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Improvements in Timing Variables for the Timed Up And Go and Its Subphases Following A Progressive Resistance Training Program

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IMPROVEMENTS IN TIMING VARIABLES FOR THE TIMED UP AND GO AND ITS SUBPHASES FOLLOWING A PROGRESSIVE RESISTANCE TRAINING PROGRAM

By

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THESIS ACCEPTANCE PAGE

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This thesis is approved as a creditable and independent investigation by a candidate for the master's degree and is acceptable for meeting the thesis requirements for this degree. Acceptance of this does not imply that the conclusions reached by the candidate are necessarily the conclusions of the major department.

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To my family— Thank you for always believing in me, your love, and support.

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ABSTRACT

IMPROVEMENTS IN TIMING VARIABLES FOR THE TIMED UP AND GO AND ITS SUBPHASES FOLLOWING A PROGRESSIVE RESISTANCE TRAINING PROGRAM

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Purpose: To evaluate the effectiveness of progressive resistance training (PRT), with the inclusion of balance and stretching exercises, on the timed up and go (TUG) task. Specifically, we investigated the TUG in regard to changes in timing variables for the entire movement and the subphases, in association with muscular strength, ambulation, fatigue, and perceived disability in patients with Multiple Sclerosis (PwMS). **Methods:** Fifteen PwMS volunteered twice weekly for a twelve-week PRT exercise training program. The participants underwent an assessment at baseline (strength assessments using a Biodex dynamometer and one repetition max (1RM); the TUG and its subphases using Qualysis Track Manager; and the six-minute walk test (6MWT) and patient oriented outcome measures (POOMs). In subsequent sessions, the strength training intervention was conducted. Following the intervention, baseline assessments were re-performed to establish post training values. **Results:** Muscular strength showed an increased percent change for isometric testing (11% for the left leg and 5.5% for the right leg). Isokinetic variables improved for both testing parameters, as well as the 1RM for the leg press ($p \leq 0.05$). Total TUG time decreased by (8%). The sit to stand phase significantly improved (22%) as evidenced by an improvement in trunk flexion (18.5%) and rise time (24.6%). Timing from the start of the movement to the three-meter mark improved significantly (12.8%). Self-reported fatigue and patient reported affliction from MS also decreased ($p \leq 0.05$) following the intervention. **Conclusion:** PwMS are capable

of making positive changes in the timing variables for the TUG by increasing muscular strength following a PRT program. These changes are associated with improved QOL and decreased fatigue.

MANUSCRIPT

INTRODUCTION

Multiple Sclerosis (MS) is a progressive and disabling neurologic disease resulting in various amounts of damage to the myelinated axons of the central nervous system (CNS).[1] The demyelination of the nerve tissue can produce a wide variety of symptoms that may hinder both physical and cognitive function.[2] Common symptoms exhibited by patients with multiple sclerosis (PwMS) relating to physical activity include excessive fatigue, muscular weakness, spasticity, and impaired balance.[3] As a result, many PwMS present with a decreased ability to perform functional movements and will exhibit changes in movement patterns. Studies have found adaptions in movement patterns in PwMS during various tasks including the sit to stand[3-5], walking gait[6-9], timed functional tests[5 10], and balance[11]. This limited ability to successfully complete functional movements may decrease the ability of PwMS to complete activities of daily living (ADLs) that are required for independence.[12] Thus, developing strategies for improving the functional movement patterns in PwMS is of high importance as the disease is the most common cause of non-traumatic disability in young adults, affecting over 2.5 million people worldwide.[13]

There are numerous clinical assessments designed to assess functional mobility and gait in various populations with pathological conditions. The Timed Up and Go (TUG) test is a widely used, clinical testing measure and has been recommended by the Multiple Sclerosis Outcome Measures Task Force for use in assessing gait/walking ability, possible fall risk, quality of life (QOL), and disability.[14] The TUG task is unique in that it requires participants to perform multiple basic activities including standing up from a chair, walking forward, turning around, walking back to the chair, turning, and sitting down. Conventionally, TUG is assessed by evaluating the total time to complete the entire movement; with a longer completion time being linked to higher levels of impaired mobility, decreased QOL, and an increase risk of falling in PwMS, Parkinson's and stroke.[15] More recently, research has focused on investigation of the subphases of the TUG movement in the frail, elderly, and neurologically impaired population such as PwMS and Alzheimer's. [5 16-22]Results of these studies have found that impaired populations exhibit longer total time to completion in each subphase[16 18-20], decreased angular velocity at the trunk[16-19], knee[5] and hip[5], balance[20], and altered gait parameters—including slower gait speeds, increased cadence, longer support phases, and shortened stride length[16-18 21 22], as compared to healthy controls.

Commonly in PwMS, reductions in strength have been associated with impairments in functional movement patterns and strongly associated with gait and balance difficulties.[23] To address this concern, various studies have investigated the effect of resistance training on PwMS in terms of adaptions in muscular strength and in association with functional movement patterns.[2 12 24-32] The general findings from these studies suggests that muscular strength will improve following a resistance training program. However, the results regarding changes in other parameters such as walking ability[24 27 29], gait speed[24 27], functional mobility[12 25 28], and balance[2 32] were ambiguous between studies. Of particular interest, the effects of resistance training on the TUG test have yielded inconsistent results with some studies showing improvement in the TUG task[29 32-37] and others reporting no significant difference[2 28]. To our knowledge, an investigation of the effects of resistance training in regard to the subphases of TUG has yet to be conducted. Thus, the primary purpose of this study was to evaluate the effectiveness of progressive resistance training (PRT), with the inclusion of balance and stretching exercises, on the TUG task. Specifically, we investigated the TUG in regard to changes in timing variables for the entire movement and the subphases, in association with muscular strength, ambulation, fatigue, and perceived disability. Following a PRT intervention, we hypothesized that PwMS would display increased muscle strength. Subsequently, we hypothesized that PwMS would also complete the TUG in less time following the intervention. Additionally, we hypothesized that PwMS would display improvements in the time to completion for all subphases of the TUG movement— sit to stand, gait/walking, turning, and stand to sit. Lastly, we hypothesized further walking distances for the 6MWT, reduced fatigue, decreased disability, and improved quality of life following the intervention. The result of this study will help clinicians and health care providers to establish effective treatment and rehabilitation programs to increase functional mobility, decrease fatigue, and improve overall QOL in PwMS.

METHODS

The data for this study was derived from a larger overall study conducted from Sep 2015-Oct 2017 investigating the effects of a progressive resistance training program on movement mechanics, balance, strength, and muscle activation in PwMS. As our study focuses on the changes in timing variables for the TUG, the subset of data from the functional movement and strength categories were extracted, analyzed, and reported. In addition, any secondary outcome measures that could help explain our findings are also reported.

Participants

Fifteen PwMS (age= 49±10.12yrs, height=1.68± 1.0m, mass=79.64± 21.44kg, sr-EDSS=3.83±2.18) suffering from relapsing-remitting multiple sclerosis (RRMS) participated in this study. A medical health questionnaire was completed by each participant to ensure safety and qualification for the study. To be included, participants were required to be 18 years of age or older, have physician approval, a physician diagnosis of RRMS, able to walk unassisted for twenty feet in a controlled environment, and an expanded disability status score (EDSS) of <6.5. Continued use of pharmacologic therapy consisting of disease modifying drugs (interferon beta 1α and 1β) was acceptable— although the participants could not have started a new prescription drug within the previous three months of the study. Exclusion criteria included any participant who was pregnant; had orthopedic limitations of the lower extremity or trunk that prohibited ambulation or sit-to-stand; or had used prednisone or other steroids for MS flare ups during the previous three months. All participants provided written informed consent as approved by the local institution human subject's review board.

Participants were recruited from the Brookings, SD and Sioux Falls, SD communities and MS support groups. Recruitment occurred through word of mouth and in association with Avera McKennan Hospital and University Health Center in Sioux Falls, SD who provided our contact information to patients with MS being seen in their clinics. Additionally, informational sheets were sent to local physicians to assist in recruitment. Incentive to participate in this study included a fifty-dollar Amazon gift card.

Instrumentation

For the TUG test, eight high-speed cameras (Oqus 3+, Qaulisys Inc., Gothenburg, Sweden) were used to capture the motion and identify critical events and timing variables of the movement. Three force plates (Advanced Mechanical Technology Inc., Watertown, MA, USA) were used to identify seat off, gait initiation, seat on, and gait termination during the TUG. A Biodex dynamometer (System Quickset 4, Biodex Medical Systems Inc., Shirley, NY, USA) was used to assess lower extremity muscular strength. A Cybex® leg press machine (Cybex International Inc., Medway, MA, USA) was used for the one repetition max (1RM). A flat, 30-meter walkway, measured with a tape measure, was used for the Six-Minute Walk Test (6MWT). Brightly colored cones were placed at the end of the walkway at the 30m mark and had chairs for resting if necessary.

Procedures

This study consisted of six data collection sessions (3 pre-intervention and 3 post-intervention). The intervention portion of the study lasted twelve weeks with sessions occurring twice per week on non-consecutive days. All testing sessions were conducted in either the Human Performance Lab or Biomechanics Laboratory on a university campus. The intervention sessions took place in the Exercise Science resistance training lab at South Dakota State University in Brookings, SD or the Orthopedic Institute's Physical Therapy clinic in Sioux Falls, SD, depending on travel distance. All data collection sessions occurred within the span of a week, with a minimum of 48 hours of rest between visits.

An informed consent form was completed by all participants prior to starting testing or intervention sessions. The pre-intervention testing sessions were conducted in a randomized order for each participant. Sessions included 1) The Timed-Up-and-Go test - to assess functional movement; 2) Biodex testing- to assess lower extremity muscular strength; 3) Six-Minute Walk Test (6MWT) and Patient Oriented Outcome Measures (POOMS)- to assess ambulation, fatigability, and the participants perceived impact from MS. These same three testing sessions were repeated in randomized order within one week of completing the twelve-week intervention. The 1RM for leg press was tested during the first and last weeks of the training intervention.

Timed Up and Go Testing Session-

High speed motion capture (200 Hz) and ground reaction forces (1000 Hz) were used to evaluate the TUG. After familiarizing participants on what they would be doing during this session, retro-reflective markers were placed on bony landmarks of the lower extremity and trunk; with clusters placed on the upper and lower legs, and trunk (C7; Left acromion; Right acromion; sternum; T10; L5/S1; sacral cluster top, left, right; thigh cluster- top medial, top lateral, bottom medial, bottom lateral; lower leg/shank cluster- top medial, top lateral, bottom medial, bottom lateral; proximal heel; distal heel; distal shoe; lateral heel; 2nd metatarsal head.) After placing the markers on the participants, the participant was instructed on how to perform the TUG trials.

