3 years) and/or those who have minimal disability (EDSS ≤3.5, no impairment to walking) is more effective than no intervention, in delaying or decreasing gait abnormalities. Studies that evaluate interventions related to gait and balance in this specific population will be reviewed. The results of this review will help justify the role of physical therapy in early MS, when clinical disability is minimal. The potential to affect disease progression and improve physical functioning make this a compelling question.

**Literature Review:**

Many factors can influence gait dysfunction in people with MS. While these may be minimal when someone is newly diagnosed with MS, various impairments can affect gait including weakness, spasticity, imbalance, and reduced gait velocity.9 Interventions to improve gait in people with MS have led to improvements of underlying impairments, improvements in gait quality and efficiency, and consequently improvements in activity, participation and quality of life.9 The studies in this review focus on various interventions that target changes in individuals with minimal disability and/or newly diagnosed. Various study designs were used to evaluate areas related to gait impairment for the defined population. All studies include subjects with Multiple Sclerosis, but sample characteristics vary in terms of age, time since diagnosis, and EDSS level (1-6.5). Many of these studies were cohort studies and individuals with MS were monitored pre and post intervention, although two RCTs and two case series were included.10-17

Many measures were used to assess impairments affecting gait, as well as detect subtle gait changes in the reviewed studies. Strength was commonly assessed with dynamometry.10,11 Gait kinematics are commonly measured using advanced technology: force platforms, and reflective marker trajectories can be used to assess gait parameters.10,13-15 Parameters tracked include ground reaction force data, walking velocity, stance time, swing time, step length, base of support, joint kinematics, etc.10,14 A force platform can also be used to assess postural sway and balance.11,15 EMG records can detail muscle activation during gait.15 Gait speed can be measured by 10m walk or 25ft walk tests.11,12,16 6 minute walk test measures endurance.13,17Modified Fatigue Impact Scale (MFIS) is a questionnaire to assess effects of fatigue.17 EDSS was self-reported in one study to measure disability, and assessed by professionals in others.10,11,13 Another measure of disability is the Guys Neurological Disability Rating Scale, which includes subscales such as mobility.17 Many functional measures can assess gait and balance including Timed Up and Go (TUG), Berg Balance Scale, Dynamic Gait Index (DGI), and Mini-BESTest.12,16 Questionnaires such as Activities Specific Balance Confidence Scale (ABC), Multiple Sclerosis Quality of Life-54 (MSQOL-54), MS Walking Scale (MSWS-12), and Multiple Sclerosis Impact Scale 29 (MSIS-29) can expand on the influence of impairments.12,16,17 Energy cost can be measured using spirometry.15 Visual Analogue Scales (VAS) can be used to assess difficulty of various tasks, such as carrying a drink while walking.12 While most of these measures have been validated in MS, limitations still include lack of MCID for some measures, as well as difficulty comparing results when multiple measures can track similar impairments. Current research is evaluating the most reliable measures to detect subtle changes in early MS.

*Resistance training*

There is evidence that resistance training can lead to improved gait and balance (12, 10, 11). An 8-week resistance training program was implemented by 8 participants with MS (EDSS 2.5-5.5) to evaluate the effects on gait kinematics.10 Training focused on lower extremity and trunk strengthening.10 Various gait kinematics that can be affected in early MS were significantly improved including decrease in stance time, and double limb support as well as increases in swing phase, step length, and foot angle.10 Other improvements were seen in self-reported disability, 3-minute stepping, fatigue, and lower extremity strength.10 95 people with MS (EDSS 1-5.5) participated in a RCT of a six-month home exercise program compared to no intervention.11 The HEP also involved aerobic training, but the focus was resistance training.11 Intervention was initiated as subjects were all recruited during inpatient rehab, but weeks 4-26 were home-based exercises with 3-4x/week strengthening sessions and 1 aerobic session.11 Subjects were contacted by phone to monitor adherence. Significant improvements were seen with walking speed and knee flexion strength.11 A case series of 8 individuals evaluated the effectiveness of core stability training on balance and mobility.12 The ability to control the trunk in response to movement can affect balance, especially with reaching and stepping.12 These participants were ambulatory, but had EDSS 4.0-6.5.12 As a group, significant improvements were seen in timed walk, MSWS-12, forward and lateral reach.12 Two subjects were within 1 and 3 years from diagnosis, but would not be classified as minimally impaired; one of the two demonstrated improvements after intervention.12 It is unclear if core strength could affect gait parameters in early MS with less disability, or if this intervention helps once disability has increased. While the interventions are diverse, these various forms of resistance training all lead to improvements in gait parameters, and may be effective in minimizing physical limitations caused by MS.