The set up for the TUG included a height adjustable chair, placed on a force platform, set to a height that created a 90° angle at the knee. Tape was placed on a second and third force plate to ensure that the starting position for the feet was shoulder width apart and foot position remained consistent for each trial. A piece of tape was placed three meters from the chair to mark the spot where the participant would turnaround and walk back to the chair. To perform the movement, the participant was instructed to stand up from a seated position, walk three meters, turn around, walk three meters back to the chair, and sit down. The participants were asked to keep their arms crossed and try to limit shifting their feet backwards while moving from the seated to standing position. The

FIGURE 1. Chair and GRF platform set up

TUG was performed 5-10 times at a self-selected speed with a minimum of two minutes between trials. For safety purposes, an investigator remained in close contact to the participant while the trial was performed. A visual representation of the set up for the TUG is shown in Figure 1 and Figure 2.

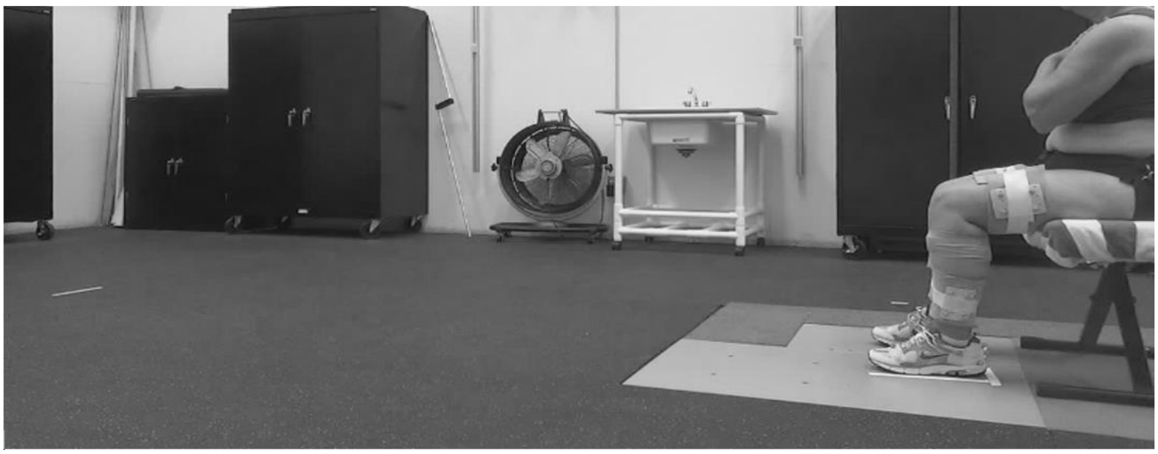

FIGURE 2. TUG test set up and patient positioning

Biodex Testing Session-

For the Biodex muscular strength test, participants were seated in the dynamometer chair. The chair was adjusted to ensure that the patient's trunk was flat against the seatback and the posterior aspect of the knee was two finger widths from the chair while flexed at 90°. The axis of the dynamometer was positioned at the lateral epicondyle for the testing limb. A strap was position around the lower shank of the testing limb at the bottom portion of the gastrocnemius. Additional straps were placed over the thigh, hips, and shoulders of the participants to prevent unwanted movement during testing. The participants performed three maximal isometric and three isokinetic leg extensions, for each of the testing velocities, bilaterally. Testing order was randomized for each participant. Isometric trials were conducted with the knee positioned at 90°. The participant was instructed to push against the dynamometer with maximal force for three consecutive seconds. For the isokinetic knee extension trials, participants started at 90 degrees of knee extension and extended their knee 60 degrees at two different velocities, 60 and 90 deg/s. A minimum rest period of two minutes was given between each trial for all strength tests.

Six Minute Walk Test (6MWT) and Patient Oriented Outcome Measures (POOMs)-

To assess ambulation and fatigue, participants performed the 6MWT. The walking surface was flat and consisted of a walkway that was 30 meters in length. The end point for the walkway was marked with cones and had chairs for resting. The participants were asked to walk as far as they could for six minutes. The use of assistive devices was allowed, and participants were provided the ability to rest at any point throughout the six minutes. The participants total distance covered in six minutes was recorded and used for assessment. Following the 6MWT, three POOMs questionnaires including the Self-Reported Expanded Disability Status Scale (sr-EDSS), the Multiple Sclerosis Impact Scale-29 (MSIS-29), and the Modified Fatigue Impact Scale (MFIS- 5 item version) were completed by the participants.

Intervention

Participants completed a combination of resistance, balance, and stretching exercises during the 12-week intervention. Two 60–90-minute sessions were performed twice per week on non-consecutive days. In week one, participants were familiarized to exercises and completed a one-repetition maximum (1RM) protocol for each resistance exercise. The resistance exercises included, single leg curls and extensions, leg press, calf raises, bench press, military press, lat pull down, and seated row. Prior to the 1RM, participants performed a warm-up by completing 10-12 submaximal repetitions, beginning at a weight that was approximately 50% of their perceived maximal effort for each lift. Weight was progressively increased by 5-10lbs until the participant could no longer complete the repetition with full ROM.

During weeks 2-11, supervised exercise training sessions were conducted. Prior to starting exercise, participants warmed up for 5-10 minutes using a cycle ergometer. For the selected resistance training exercises, following standard American College of Sports Medicine (ACSM) training guidelines[38], participants performed two sets of 10-15 repetitions at 60%-80% of their 1RM for each exercise with 2-5 minutes of rest between sets. When the participants were able to perform all repetitions for both sets for two consecutive sessions, resistance was increased by 2-5% for that exercise.[12] Balance exercises were included in each training session and consisted of standing on a foam pad while maintaining balance for both mediolateral and anteroposterior perturbations. Stretching exercises for each session included two, 30 second static stretches to each of the major muscle groups. In the final week of the intervention, the 1RM protocol was performed again to obtain post training values.

Data Analysis

For the TUG trials, the reflective markers were labeled using *Qaulysis Track Manager* Software (Oqus 3+, Qualisys Inc., Gothenburg, Sweden) then exported into Visual 3D (v.5, C-Motion Inc. Germantown, MD, USA). A 4th order recursive lowpass Butterworth filter with a cutoff frequency of 50 and 6 Hz was used to filter ground reaction forces and marker trajectories, respectively. The data was then exported into a custom-made LabVIEW program (v. 2015, National Instruments, Austin, TX, USA) where timing variables of the TUG were calculated. In addition to the total TUG time, the TUG was divided into several different phases. The following critical events were identified and used to divide the movement into various phases. The critical events are defined as follows:

Start of movement: The instant the trunk started to move into flexion

Seat off: The instant the vertical force for the force plate under the seat dropped below 10 newtons.

Gait Initiation (GI): The instant the vertical force of either of the plates the participant was standing on went below 10 newtons

Start of Turn: The instant both acromion markers anterior/posterior position were greater than 2.75m from the seat.

End of Turn: The instant when both acromion markers position was less than 2.75m from the seat.

End gait: The instant the vertical force from either force plate reached 10 newtons.

Seat On: The instant the vertical force of the force plate placed under the seat reached 10 newtons.

End of movement: The participant was seated, and the trunk stopped extending.

The TUG was divided into the following phases and sub-phases:

Sit-to-stand: Start of movement to Gait initiation

Trunk flexion: Start of movement to Seat off

Rise: Seat off to Gait initiation

Forward gait: Gait initiation to Start of turn

Turn: Start of turn to End of turn

Return gait: End of turn to End gait

Turn and sit: End gait to End of movement

Turn and descend: End of gait to Seat on

Trunk Extension: Seat on to End of movement

Timing variables of interest included, total TUG time, time spent in each phase and sub-phase of the TUG, total gait time, time from start to three meters, and time from three meters to the end of the movement. Time will be reported in both absolute time and as a percentage of the total TUG time. The average value for all timing variables across the five TUG trials was calculated and used for statistical comparisons. Figure 3 provides a visual of each of the phases of the TUG.

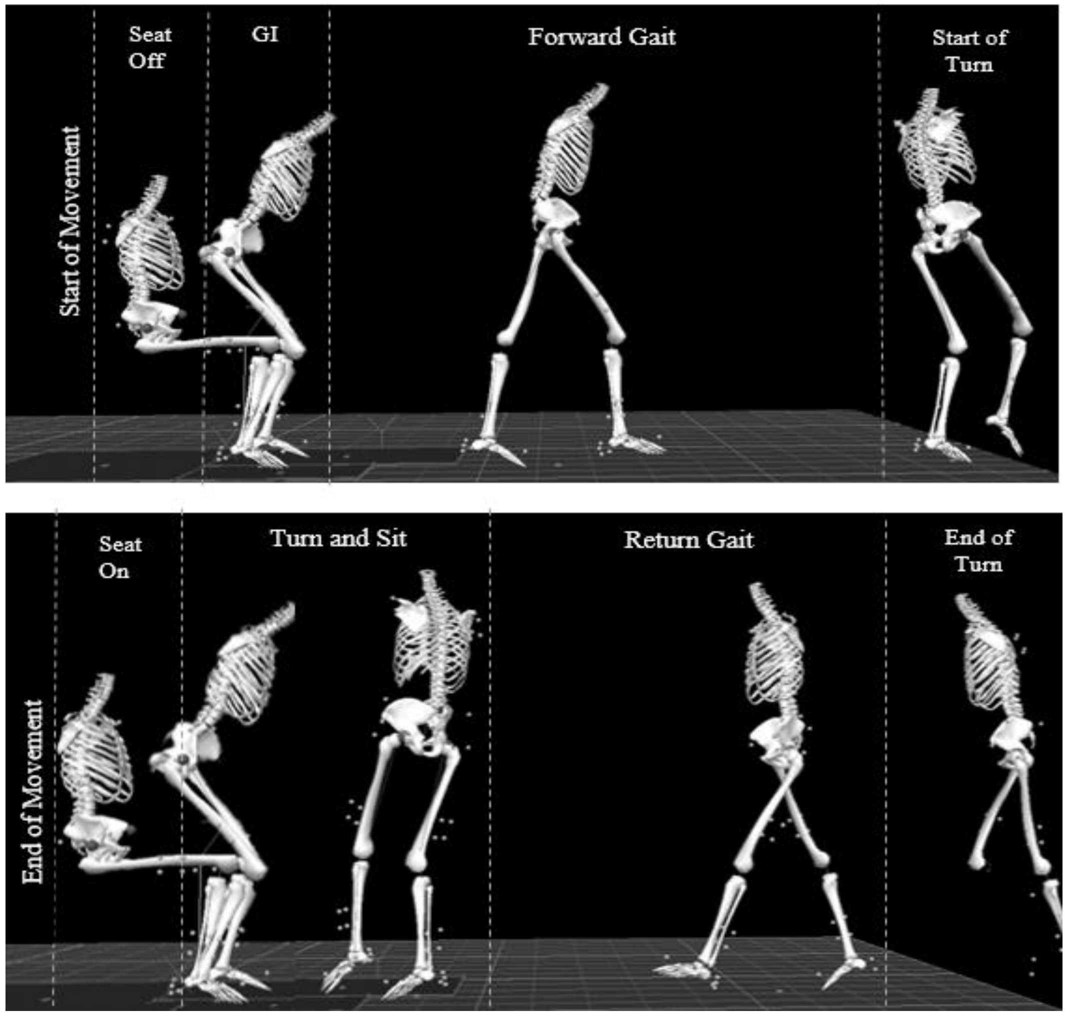

FIGURE 3- Diagram of TUG movement separated into subphases

For the Biodex, bilateral peak torque data for all testing parameters was exported from the dynamometer software. The highest value for each condition was used for the pre-post comparisons. Peak torque for both the right and left limb were scaled to body mass. This method has been proposed by Schilling et al as body weight is the most common load encountered during ADLs; thus, it is a better indicator of functional mobility.[36]

For the 1RM, the amount of weight pressed during the 1RM for the leg press exercise was obtained from the participants data collection sheets. The data was scaled to body mass. For the 6MWT, the total distanced walked for each participant was recorded. Lastly, for the POOMs, the questionnaires were scored and totaled.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Science (SPSS) software. Paired sample t-tests were used to determine pre-post differences for each of the variables of interest. The output was graphed for visual representation when applicable. For all variables, a significance level of $p \leq 0.05$ was utilized. The percent change and effect sizes (Cohen's *d)* were also calculated.

RESULTS

Participants-

Fifteen participants (2 male, 13 females; age, 49 ± 10.12 yr; height, 1.68 ± 0.09 m; mass, 79.64 ± 21.44 kg; sr-EDSS, 3.83 ± 2.18) completed the study.

Muscular Strength-

All strength measures were scaled to body weight. For isometric measures, only strength measurements for the left limb reach statistical significance (*p*=.021). For the left leg, isometric peak torque improved by 11.27%. No significant difference in the right limb was detected. For isokinetic measurements, both limbs showed a statistical difference for all testing parameters. In the following order (90, 180 degrees/second), left peak torque increased by 20.05%, and 17.34%. For the right limb, both velocities also showed a significant difference. A gain in peak torque of 10.58% at 90° and 12.10% at 180° were found.

TABLE 1. Biodex Strength Data (Scaled to Body Weight)

Variable	Tested Limb	Pre Mean (SD)	Post Mean (SD)	Mean Difference (SEM)	*p-value*	*d*	% Increase
Isometric	Right	1.19 (0.55)	1.26 (0.51)	-0.07 (0.19)	0.207	0.34	5.51
	Left	1.10 (0.55)	1.22 (0.57)	-0.12 (0.19)	0.021*	0.67	11.27
Isokinetic 90°	Right	0.85 (0.43)	0.94 (0.42)	-0.09 (0.16)	0.049*	0.56	10.58
	Left	0.73 (0.40)	0.88 (0.42)	-0.15 (0.18)	0.008*	0.80	20.05
Isokinetic 180°	Right	0.65 (0.36)	0.73 (0.35)	-0.08 (0.11)	0.018*	0.69	12.10
	Left	0.58 (0.34)	0.68 (0.32)	-0.10 (0.13)	0.012*	0.75	17.34

* indicates significant difference from pre-intervention ($p \leq 0.05$)
SEM, standard error of the mean difference

The average 1RM for the leg press was scaled to body weight. The difference in the means reached statistical significance (pre=1.32BW, post=1.61BW; $p<0.01$; $d = 1.65$; % change=22%)

Tug Timing Variables-

Table 2 presents the pre-post changes in timing variables following the intervention. Total TUG time significantly improved by 1.44 seconds (8.32%) following the intervention. In regard to the phases of the movement, the sit to stand phase showed improvement by 0.48 seconds; thus, increasing overall performance in terms of time to completion by 22.4%. This is evidenced by an improvement in trunk flexion (18.5%) and rise time (24.6%). Additionally, the start of the movement to the three-meter mark also showed a significant reduction in time by 0.72 seconds or 12.8%. No other significant differences in absolute TUG timing variables were detected.

TABLE 2. Absolute Pre-Post changes in timing variables.

Timing Variable	**Pre mean(SD)**	**Post Mean(SD)**	**Mean Difference (SEM)**	***p*-value**	***d***	**% Change**
Total TUG Time	17.3 (6.22)	15.9 (5.04)	1.44 (2.48)	0.04*	0.58	8.32
Trunk flexion	0.85 (0.25)	0.69 (0.08)	0.16 (0.25)	0.03*	0.63	18.5
Rise	1.30 (0.76)	0.98 (0.60)	0.33 (0.41)	0.01*	0.79	24.9
Forward gait	3.47 (1.36)	3.23 (0.95)	0.24 (0.63)	0.16	0.38	6.9
Turn	2.67 (1.34)	2.66 (1.22)	0.01 (0.86)	0.97	0.01	0.3
Return gait	2.27 (0.64)	2.20 (0.68)	0.07 (0.25)	0.32	0.26	3.0
Turn and descend	5.70 (2.51)	5.09 (2.42)	0.60 (1.71)	0.19	0.35	10.7
Trunk Extension	1.06 (0.31)	1.01 (0.30)	0.05 (0.27)	0.52	0.17	4.3
Sit-to-stand	2.15 (0.93)	1.67 (0.64)	0.48 (0.60)	0.01*	0.81	22.4
Turn and sit	6.75 (2.58)	6.11 (2.34)	0.65 (1.77)	0.18	0.37	9.6
Start of Movement to 3M	5.62 (2.25)	4.90 (1.51)	0.72 (1.12)	0.03*	0.64	12.8
3M to End of Movement	9.02 (3.18)	8.31 (2.96)	0.71 (1.88)	0.16	0.38	7.9
Combined Gait	5.74 (1.96)	5.43 (1.61)	0.80 (0.21)	0.16	0.38	5.3

* indicates significant difference from pre-intervention (P=0.05, respectively)
SEM, standard error of the mean difference

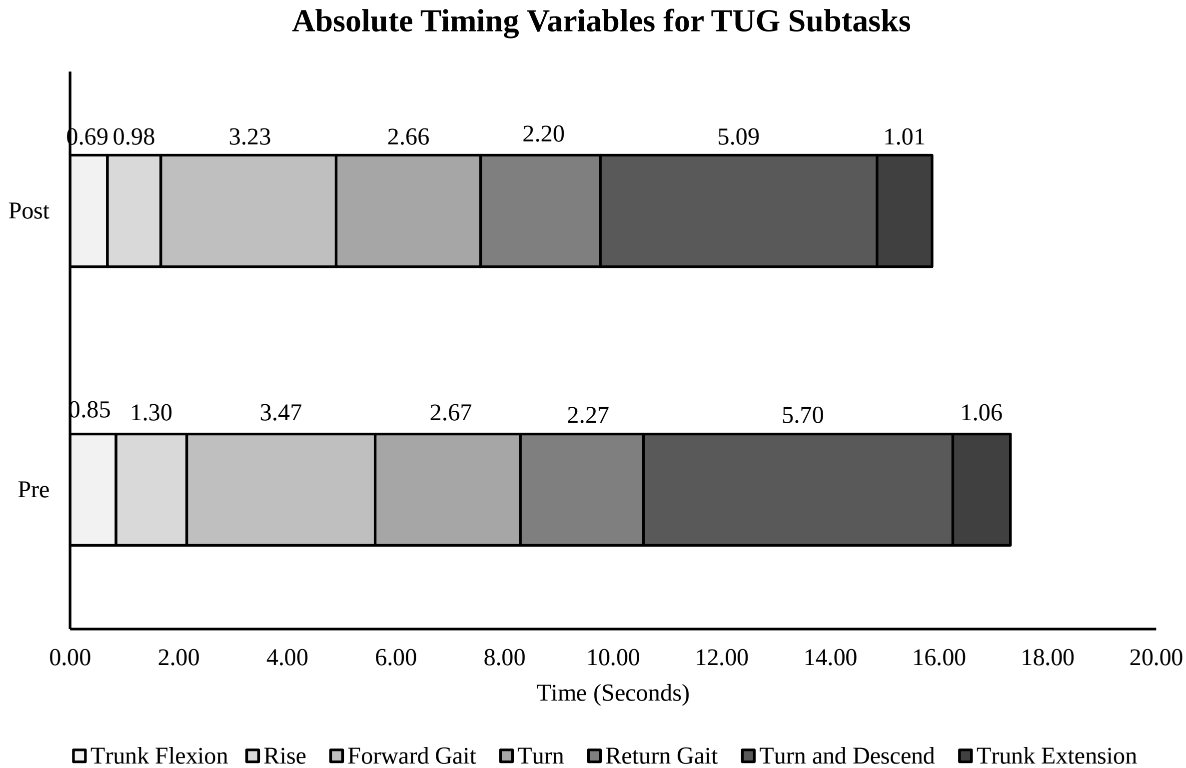

FIGURE 4- A comparison of completion time for each sub following a PRT intervention

Timing variables were also investigated in terms of the average percent of the time spent in each subphase relative to the total movment. Following the intervention, participants spent a significantly less percentage of time in the rise phase of the movement, decreasing the percent of time by 17%. In association, a significant reduction in the sit to stand phase was also detected with a reduction of 14%. Additionally, the participants spent a significantly larger percentage of time in combined gait. No other subphases, relative to total TUG time, displayed significant differences as shown in Table 3.