*Treadmill/Elliptical Training*

 More specific to gait deviations, multiple studies evaluated gait changes after treadmill or elliptical training. Task specific training attempts to improve gait patterns through practicing repeated motions.13 24 subjects with MS (mean EDSS 2.5) were compared to 24 healthy subjects before and after 6 weeks of elliptical training to assess changes in gait parameters and joint kinematics.14 Results indicate subjects with MS significantly altered joint torques at the ankle and hip, and joint power at the ankle during stance.14 Power absorption and generation at the ankle and hip both increased to be equal to the control group.14 This is significant as ankle kinematics can be affected in early MS and can normalize gait pattern. Strengthening of plantar flexors and hip extensors, especially through the elliptical, may be an effective intervention in early MS. A case series of 3 individuals with MS (EDSS 1.5-2.5) evaluates the effect of aerobic treadmill training on walking parameters, muscular activity and postural balance.15 10 sessions over 4 weeks of endurance treadmill training was completed and led to decreased oxygen cost in all 3 subjects, improved postural sway in 2/3, and improved timing of gastrocnemius activation at heel strike in 2/3.15 These improvements are specific to individuals with minimal impairment, although sample size is very small and require further study to generalize results.15 A cohort study of 13 individuals with MS (able to walk 25ft without assistance) completed 6 weeks of body weight supported treadmill training with or without robot-driven orthotic.13 No significant differences were seen between the groups, suggesting the benefit of body weight supported treadmill training alone.13 Improvements in outcome measures were seen in both groups including improvements in timed 25ft walk, 6 minute walk, decrease in percentage of double limb support time, and overall decrease in mean EDSS score.13These findings suggest that task-repetition, potentially with body weight support, on treadmill, or elliptical, can significantly improve gait.13-15 Further research may assess the benefits of treadmill training compared to over ground gait training and other forms of training (resistance training, balance training, etc).

*Community based exercises*

Individuals with minimal disability may be appropriate for community based exercises. Some studies evaluates different community based exercises and the effect on gait and physical functioning. 11 individuals with MS (6 with EDSS ≤3.5, overall sample 4.1±2.1) participated in 5 weeks of kickboxing with pre and post intervention measures to assess balance, mobility, and quality of life.16 Classes were taught by experienced martial arts instructors.16 In applying these results, it’s important that participants wore safety harnesses during exercise.16 Improvements were seen with gait speed, TUG, DGI, Mini-BESTest, and ABC scale, even when analyzing only those with EDSS ≤3.5.16 This intervention affects multiple domains of balance and mobility and may be safe and feasible community option. A RCT involving 242 individuals with minimal gait impairment evaluated the effectiveness of community based exercise interventions.17 Participants were randomized to PT led class, fitness instructor (FI) led class, yoga class, or control group.17 PT exercises focused on resistance exercises both in the clinic and through HEP. FI lead classes were not pre-defined in order to study what a patient may be involved with in the community; they involved aerobic and progressive resistance exercises.17 Yoga included stretching and dynamic weight-bearing exercises.17 Unfortunately the study was not powered to compare groups, although within group differences showed improvements in the MFIS-29 v2 psychological component, as well as the MFIS total and physical subscales for all 3 interventions.17 FI and PT led classes improved with 6 minute walk test.17 Because it is important to help patients stay active when not working with PT, the results of these community based interventions could be good resources.

**Limitations:**

There are several limitations of these studies including small sample sizes, no control groups, little discussions of power, and designs that were not blinded or randomized. While Garrett had 242 participants, there was still not enough power to compare results between groups.17 Other studies ranged from 3-24 participants, and not were newly diagnosed and/or minimally impaired.10,12,13-,15 Because MS affects individuals in variable ways, subject characteristics can be very diverse, so small samples limits the ability to detect change and generalize results. Assessors were not blinded in 4 of the 8 reviewed studies.10-13 While 3 studies had control groups, the other 5 only had an experimental group. Selection bias may also be an issue based on recruitment to some studies.17 It is difficult to directly compare many of these interventions as they use different outcome measures. Despite this, individual studies are able to show positive evidence for several interventions to improve gait. While these limitations decrease the quality of the evidence and the generalizability of the results, many of these studies are asking new questions and guiding new research. These findings can now be used to guide future studies so that results can be validated by larger and randomized studies.