TABLE 3. Average Percentage of Time Spent in Each Subphase of the TUG

Variable	Pre mean(SD)	Post mean(SD)	Mean Difference (SEM)	*p-value*	*d*	% change
Trunk Flexion	5.15 (1.42)	4.66 (1.09)	0.49 (1.08)	0.10	0.45	-9.54
Rise	7.16 (2.23)	5.96 (1.76)	1.20 (1.87)	0.03*	0.64	-16.8
Forward Gait	20.0 (1.49)	20.5 (1.29)	-0.51 (1.09)	0.09	0.47	2.53
Turn	15.5 (4.60)	16.9 (4.94)	-1.36 (5.90)	0.39	0.23	8.79
Return Gait	13.4 (1.39)	13.9 (1.19)	-0.51 (1.36)	0.17	0.04	3.80
Turn and descend	32.1 (6.24)	31.0 (7.26)	1.12 (7.21)	0.56	0.16	-3.48
Trunk extension	6.61 (2.09)	7.04 (2.83)	-0.43 (1.65)	0.33	0.26	6.50
Sit to Stand	12.3 (2.36)	10.6 (1.75)	1.69 (2.22)	0.01*	0.76	-13.74
Turn and Sit	38.7 (5.61)	38.1 (6.04)	0.69 (7.02)	0.71	0.10	-1.78
Start of Movement to 3M	32.3 (2.93)	31.1 (2.27)	1.18 (2.45)	0.08	0.48	-3.66
3M to End of Movement	52.2 (5.81)	51.9 (6.21)	0.18 (6.67)	0.92	0.03	-0.34
Combined Gait	33.4 (1.20)	34.5 (2.08)	-1.02 (1.85)	0.05*	0.55	3.04

* indicates significant difference from pre-intervention (*p*≤0.05, respectively)
GI- Gait Initiation
3M, 3-meter mark
SEM, standard error of the mean difference

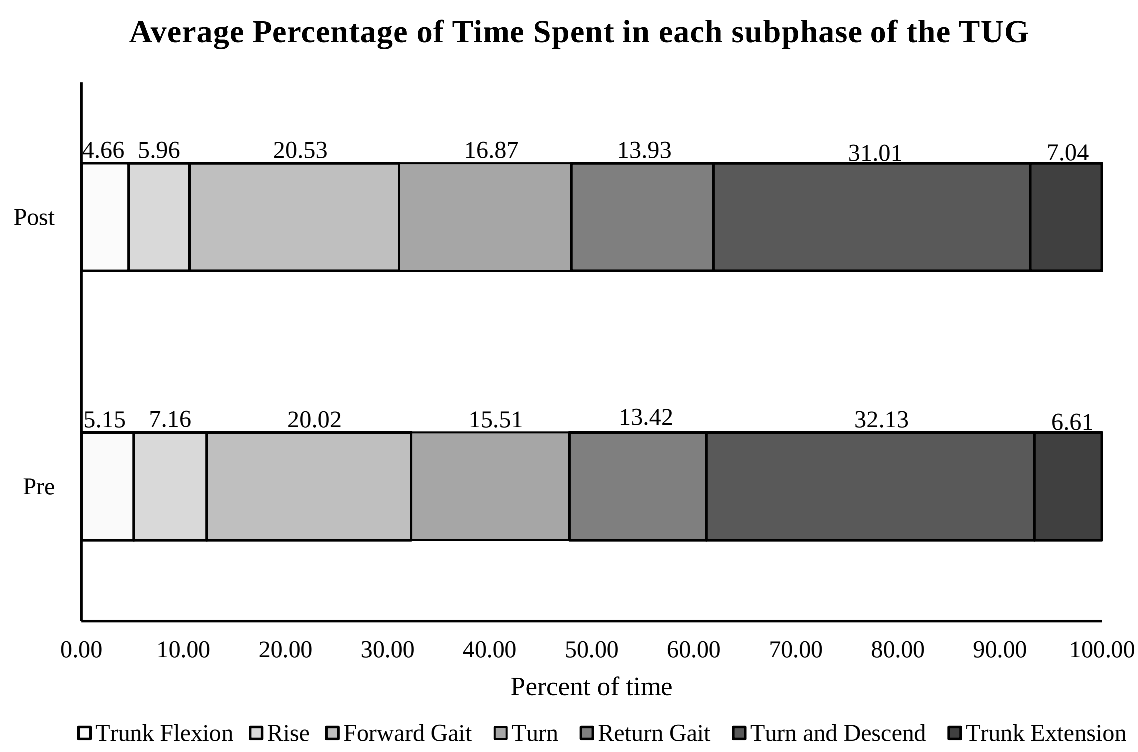

FIGURE 5- Average Percentage of Time Spent in Each sub-phase of the TUG

Patient Oriented Outcome Measures (POOMs)-

The MFIS-5 and MSIS were used to assess fatigue and perceived affliction from MS following the twelve-week intervention. There was a significant difference for both outcome measures. For the MFIS-5, participants noted an average reduction in fatigue levels by 20%. For the MSIS, a 25% improvement was observed following intervention. There was no change observed for the sr-EDSS values.

TABLE 4. Patient Oriented Outcome Measures

Variable	**Pre Mean (SD)**	**Post Mean (SD)**	**Mean Difference (SEM)**	***p-value***	***d***	**% Reduction**
sr-EDSS	3.83 (2.18)	3.63 (2.13)	0.20 (0.70)	0.29	0.28	5.22
MSIS	58.7 (24.6)	46.8 (15.1)	11.93 (17.13)	0.02*	0.70	24.7
MFIS-5	7.80 (4.54)	5.87 (4.17)	1.93 (2.87)	0.02*	0.67	20.1

* indicates significant difference from pre-intervention ($p \leq 0.05$, respectively)
Sr-EDSS, Self-reported Expanded Disability Severity Scale
MSIS, Multiple Sclerosis Impact Scale
MFIS-5, Modified Fatigue Impact Scale
SEM, standard error of the mean difference

Six-Minute Walk Test (6MWT)-

The 6MWT test was used to assess ambulation and fatigability of the participants. The difference in the means reached statistical significance (pre=355m, post=384m; p=0.04; = 0.59; % change=8.2%).

DISCUSSION

The purpose of this study was to examine the effect of a progressive resistance training program, that also included balance and flexibility exercises, on the timing variables for the TUG. Using a repeated measure design, the participants served as their own controls for the intervention. Specifically, our study aimed to analyze the subphases of the TUG to determine which phases of the movement elicited change following a resistance training intervention. Following a PRT intervention, we hypothesized that PwMS would observe improvement in the overall time to complete the TUG task. Additionally, we postulated that PwMS would observe improvements in the time to completion for all subphases of the TUG movement— sit to stand, gait/walking, turning, and stand to sit. Lastly, we speculated that muscular strength would increase; ambulation would improve as addressed by the 6MWT; and fatigue, QOL, and disability status would improve, as reflected in the POOMs.

Muscle weakness, particularly noted in the lower extremity, is a common symptom in PwMS and has been associated with reduced functional capacity, fatigue, and increased disability.[12] Additionally, muscle weakness and fatigue are main contributors in the reduction of physical activity in PwMS.[27] This reduction likely leads to inactivity, which may further deteriorate muscle mass and decrease the individual's ability to perform daily activities (ADLs). Without intervention, this pattern is likely to continue and may lead to a negative cycle of deterioration associated with a downward spiral of health. As such, establishing interventions that aim to increase functional mobility, muscular strength, and overall perceptions of fatigue are of high importance.

Given this, the TUG test was utilized in this study as our primary clinical outcome as it is a functional assessment of movement and disability.[14]

Muscular Strength-

Our findings regarding improvement in isometric muscular strength are consistent with findings in the literature. Specifically, the percent change noted for the isometric contraction bilaterally (right=5.5%, left=11%) were within the ranges noted in the literature, with reports of 7%[12 27]and16%[25 31] increases in unilateral lower limb strength following a resistance training intervention in PwMS. The isokinetic strength data showed significant changes at 90°/s and 180°/s bilaterally. These variables are highly relevant to the participants ability to perform the TUG test as the movement requires adequate angular velocity of the knee to complete the task more quickly.

The 1RM max for the leg press was chosen as it most resembles the movement for the sit to stand phase performed in the TUG.[36] The results from our study indicate a significant increase in leg press 1RM strength by 22%. This is consistent with previous studies that have analyzed 1RM max leg press strength data following a resistance training program in PwMS and other neurologically impaired populations, such as Parkinson's.[24 25 29 36] Similar to our results, leg press 1RM strength improved significantly with increases of 17-37%.[24 25 36]

The effect of the PRT program and increased muscular strength may produce multiple positive adaptions in PwMS including improved physical performance, enhanced motor control, and increased independence. Additionally, strength training and exercise have the ability to elicit positive adaptations in the overall health. Furthermore, increased muscular strength may affect the perceived impact of MS by improving functional movement and decreasing fatigue; thus, improving quality of life in PwMS.

Total TUG and the Subphases of TUG-

The improvement noted in muscular strength for both the Biodex and the 1RM are of high importance as they play an influential role on the TUG and its subphases. Following the intervention, total TUG time decreased by 8%. The reduction in completion time is likely due to the increase in muscular strength. Our results are consistent with previous studies that likewise found significant decreases in the total TUG time in PwMS who increased lower limb strength through participating in a resistance training program.[24 29 32-35 37 39 40]

The sit to stand phase of the TUG, including both trunk flexion and rise time, showed the largest change in our study. The improvement in this phase is highly relevant to the functional movement of PwMS considering the sit-to-stand movement is the most mechanically demanding and common ADL.[5] Specifically, our study noted an overall improvement in the time to perform the sit to stand task by 22.4%. Additionally, the percentage of the total TUG time spent in the sit to stand phase was 14% less following the intervention. This improvement is likely due to the increase in muscular strength. Bowser et al. noted that PwMS who demonstrated increased lower limb strength and more effective movement patterns are able to perform the sit to stand task faster than participants with weaker limbs.[3] In addition, Bowser et al. also reported that rise time was slower in patients with leg weakness. As leg weakness inhibits the ability to rise from a seated position, the improvement in rise time by 25% noted in our study is likely a result of an increase in lower limb strength. To further support this idea, Witchel et al. found that a decreased angular velocity of the thigh, that produced a decreased ability to perform the sit to stand, was likely associated with knee extensor weakness.[5] Trunk flexion is also included within the sit to stand movement. On average, following the intervention, participants decreased trunk flexion time by 19%; thus, performing the task more efficiently. In a previous study, enhanced trunk movement, as assessed by the trunk impairment scale, was related to good balance, mobility, and walking ability.[41] Thus, the improvement in the time to complete the trunk flexion phase may be associated with better movement mechanics.

When investigating gait parameters, compared to healthy controls, PwMS tend to display decreased gait speed, increased cadence, increased support time, and shortened step length while walking. These variables have been shown to improve following resistance training in previous studies. Gutierrez et al. found that after an 8-week training intervention, stride length, step length, and time spent in support improved due to increased muscular strength.[27] In contrast, Dodd et al. reported no change in gait parameters following a ten-week resistance training program.[24] The latter study is consistent with our findings. Following intervention, both the separate and combined gait timing variables improved marginally; however, they did not reach statistical significance. In our study, timing variables for gait were investigated both separately (forward gait and return gait) and combined (forward gait + return gait) to assess the change in timing for the gait phases of the movement. The percentage of time spent in the combined gait phase relative to total time was significantly different. This finding can be explained in relation to the enhanced performance noted in the sit to stand phase. Due to the ability of the participant to perform the sit to stand task more efficiently, as noted by a faster completion time, the percentage of time spent in combined gait relative to total time is expressed as a longer percentage for the movement. Despite the increase in percentage, the percent increase does not equate to an increased total time for gait completion as the gait timing variables were not statistically different following the intervention as seen in Table 2. Additionally, the time from start of the movement to the three-meter mark also reached significance. Although it is possible that the ability to ambulate and some gait parameters may have been improved; as noted by the increased distance for the 6MWT, it is more likely that the overall enhanced TUG performance for this phase was due to the faster sit to stand phase.

To perform the TUG correctly, sufficient balance is needed. Although balance is needed throughout the movement, the phases that encompass a turn, may require considerably greater balance. For the turn phases in our study, no significant differences were found. Although not significant, the sit and descend phase showed marginal improvement. Weiss et al. found that a decreased ability to transition between the stand to sit phase is indicative of a worse TUG performance and poorer motor function in cognitively impair populations.[19] Hence, the improvement in muscular strength noted in this study may account for the minimal improvement in the turn and descend phase. The first turn performed in the TUG task remained unchanged following intervention. The reason for this observation is not clear. Previous studies have investigated balance in PwMS following a resistance training program without the inclusion of specific balance exercises and found no improvement.[2 29] However, Cakt et al. found that balance did improve following a combined cycle ergometer resistance training and balance program. In the referenced study, multiple functional balance exercises were performed for 20-25 minutes consisting of balance board exercises, retro walking, toe walking, leaning to the sides, and lower-body plyometric exercises.[42] In our study, only one balance exercise was included. Thus, it is possible that the inclusion of more balance exercises and more time spent working on balance are needed to elicit a change.

6MWT, POOMs, Fatigue, and Perceived Disability-

The observed strength improvement found in our study also has an influence on fatigue and disability status. Fatigue and disability status, as reported by the POOMs questionnaire, confirmed our hypotheses by observing an improvement in the 6MWT, MSIS-29, and MFIS-5. Similar to previous studies, our study confirms that resistance training has a positive effect on perceived fatigue in PwMS.[12 24 27 32] Specifically, Dodd et al. and Gutierrez et al. observed a decrease in MFIS scores following a 10 and 8-week strength training intervention.[24 27] Additionally, our results are consistent with other studies that consistently show that PwMS walk longer distances during the 6MWT following an exercise intervention.[32-34 36] The increased ability to perform the 6MWT is likely associated with decreased levels of fatigue; thus allowing the participant to walk further for longer periods of time. Additionally, increased muscular strength may play a factor by possibly enhancing gait performance. These findings are important in PwMS as physical fatigue, poor muscle endurance and muscle weakness are common symptoms reported by people with MS.[24] By reducing these symptoms, PwMS can perform functional movements more readily, leading to an increased independence and overall QOL. Additionally, although there are pharmacologic drugs used to improve fatigue in PwMS, they are not always effective.[24] In regard to the sr-EDSS, our study found no significant change in disability level. Dalgas et al. and Fimland et al. noted similar findings[25 30]; although it should be noted that, in contrast, other studies have noted a difference in EDSS score following a strength training program.[27 29] The reason for the disparity could be due to inclusion of participants with lower EDSS scores (2.5) in other studies.[27]Additionally, it has been shown in a previous study that 50% of participants inaccurately estimate their walking ability when completing the sr-EDSS; thus, leading to inaccurate estimations of EDSS scores.[43] As the distinction between walking ability and total achievable walking distance is small per each disability score, minimal changes in walking performance following an intervention may be hard to detect. Thus, the use of the sr-EDSS could be another reason that no change was observed in the sr-EDSS in our study.

Limitations-

The present study contains a number of limitations. First, our sample size (n=15) was slightly underpowered. Although the sample size was great enough to find a statistical difference, this could disrupt our ability to find significant differences for other variables. Additionally, participants in this study were diagnosed with the relapsing-remitting form of MS (RRMS) and were relatively high functioning. This may limit the generalizability of the study in regard to the broader MS population or even PwMS who are diagnosed with RRMS and are less high functioning. Although our findings may not be generalizable to all PwMS, it is a valid measure for PwMS who are ambulatory with a EDSS score $\leq$ 6.5. Furthermore, the TUG task was only performed at a self-selected speed; thus, making our study less comparable to other studies that looked at forced/fast TUG speed. However, this speed was chosen as ADLs are generally performed at a self-selected speed. Given the nature of the disease, symptomology and disability levels are highly variable with a tendency to fluctuate; thus, possibly hindering the participants ability to perform functional tasks consistently. This could disrupt our ability to find significant differences. To limit this, testing was performed on nonconsecutive days during the same time of day to avoid inconsistency from fatigue or soreness. Lastly, the MFIS-5 and MSIS-29 were self-reported and therefore were subject to under/over reporting and possible bias. Despite being self-reported, these questionnaires demonstrate high validity and reliability and are appropriate outcome measures in PwMS. For the MSIS-29 and MFIS-5, previous studies have found these questionnaire to be clinically useful, have a high test re-test reliability, and have strong vailidty.[44 45] Additionally, the use of self-reported POOMs is more readily available; thus, making our study relatable to previous studies who have also used self-reported scales.[12 24 27 29]

Conclusion-

In summary, our results indicate that a twelve-week PRT that includes flexibility and balance training, can have a positive effect on the ability of PwMS to complete the TUG task. Our findings support that PRT is a safe and beneficial training tool that can be used to increase functional capacity and improve overall QOL in PwMS. The results for the TUG timing variables showed improvement following a PRT. Specifically, our study noted the greatest change in the sit to stand phase suggesting that an increase in muscular strength is more impactful on performance in siting to standing and standing to sitting. Our findings are important as they demonstrates that strength training and increasing muscular strength will increase functional capacity, decrease disability, and fatigue, and overall improve QOL in PwMS. Additionally, by investigating the changes in subphase timing, we can clearly observe were participants showed the most improvement. This knowledge, in association with the current literature, can aid clinicians in tailoring PRT programs for PwMS. Furthermore, addressing the improvement of fatigue levels is highly important as fatigue status may affect the ability of PwMS to perform daily tasks needed for independence regardless of functional mobility. Future research is still needed to determine the kinematic differences in each subphase following a PRT program to determine the specific mechanics behind the improvements in timing.

LITERATURE REVIEW

The purpose of this literature review is to summarize the findings from previous research in the MS population. By understanding these results, we are more clearly able to identify differences in movement mechanics and the impacts of strength and balance training on these differences in PwMS. Furthermore, we can determine the impact of interventions on perceived quality of life and fatigue levels. Populations observed in this review included PwMS, the elderly, post stroke victims, and patients with Parkinson. Comparisons between these groups is warranted given these populations share many of the same clinical symptoms. This literature review is divided into five tables that address 1) the effects of resistance training in PwMS, 2) the effects of resistance training on TUG, 3) movement differences in PwMS, 4) movement differences in the subphases of the TUG, and 5) the clinical relevance and validity of the TUG test in assessing ambulation, functional mobility, and fall risk.

Effect of Resistance Training in PwMS

Table 1 summarizes the literature regarding the effects of strength training on PwMS. The overall consensus of the literature supports that resistance training is safe and well tolerated for patients diagnosed with MS.[24 27 29 32] In studies specifically interested in the adaptions in muscular strength following a training intervention, muscular strength improved in all cases.[2 12 24-32] Several studies hypothesized that improved strength performance was associated with an increase in neural drive.[30 31] Fimland et al. and Dalgas et al. found that neural drive did improve following a resistance training program and, in association to this improvement, saw increases in maximal voluntary contractions (MVC) in knee extension, knee flexion, and plantarflexion. Specifically, Fimland et al. reported a 20% increase in knee extension and 36% increase in plantarflexion following a 3-week training intervention.[30]

Several studies investigated timed walking assessments in relation to resistance training including the 6-minute walk test (6MWT), 10-meter walk test (10MWT), 2-minute walk test (2MWT), Timed 25-foot walk test (T25WT). Studies utilizing the 6MWT found homogeneous results with improvement in total walking distance following intervention.[25 32] Two studies evaluated the 2MWT and found no significant changes in time or velocity.[24 28] The 10MWT was included in two studies and yielded different results. Moradi et al. noted that the overall time to complete the task decreased; however, the change was not significant.[29] In contrast, Dalgas et al. noted improvement to the 10MWT.[25] The T25WT was only conducted in one study and found no significant changes following intervention.[28] Functional performance was also evaluated using the TUG test following a resistance training intervention in several studies.[2 28 29 32] The results of these studies will be summarized in Table 2.

Lastly, numerous studies investigated the changes in perceived fatigue, overall quality of life (QoL), and EDSS scores as secondary outcomes of the study. In all studies, fatigue decreased significantly following intervention.[12 24 27 32] This was generally associated with improvements in functional or muscular endurance. Additionally, improvement in overall QoL was reported in two studies following a strength intervention.[24 32] EDSS values yield inconsistent findings. In two studies, no change was observed.[25 30] In contrast, Moradi et al. and Gutierrez et al. did observe a decline in EDSS scores following intervention.[27 29] Overall, the literature supports that resistance training may provide beneficial improvements in strength, function, fatigue, and QoL in PwMs.

Table 1. Effects of Resistance Training in Patients with Multiple Sclerosis (PwMS)

Author	Study Population	Sample Characteristics	Intervention	Instrumentation	Main Outcome Variables	Major Findings
(Dodd et. al., 2011)	n=71 PRT (n=36) CON (n=35)	PRT Male/Female (10/26) Age 47.7 (10.8) Gait Aid Used (12) MFIS fatigued (22) CON Male/Female (9/26) Age 50.4 (9.6) Gait Aid Used (13) MFIS fatigued (19)	10-week PRT Performed Biweekly	1 RM	2MWT, 1 RM, MFIS, WHOQoL-Bref, MSSS-88	• No change in distanced walking or walking speed • Significant ↑ leg press (16.8%), reverse leg press (29.8%) • ↑ muscular endurance (39.7%) • Significant ↓ in fatigue symptoms • Improved overall physical health
(DeBolt & McCubbin, 2004)	n=29	All female participants Age 51.1 (7.1) EDSS 1.0-6.5	8-week home-based resistance training program 3-times weekly	Force plate (AccuSway), Leg extensor power rig	Balance, leg power, TUG	• No significant difference for balance • ↑ leg power (37.4%) • ↓TUG time (12.7%)
(Dalgas et al., 2009)	n=38 PRT (n=19) CON (n=19)	Not reported	12-week PRT Post-study follow up after 12 weeks	Biodex, 1 RM, Handgrip dynamometer	Maximum voluntary contraction (KE MVC) Total functional capacity sore: Chair stand test, ascending stair-climb, 10-m walk test, 6-min walk test	• ↑ KE MVC (15.7%) • ↑ KF MVC (21.3%) • 1 RM ↑ (37.1%) • All functional scores ↑ (21.5%) • Improvements were maintained at follow up
(Medina-Perez de Souza-Teixeira, Fernandez-Gonzaloo, & de Paz-Fernandez, 2014)	n=42 RT (n=30) CON (n=12)	RT Age 49.6 (11.0) Weight (kg) 68.1 (11.4) Height (cm) 165 (8.3) BMI 25 (4.1) EDSS 4.5 (2.1)	12-week PRT Mainly focused on knee extensors	Strain gauge	Knee extension maximum voluntary isometric contraction (MVIC), muscle power, muscle endurance	• ↑ knee extension strength (7.7%) • ↑ muscle power (40%) • No significant change in muscle endurance