**Clinical Relevance**:

The research regarding early interventions for gait changes is still in preliminary stages, but there are ways to apply this information clinically. While studies showed significant improvements in many ways, it is important to consider that results are not unique to newly diagnosed and/or minimally impaired. Participants with higher EDSS scores often had greater results, although improvement was also made by participants who had little impairment at baseline. It is also important to consider that the level of supervision varied in these studies.

At this point it is difficult to compare the interventions and determine which is most effective and appropriate for specific patients. While various resistance training interventions, community based programs, and treadmill/elliptical protocols lead to improvements in various outcome measures related to gait, these studies need validated by larger randomized controlled trials. Individually these studies can provide us guidance towards treating gait changes in early MS. All of these interventions could be attempted to improve subtle changes. Clinically, these findings emphasize the importance of thorough evaluation of gait and mobility. Health care providers should be aware that gait changes are detectable even in individuals with no clinical disability. It is significant that the reviewed articles demonstrated positive changes, even when baseline impairment is subtle.

Previous studies about MS show exercise has the potential to improve underlying impairments, improve gait quality and efficiency, enhance mobility, and consequently improve activity, participants and quality of life.9 Reviews have demonstrated that resistance exercises, endurance training, and combined training can be well tolerated by individuals with MS.18 Exercise may have an effect on the immune system by increasing concentrations of brain-derived neurotrophic factor and nerve growth factor, as well as increasing antioxidant enzymes which may improve neuroprotection.18 As the understanding of the consequences of early subclinical changes increases, clinicians may begin to follow patients earlier. While some increase in disability is due to disease process, it is also true that as walking becomes more challenging and requires more energy, individuals often become sedentary and deconditioned and disability increases.15 The ability to improve walking as well as promote activity may decrease further disability. Considering the previous evidence about the importance of exercise and physical activity in MS, the findings of subtle gait changes in early MS, and the early preliminary evidence about interventions to improve gait in early MS and/or minimal disability, exercise should be emphasized for those who are newly diagnosed with MS.

**Recommendations for Further Research**:

 Future studies are needed to validate these preliminary findings that early gait training interventions can improve subtle gait changes in early MS. Studies should continue to develop the most sensitive and reliable outcome measures to detect early changes. Further studies may expand the interventions available to improve early gait changes. Additional studies may help understand the implications of early detection of changes. More research can be done to see if those who demonstrate early gait changes would be appropriate for more aggressive management with disease modifying drugs, or if findings could predict future pyramidal dysfunction.1 Related to PT, the ability to detect early gait impairments may help identify individuals appropriate for early PT intervention to optimize function and potentially affect disease course. While there is evidence that interventions can improve specific impairments, long term studies are needed to evaluate the ability of interventions to decelerate or prevent physical disability over time. Mobility issues are common for many people with MS, so the ability to answer these questions will have a significant impact on future treatment of MS.

**Conclusions:**

MS is a chronic and unpredictable diagnosis, in which subtle gait changes may begin to occur even in the absence of clinical disability. This review revealed preliminary evidence that resistance training, treadmill and elliptical training, and various community based interventions can improve measures of gait and mobility, particularly for individuals who are newly diagnosed and/or have EDSS ≤3.5. High quality studies are necessary to validate these findings as well as to better understand the implications of early detection of changes. Previous studies have demonstrated the positive effects of physical activity and exercise for individuals with MS. The ability to affect specific impairments, improve gait quality, enhance mobility, and improve activity, participation and quality of life through exercises suggests this should also be emphasized ­­­­­­ for those newly diagnosed.9,18

*Relation to Capstone*

I am curious about individuals who are newly diagnosed with MS. Several factors have led me this area for the capstone project. Because mobility becomes limited for so many with MS, and is often a concern for people even without clinical disability, it is critical to address early. Often individuals are overwhelmed with information when they are first diagnosed, and they may not begin to work with a therapist until they experience mobility issues. Audrey and I hope to explore the research to understand what changes occur early in MS. With this information we hope to develop a wellness event targeted to individuals newly diagnosed with MS. We hope to share information about various multi-disciplinary topics, and begin to promote physical activity early in the course of the disease.

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