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(Gutierrez et al., 2005)	n=8	Female/male (7/1) Age 46 (11.5) Height (m) 1.66 (0.08) Mass 77 (19.6) EDSS 3.6 (0.8)	8-week PRT Performed bi-weekly	Force platform, peak Motus 2000 motion analysis system, KinCom isokinetic dynamometer	Kinematic gait parameters (knee ROM, stance, swing, double support, step length, foot angle, stride velocity, step width, toe clearance) Isometric strength, Fatigue (MFIS), and srEDSS	• ↓ srEDSS • ↓ MFIS • ↑ Isometric knee extensor strength (7.2%) • ↑ Isometric plantarflexor strength (55%) • ↑Isometric knee flexor strength (14.5%) • Step performance ↑ (8.7%)
(Broekmans et al., 2011)	n=36 PRT (n=11) PRT with stim (n=10)	PRT Age 44.9 (11.6) Body weight 70.4 (4.2) EDSS 4.5 (1.3) PRT with stim Age 48.7 (8.6) Body weight 64.3 (3.5) EDSS 4.4 (0.9)	Unilateral 20-week PRT	Biodex	Muscular strength, functional mobility (TUG, T25FW, 2MWT, functional reach, Rivermead mobility index	• Functional mobility did not significantly change • ↑ maximal isometric knee extensor/knee flexor strength • No difference between PRT and PRT with stim
(White et al., 2004)	n=8	Age 46 (12) Height 166 (8) Mass 74 (17) % Body fat 34 (9) BMI 27 (6) srEDSS 3.7 (1)	8-week PRT Performed bi-weekly	Isokinetic dynamometer, skin fold measurements	Muscular strength, functional mobility (25-foot walking test, 3-minute step test, MFIS, srEDSS)	• ↑ knee extension (7.4%) • ↑ plantarflexion (52%) • ↑stepping performance (8.7%) • ↓ Disability and MFIS scores *Continued on next page*

(Moradi et al., 2015)	n=20	All male participants Age 34.38 (11.07) Height 1.75 (0.05) Weight 68.06 (11.13) BMI 22.15 (3.63) EDSS 3(1-6)	8-week PRT Performed 3 times per week	1 RM	Muscular strength, balance, perceived disability, ambulatory function (10-meter timed walk test, 3-minute step test, TUG)	• Significant changes in 3-minute step test • TUG time ↓ (18.76%) • Muscular strength ↑ • EDSS ↓ • No change in balance
(Fimland, Helgerud, Gruber, Leivseth, & Hoff, 2010)	n=14 Training (n-=7) CON (n=7)	Training-Female/Male (3/4) Age 53 (4) Height 172 (4) Weight 74.8 (9.6) BMI 24.7 (2.3) EDSS 4.6 (0.4) Control-Female/Male (3/4) Age 54 (2) Height 170 (2) Weight 76.6 (5) BMI 26.6 (1.8) EDSS 3.5 (0.5)	3-week training intervention	Force transducer on custom-made dynamometer, surface electrodes	Isometric strength, voluntary muscle activation	• MVC ↑ (20%) • Plantarflexion ↑ (36%) • No change was noted in the control group
(Dalgas et al., 2013)	n=38 PRT (n=15) CON (n=15)	All participants- Age 48.7 (8.8) Height 169 (10.6) Weight 67.7 (14.0) EDSS 3.8 (0.8)	12-week PRT Performed bi-weekly	Biodex, EMG, skinfold	Knee extensor maximum voluntary contraction (MVC), functional capacity score, EMG	• ↑ knee extensor strength (10.6%) • ↑ knee flexor strength (4.6%)
Grazioli et al., 2019)	n=20 CT (n=10) FKT (n=10)	Age range (22-55) EDSS range 2.5-5.5	12-week combined training (resistance and aerobic)	Functional clinical tests	Berg balance scale, TUG, 6-minute walk test, 10-m walk test	• ↑ balance (5%) • ↑ TUG performance • ↑6-minute walk and 10-m walk test

PRT= Progressive Resistance Training
CON= Control group
MFIS=Modified Fatigue Impact Scale
1RM=1 repetition max
2MWT=2-minute walk test
EDSS/sr-EDSS=Expanded disability status scale/self-reported expanded disability status scale
BMI= Body mass index
KE, KF MVC= Knee extensor, knee flexor maximum voluntary contraction
WHOQoL-Bref= World Health Organization Quality of Life Instruments
MSSS-88= Multiple Sclerosis Spasticity Scale
CT= combined training
FKT= conventional physiotherapy group

Effect of Resistance Training on TUG in Various Populations

Table 2. summarizes the post-intervention outcomes of a resistance training program on TUG performance in various populations with pathological conditions. Numerous populations including PwMS, the elderly, post-stroke victims, and individuals with Parkinson's have used the TUG test to assess functional movement, balance, and risk of falls. As these populations share many of the same clinical symptoms as PwMS, they allow for an ideal comparison.

Research investigating the effect of a resistance training program on the TUG task yield mildly inconsistent findings. In most studies, TUG performance, as assessed by overall completion time, improved following a resistance training program.[29 32-35 37 39 40] In these studies, intervention duration ranged from 8-14 weeks. For the MS population, two studies reported no change in TUG.[2 28] However, although not significantly different, DeBolt et al. did observe a reduction in TUG time by 13%; thus, showing a trend towards improvement.[2] On the contrary, four studies noted improvement with TUG[29 32 33 40] with three reporting improvement of 9%[40], 19%[29], and 8%[33], respectively following an intervention. In contrast, Broekmans et al. found no change in TUG performance.[28]

Other populations portrayed similar findings to the MS studies. In elderly patients, research found that overall TUG performance improved following a resistance training intervention.[37 39] Two other studies, one post stroke and one Parkinson's, also showed an improvement in TUG by 18%[34] and 20%[35]. Schilling et al. reported contrasting outcomes after an 8-week training intervention with patients diagnosed with Parkinson finding no significant interactions for the TUG task. Overall, despite a few studies, the literature supports that the ability to perform the TUG task may improve following a strength training intervention.

Table 2. Effect of Resistance Training on TUG in Various Populations

Author	Study Population	Sample Characteristics	Diagnosis	Intervention	Main Outcome Variables	Major Findings
(Moradi et al., 2015)	n=20	All male participants Age 34.38 (11.07) Height 1.75 (0.05) Weight 68.06 (11.13) BMI 22.15 (3.63) EDSS 3(1-6)	Multiple Sclerosis	8-week PRT Performed 3 times per week	Muscular strength, balance, perceived disability, ambulatory function (10-meter timed walk test, 3-minute step test, TUG)	• Significant changes in 3-minute step test • TUG time ↓ (18.76%) • Muscular strength ↑ • EDSS ↓ • No change in balance
(DeBolt & McCubbin, 2004)	n=29	All female participants Age 51.1 (7.1) EDSS 1.0-6.5	Multiple Sclerosis	8-week home-based resistance training program 3-times weekly	Balance, leg power, TUG	• No significant difference for balance • ↑ leg power (37.4%) • ↓TUG time (12.7%)
(Broekmans et al., 2011)	n=36 PRT (n=11) PRT with stim (n=10)	PRT Age 44.9 (11.6) Body weight 70.4 (4.2) EDSS 4.5 (1.3) PRT with stim Age 48.7 (8.6) Body weight 64.3 (3.5) EDSS 4.4 (0.9)	Multiple Sclerosis	Unilateral 20-week PRT	Muscular strength, functional mobility (TUG, T25FW, 2MWT, functional reach, Rivermead mobility index	• Functional mobility did not significantly change • ↑ maximal isometric knee extensor/knee flexor strength • No difference between PRT and PRT with stim
(Grazioli et al., 2019)	n=20 CT (n=10) FKT (n=10)	Age range (22-55) EDSS range 2.5-5.5	Multiple Sclerosis	12-week combined training (resistance and aerobic)	Berg balance scale, TUG, 6-minute walk test, 10-m walk test	• ↑ balance (5%) • ↑ TUG performance ↑6-minute walk and 10-m walk test
(Sabapathy, Minahan, Turner, & Broadley, 2011)	n=16	Age 55 (7) Male/Female (4/12)	Multiple Sclerosis	8-week endurance 8-week resistance training	Grip strength, functional reach, four step square, TUG, 6-minute walk test, MSIS, MFIS, SF-36	• ↓ TUG time (8%) • 6MWT distanced ↑ • No between group differences for endurance vs resistance

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(Flansbjer, Miller, Downham, & Lexell, 2008)	n=24 PRT (n=15) CON (n=9)	PRT- Age 61(5) Male/Female (9/6) Assistive device used (4) CON Age 60 (5) Male/Female (5/4) Assistive device used (3)	Post-stroke	10-week PRT Performed bi-weekly	Dynamic and isokinetic muscle strength, muscle tone, gait performance (TUG, 6MWT, fast gait speed (FGS)), and perceived participation (stroke impact scale)	• ↑ dynamic strength (34%) • ↑Isokinetic strength bilaterally • ↑6MWT (10%) • ↓ TUG time (18%)
(Vieira de Moraes Filho et al., 2020)	n=40 PRT (n=25) CON (n=15)	PRT- Male/Female (20/5) Age 64.7 (1.8) Weight 74.5 (2.5) Height 1.65 (.02) BMI 27.5 (0.8) CON Male/Female (10/5) Age 64.4 (3.7) Weight 79 (5.4) Height 1.67 (.02) BMI 27.8 (1.9)	Parkinson's	9-wekk PRT Performed bi-weekly	Functional performance (10-meter walk test, TUG, 30 second chair stand test), Isokinetic muscular strength (Biodex)	• Improved TUG time (20.3%) • All functional tests where statistically significant after the intervention • ↑ Isokinetic muscle strength (2.9%)
(Schilling et al., 2010)	n=18 PRT (n=8_ CON (n=7)	PRT- Age 61.3 (8.6) Weight 76 (25.4) CON Age 57 (7.1) Weight 79.2 (27.6)	Parkinson's	8-week PRT Performed bi-weekly	Leg press strength, TUG, 6MWT, activities-specific balance confidence questionnaire	• ↑ relative and absolute leg strength • No significant interactions were noted for TUG • ↑ in time effect for 6MWT
(Sousa & Sampai, 2005)	n=20	All male participants Age 73 (5) BMI 23.4 (1.2)	Elderly patients	14-week PRT 3 times per week	TUG, Functional Reach test, 1 RM	• Tug performance improved • Mean TUG results were significantly ↓ • 1 RM improved *Continued on next page*

(Lacroix et al., 2016)	n=66 BST with supervision (n=22) BST without supervision (n=22) CON (n=22)	Male/Female (25/41) Average Age (72.7) Average Height (168.8) Average Body Mass (73.7)	Elderly patients	12-week balance and strength training 3 times per week	Balance (Rhomberg test, OptoGait), Functional Sit and Reach, TUG, Chair Stand Test, Ascent Test	• ↓ TUG time • Significant improvements in lower extremity power
(de Souza-Teixeira et al., 2009)	n=13	Average age 43 (range 35-51)	Multiple Sclerosis	8-week Performed bi-weekly	Isometric strength, muscular endurance, maximal power, muscle hypertrophy, functionality (TUG)	• ↑ Isometric strength (16%) • ↑ muscular endurance (84%) • ↑ muscular power by (51%) • Functionality improved. Improved TUG by 9%

BMI= Body mass index
EDSS/sr-EDSS= Expanded disability severity scale/ self-reported expanded disability severity scale
PRT= Progressive resistance training
CON= Control group
PRT c stim= Progressive resistance training with electrical stimulation
T25FT= Timed 25-foot walk test
2MWT= 2-minute walk test
CT= Combined training
FKT= conventional physiotherapy group
1 RM= 1 repetition max

Movement Differences in PwMS

Table 3 summarizes the movement differences commonly exhibited by PwMS. Specifically, literature relating to the movements that are required to perform the TUG task— sit to stand, gait, and balance; were investigated.

In regard to the sit to stand motion, trunk, hip, and knee movement were evaluated. Bowser et al. compared MS participants with leg strength comparable to a healthy population to MS participants with leg weakness. From this study, it was concluded that PwMS that exhibit leg weakness had a faster trunk velocity, increased trunk flexion, and slower rise times than that of the stronger participants/control group.[3] Nilsagård et al. further confirmed that enhanced trunk movement is related to good basic balance, mobility, function, and walking ability in PwMS after comparing the Trunk Impairment Scale (TIS) to a wide variety of functional tests.[4] Lastly, Witchel et al. found that PwMS present with a decreased angular velocity of the knee and hip during the sit to stand movement which was overall correlated with knee extensor weakness.[5]

Numerous studies evaluated gait/walking differences in PwMS. In most studies, individuals affected by MS displayed a slower walking velocity, decreased stride length and cadence, increased step width, and a longer support time during stance.[6 8 9] Carpinella et al. also noted an altered gait pattern in PwMS[46]. These studies were further supported by Pau et al., Plotnik et al., and Sosnoff et al., who concluded that ambulation and velocity tend to deteriorate as the disease and disability status progress.[7 8 10] Additionally, Pau et al. correlated that the deterioration is also associated with fatigue and endurance as evidenced by the 6-minute walk test.[8]

Balance during standing and functional tasks were assessed in two studies. The first study observed quiet standing and utilized a force platform to evaluate proprioception, postural control, and overall balance.[11] Findings suggest PwMS display increased postural sway which is correlated to decreased balance.[11] Carpinella et al. also observed a larger trunk pitch sway and alteration in gait during a stair ascent task.[46] In conclusion, from the literature, PwMS may present with altered gait patterns with walking, difficulty with the sit to stand task, and decreased balance and proprioception. These alterations in functional movement may cause activities of daily living to be more difficult in PwMS.

Table 3. Movement Differences in Patients with Multiple Sclerosis

Author	**Study Population**	**Sample Characteristic**	**Diagnosis**	**Variables of Interest & Movement Analyzed**	**Instrumentation**	**Major Findings**
(Bowser, O'Rourke, White, & Simpson, 2015)	MS CS (n=10) MS LW (n=11) CON (n=12)	MS- CS EDSS 1.6 (2.2) BMI 27.5 (6.9) MS LW EDSS 4.3 (1.4) BMI 29.5 (4.7) CON EDSS na BMI 26.8 (5.0)	Multiple Sclerosis	STS movement times, trunk kinematics. COM placement, lower extremity sagittal plane kinematics and kinetics Sit-to-Stand at self-selected speed	Sit to stand test, ground force reactions, cameras	• MSLW displayed greater muscle weakness, faster trunk velocity, greater trunk flexion, slower rise times than CON
(Carpinella et al., 2018)	n=50 NEU (n=30) MS (n=10) ST (n=10) PD (n=10) HS (n=20)	HS- Male/Female (10/10) Average age (57) MS- Male/Female (4/6) Average age (51) ST- Male/Female (4/6) Average age (59) PD- Male/Female (2/8) Average age (73)	MS, Stroke, Parkinson	Step frequency and symmetry, stride regularity, ground reaction forces, trunk sway Stair Ascent	10-step accelerometer, gyroscope	• Altered pathology in all groups compared to control • MS showed the worst performance with alterations of all gait patterns aspects and larger trunk pitch sway
(Witchel et al., 2018)	n=40 MS (n=17) CON (n=23)	MS Female/Male (13/14) Age 53.06 (11.06) Height 167.8 (11.2) Weight 74.9 (26.2) EDSS 4 (1.80)	Multiple Sclerosis	Angular velocity, duration, peak movement attributes Sit to stand, stand to sit during TUG	Sensor to examine accelerometer, gyroscopy, and magnetormetry	• Decreased in angular velocity of the thigh and knee • This decrease is likely due to knee extensor weakness

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(Benedetti et al., 1999)	n=7	Male/Female (2/5) Age Range (22-44) EDSS Range (0-2)	Multiple Sclerosis	Gait, time, distance, velocity, force plates, stride length, stance support, lower limb kinematics, muscle activation Gait	ELITE stereophotogram metric system, force plates	• Gait control dysfunction • Slower walking velocities • Reductions in stride length and cadence and increase support time in stance • Increase sagittal hip motion • Decreased in ankle motion
(Sosnoff, Goldman, & Morl, 2010)	n=77	Mild (n=33) Age 47.4 (10.1) Female/Male (27/6) srEDSS 2.10 (0.77) Moderate (n=20) Age 49.4 (13.1) Female/Male (20/0) srEDSS 6.02 (.12) Severe (n=17) Age 53. 2 (10.3) Female/Male (9/8) SrEDSS 6.02 (.12)	Multiple Sclerosis	Velocity, ambulatory status during ADLs Walking gait	ActiGraph accelerometer	• There are differences between mild, moderate, and severe cases of MS in terms of reduction in velocity and daily ambulation
(Rougier et al., 2007)	n=79 MS (n=56) CON (n=23)	Male/Female (12/11) Age Range (26-57) Height 1.69 (0.1) Weight 65 (11)	Multiple Sclerosis	Proprioception, postural control, center of gravity, center of pressure Quiet standing	Force platform	• MS display larger vertical projection and center of pressure • Increased postural sway *Continued on next page*

(Plotnik, Wagner, Adusumilli, Gottlieb, & Naismith, 2020)	n=92	Age 46.6 (10.9) EDSS (2.0-6.5) Female % (83%)	Multiple Sclerosis	Gait variability, bilateral coordination of gait, gait asymmetry, phase coordination index, total distance 6-minute walk test	Opal motion sensor-based gait analysis system	• Gait is more asymmetric and less coordinated as the disease progresses • Gait asymmetry and phase coordination index deteriorated significantly for each minute during the 6MWT
(Coghe et al., 2019)	n=49 MS (n=28) CON (n=21)	Male/Female (14/14) Mean disease duration in years 18.5 (4.8) EDSS 4.0 (1.8) Body Mass 64 (12.5) Height 166 (9,3)	Multiple Sclerosis	Lower Limb: Gait speed, stride, stride length, cadence, step width Upper Limb: velocity, going phase, adjustment phase, return phase Gait and upper arm movement	Gait analysis for lower limbs, hand to mouth task for the upper limb Motion capture system	• PwMS exhibit a significant reduction in gait velocity, stride length, and cadence • Step width is increased in PwMS • For the upper extremity, PwMS had reduced velocity and spent longer in the adjusting phase.
(Nilsagård, Carling, Davidsson, Franzen, & Forsberg, 2017)	n=47	Female/Male (32/15) Age 57.5±10.2 EDSS 6.0 (4.0-7.5)	Multiple Sclerosis	Correlations between trunk impairment scale and functional assessments Walking, balance, TUG, sit to stand	2MWT, trunk impairment scale, Berg balance test, 10MTW, TUG, Sit to Stand	• Suggest that good trunk movement is related to good basic balance, mobility function, and walking ability in pwMS *Continued on next page*

(Pau et al., 2016)	n=152 MS Class 1 (n=54) MS Class 2 (n=31) MS Class 3 (n=20) CON (n=47)	Age- Class 1 39.6±8.3 Class 2 43.6±9.3 Class 3 52.1±10.2 CON 39.4±12.7 Height- Class 1 163.9±8.5 Class 2 164±.9.2 Class 3 162±8 CON 163.9±8.5 Body Mass- Class 1 62.2±13.0 Class 2 59.6±10.4 Class 3 55.9±10.8 CON 60.7±12.0 EDSS- Class 1 1.0±0.2 Class 2 2.6±0.6 Class 3 4.6±1.1 CON NA	Multiple Sclerosis	Gait speed, cadence, stride length, stance phase, swing phase, double support time Gait- T25FT	Inertial sensor	• Higher levels of disability (EDSS) led to slower gait speed, decreased cadence, and longer time to complete the movement

PwMS= Patients with Multiple Sclerosis
MS= Multiple Sclerosis
CON= Control
EDSS/sr-EDSS= Expanded disability status scale/ self-reported expanded disability status scale
T25FT= Timed 25-foot walk
2MWT= 2-minute walk test
10MWT= 10-meter walk test
ST= Stroke
PD= Parkinson’s disease
HS= Control group
NEU= 3 pathological samples combined (ST, PD, MS)
MS- CS= MS participants with comparable strength to healthy controls
MS LW= MS participants with leg weakness
BMI= Body mass index

Movement Differences during the Subphases of TUG in Various Populations

Table 4 summarizes the movement differences in the specific subphases of the TUG movement in various populations. Findings in these studies are similar to the movement differences reported in Table 3.

Angular velocity was examined for the trunk, hip, and knee. In all cases, trunk velocity was found to be lower in populations with a decreased ability to perform functional movements.[16-18] The trend in decreased angular velocities continued down the kinetic chain and were observed in the hip and knee in Witchel et al.[5] Gait patterns were also altered in the subphases of TUG and were characterized by slower gait velocities[16 18 21], an increased number of steps taken[16-18 21], and increased double support time during gait.[21] When observing the turning movement in TUG, studies found that participants took longer to complete the turn.[16 22] Additionally, when turning to sit in the chair at the end of the movement, Weiss et al. described two specific transitions for the movement. The transitions being classified as direct transition or overlapping. In the direct transition, participants finished the turn before starting the motion to sit. In the overlapping transition, participants turned and began the sitting motion during the same movement.[19] Additionally, one study noted that PwMS present with increased sway which was correlated with a decrease ability to balance.[20] In conclusion, the movement patterns observed in the subphases of the TUG movement included decreased angular velocity, altered gait patterns, and slower turning time. Additionally, the changes in movement patterns are similar to the general movement differences observed in PwMS during the sit to stand task, gait, stair ascent, 6MWT, and quiet standing.

Table 4. Movement Differences in the Subtask Phases of TUG in Various Populations

Author	Study Population	Sample Characteristics	Population	Instrumentation	Variables of Interest	Major Findings
(Ansai et al., 2019)	n=80 Nonfrail (n=43) Prefrail (n=30) Frail (n-=7)	Not reported	Frailty Syndrome	Qualisys motion system, Visual 3D software	Peak and average velocities angular velocities, total time, gait speed	• Peak velocity of the trunk was significantly lower in the frail group as compared to the nonfrail group for sit to stand and stand to sit • Time to complete the turn took longer in the frail population • Gait speed was slower for frail individuals • Frail subjects took more steps during gait • Longer TUG time for frail subjects
(Mirelman et al., 2014)	n=347 Mild Cognitive Impairment (n=67) No Cognitive Impairment (n=280)	MCI- Age 83.35± 3.50 Sex (% female) 75% BMI 27.92±5.36 NCI- Age 82.75±4.17 Sex (% female) 74% BMI 27.22±5.61	Elderly adults with mild cognitive impairment	Body-fixed sensor	TUG subtask duration, number of steps, step symmetry, angular velocity	• Total TUG duration did not differ • MCI patients had lower step regularity, lower angular velocities
(Witchel et al. 2018)	n=40 MS=17 CON=23	PwMS- Female/Male (13/4) Age 53.06± 11.06 Height(cm) 167.8±11.2 Weight(kg) 74.9±26.2 EDSS 4+1.80	MS	Sensor to examine accelerometer, gyroscopy, and magnetometry	Sit to Stand, stand to sit in TUG Angular velocity, duration, peak movement attributes	• Decrease in angular velocity of the thigh and knee. This decrease is likely due to knee extensor weakness

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(Ansai, Andrade, Nakagawa, & Rebelatto, 2018)	n=75 Non-fallers with MCI (n=18) Fallers with MC (n=20) Non-fallers with AD (n=18) Fallers with AD (n=19)	Non-fallers with MCI Mean Age 72.5 Female gender 16% Mean BMI 30.4 Fallers with MC Mean Age 77 Female gender 16% Mean BMI 29.0 Non-fallers with AD Mean age 78 Female gender 11% Mean BMI 27.7 Fallers with mild AD Mean Age 79 Female gender 10% Mean BMI 27.3	Elderly adults with Alzheimer's Disease	Qualisys Track Manager, Visual 3D	Fall vs non-fallers: Gait speed, number of steps, completion time for each subtask, average velocity of the trunk	• Non fallers with mild cognitive impairment spent less overall time to complete TUG than fallers • Non-fallers had higher gait speeds • Non-fallers had higher trunk velocities • Non-fallers took less steps
(Weiss et al., 2016)	n= 1055	Age 80.33±7.57 Gender (% women) 76.96% Height (m) 1.63±0.09 Weight (kg) 74.81±17.46	Elderly	Body fixed sensor (DynaPort Minimod)	Turning to sitting movement strategies of the TUG movement, acceleration and angular velocity	• Subjects used 2 movement strategies for turning to sitting: distinct transition (77.34%) and overlapping transition (22.65%) • Higher duration between subtasks was associated with worse TUG performance, motor and cognitive function, and mobility disability. *Continued on next page*

(Pau et al., 2017)	n=148 CON (n=42) MS Class 1 (n=57) MS Class 2 (n=32) MS Class 3(n=17)	CON Age 39.6 Height (cm) 168.7 Body mass (kg) 66.6 EDSS NA Class 1 Age 39.8 Height (cm) 163.5 Body mass (kg) 62.4 EDSS 1.0 Class 2 Age 43.5 Height (cm) 61.3 Body mass (kg) 61.3 EDSS 2.6 Class 3 Age 48.6 Height (cm) 160.4 Body Mass (kg) 54.3 EDSS 5.2	Multiple Sclerosis	Single wearable miniaturized inertial sensor	Balance; sway area, sway path, displacement TUG; timing for overall movement and subphases	• Balance and sway parameters were increased for patients with higher disability status • Total tug time was longer for patients with higher disability
(Mulas et al., 2020)	n=213 Healthy controls young age (HC-YO) (n=64) Health controls old age (HC-OO) (n=78) CI young-old (CI-YO) (n=28) CI old-old (CI-OO) (n=43)	HC-YO Age 71.9±2.3 BMI 66.1±12.8 Height (cm) 158.8±7.5 HC-OO Age 80.7±2.5 BMI 65.4±12.1 Height (cm) 160.5±12.1 CI-YO Age 71.3±2.9 BMI 62.5±12.3 Height (cm) 159.9±9.5 CI-OO Age 81.5±4.2 BMI 61.5±14.6 Height (cm) 157±8.6	Elderly subjects with cognitive impairment	Wearable inertial sensor	Gait analysis; gait speed, stride length, cadence, stance phase, swing phase, double support, overall timing TUG; total time, subphase times	• CI subjects had reduced speed (34%), stride length (11%), cadence (-9%), and double support duration (+11%) • CI took longer to complete total tug and subphases

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(Kurosawa, Shimazu, & Yamamoto, 2020)	n=50 Older (n=28) Younger (n=22)	Older Age 71.1±5.0 Height (m) 1.57±0.88 Weight (kg) 55.9±10.4 Gender (Male/Female) 10/18 Younger Age 20.8±0.8 Height (m) 1.61±0.62 Weight (kg) 54.4±4.8 Gender (Male/Female) 7/15	Elderly	Camera motion measurement system (Vicon612)	Time ratio of each subtask, body inclination angle	• Older adults took longer to complete the TUG task • Older adults took longer during the turn subtask and the turn and sit subtask

BMI= Body mass index
CON- Control group
EDSS/sr-EDSS= Expanded disability status scale/ self-reported expanded disability status scale
MCI= Mild cognitive impairment
NCI= No cognitive impairment
AD= Alzheimer’s disease

Clinical Relevance, Reliability, Reproducibility, and Validity of the TUG

Table 5 summarizes the clinical relevance, reliability, reproducibility, and validity of the TUG test as a measure of functional mobility in various populations. The literature concludes that the TUG test has a high reproducibility rate, strong reliability, and is a valid measure of functional mobility.[41 47 48] Additionally, Valet et al. found that the immediate reliability of TUG was excellent and maintained its reliability after 2 weeks.[49] Additionally, the TUG task has an excellent test-retest rate as reported by Chan et al.[50] Lastly, it has been found that strength changes, gait parameters, and walking endurance are all correlated with a TUG performance.[48] In conclusion, the TUG task is a valid and clinically relevant measure of functional mobility in various populations with pathological differences.

Table 5. Clinical Relevance and Validity of TUG in Various Populations

Author	**Study Population/Characteristic**	**Population**	**Study Aim**	**Instrumentation /# of Trials performed**	**Major Findings**
(Nislagard, Lundholm, Gunnarsson, & Dcnison, 2007)	n=43 Male/Female (13/30) Height(cm) 170 (9) Weight(kg) 74(15) Age(yrs) 52(9) EDSS ≤ 4= 19 EDSS ≥ 4= 24	Multiple Sclerosis	Determine smallest percentage needed to be able to detect a genuine change and examine the reproducibility of the 10-m and 30-m walks, and TUG	10-m timed walk (10TW) at SS speed 30-m timed walks (30TW) as forced speed TUG at forced speed Number of Trials: Time walks= performed 3 times TUG= performed 2 times	• Reproducibility was very high • Interclass correlation 0.97=10TW, 0.98= 30TW and TUG • Smallest percentage difference needed to detect change= -23% or +31% for 10WT or TUG • Correlation between all tests was 0.85
(Sebastiao, Sandroff, Learmonth, & Morl, 2016)	n=47 Females= 89.4% Age 53.0±11.4 Median EDSS= 4	Multiple Sclerosis	To examine the validity of the timed up and go (TUG) as a measure of functional mobility in pwMS	TUG test, timed 25-foot walk test, 6MWT, and more Number of Trials: TUG= performed 2 times	• TUG test strong convergent validity • TUG is a valid measure of functional mobility • All other tests were valid
(Valet et al., 2019)	n= 63 EDSS≤4	Multiple Sclerosis	Explore intra-rater reliability and minimal detectable change for 2MWT and TUG	TUG 2MWT Number of Trials: TUG= performed 2 times 2MWT= performed 2 times Testing session were repeated 2 weeks later	• Immediate reliability was excellent for both tests (2MWT= ICC=0.98; TUG= ICC=0.98) • Reliability was maintained after 2 weeks (2MW ICC=0.05; TUG= ICC=0.90)

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(Chan & Pin, 2019)	n=39 Age 87.1±6.2 Male/Female (3/36) BMI 22.0±3.3	Elderly adults with dementia/ Alzheimer	Examine the test-retest and inter-rater reliability for the 2-minute walk, 6-minute walk, and 10-meter walk	2MWT 6MWT 10MWT Number of Trials: All test repeated 6 times on separate occasions	• Excellent test-retest (ICC=0.91-0.98) and inter-rater reliability (ICC=0.86-0.96) for all tests • Walking tests are strong correlated with each other
(Ng & Hui-Chan, 2005)	n=21 n=21 Stroke (n=11) CON (n=10) CON consisted of healthy elderly subjects Stroke- Age 61.±6.8 Sex (Male/Female) 6/5 Height (m) 1.6±0.1 Weight (kg) 61.3±10.3 BMI 23.2±2.8 CON- Age 63.5±6.1 Sex (Male/Female) 5/5 Height (m) 1.6±0.1 Weight (kg) 59.6±9 BMI 22.8±2.7	Stroke	Quantify the reliability of TUG and examine if TUG can be used to detect difference in functional mobility	TUG, 6MWT, EMG Number of Trials: 2 testing sessions on different days	• TUG showed excellent reliability • Strength changes, gait parameters, and walking endurance are all correlated with TUG scores.

CON= Control
BMI= Body mass index
6MWT= Six-minute walk test
2MWT= Two-minute walk test
10MWT= 10-meter walk test
EMG= Electromyography
EDSS/sr-EDSS= Expanded disability status scale/ self-reported expanded disability status scale

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