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REVISIÓN SISTEMÁTICA

“EFECTO DEL EJERCICIO TERAPÉUTICO EN PACIENTES CON ESCLEROSIS MÚLTIPLE”

TESIS PARA OPTAR EL TÍTULO DE LICENCIADO EN TECNÓLOGÍA MÉDICA EN TERAPIA FÍSICA Y REHABILITACIÓN

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DEDICATORIA

A nuestros padres y hermanos, que bajo sus amparos y afectos nos han permitido ver la luz en todo el trayecto de este camino educativo.

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RESUMEN

Objetivo: Determinar el efecto del ejercicio terapéutico en pacientes con esclerosis múltiple.

Método: Se ha realizado una revisión sistemática analizando cuatro bases de datos de estudios publicados en distintos idiomas entre 2006 hasta 2017, los cuales miden la efectividad del ejercicio terapéutico en pacientes con esclerosis múltiple y observar si ello les mejora su estilo de vida. Se encontraron 24 artículos de los cuales se seleccionaron 4 de ellos para su análisis.

Resultados: Los estudios demuestran la viabilidad de un enfoque de rehabilitación personalizado y su efectividad para mejorar el equilibrio (puntaje BBS) y el control postural vertical (puntaje compuesto),con la excepción de la fuerza de agarre, el análisis de los datos encontró que todas las medidas de la capacidad física mejoraron significativamente con ocho semanas de entrenamiento físico, sobre el efecto sobre la calidad de vida en personas con esclerosis múltiple los resultados no son concluyentes.

Conclusión: Se verifica el efecto positivo del ejercicio fisioterapéutico en la mejora del equilibrio de personas con esclerosis múltiple.

Palabras Clave: Equilibrio, esclerosis múltiple, ejercicio terapéutico.

SUMMARY

Objective: Determine the effect of therapeutic exercise in patients with multiple sclerosis.

Methods: A systematic review was carried out analyzing four databases of studies published in different languages between 2006 and 2017, which measure the effectiveness of therapeutic exercise in patients with multiple sclerosis and observe if this improves their lifestyle. 24 articles were found, of which 4 of them were selected for analysis.

Results: Studies demonstrate the feasibility of a personalized rehabilitation approach and its effectiveness to improve balance (BBS score) and vertical postural control (composite score), with the exception of the grip strength, data analysis found that all measures of physical capacity improved significantly with eight weeks of physical training, on the effect on the quality of life in people with multiple sclerosis the results are inconclusive

Conclusion: The positive effect of physical exercise on improving the balance of people with multiple sclerosis is verified

Keywords: Balance, multiple sclerosis, therapeutic exercise.

CAPÍTULO I: INTRODUCCIÓN

1.1. Planteamiento del Problema

La esclerosis múltiple es una enfermedad autoinmune, crónica, inflamatoria, desmielinizante del sistema nervioso central (SNC) que se presenta en individuos genéticamente susceptibles y que se involucra a factores inmunológicos como anticuerpos, complemento y mediadores de la respuesta inmune innata(1).El nombre "esclerosis múltiple" significa tanto el número (múltiple) como la condición (esclerosis, del término griego que describe el cicatrizado o endurecimiento) de las áreas en las que se ha eliminado la mielina en el sistema nervioso central.(1)

La esclerosis múltiples es una enfermedad de los adultos jóvenes, la edad de comienzo esta entre los 20 y 40 años en alrededor del 80 % de los pacientes.(1).En la mayoría de las series predominan ligeramente las pacientes del sexo femenino sobre los hombres, y esto es particularmente notables en áreas de baja incidencia, la prevalencia más elevadas se presenta en personas de raza blanca y la presencia en vínculos familiares, en el 6-12% de los casos sugieren la implicación de un factor genético. (1)Se sabe poco sobre el gen involucrado. Comienza típicamente en la edad adulta con pronóstico variable y amplio espectro clínico, con formas extremas malignas o benignas entre el 20-40% y formas intermedias en el resto. (2)

Los estudios epidemiológicos han podido determinar que es imprescindible la participación de un factor medioambiental, y en últimos años se están estudiando intensamente factores infecciosos, sobre todo virales, que podrían estar implicados.

Buena parte de los pacientes se ven ligeramente afectados y en los casos más severos de esclerosis múltiple, una persona puede desarrollar incapacidad para realizar sus actividades de la vida diaria (AVD). Durante la esclerosis múltiple, se produce una alteración mediada por el sistema inmune, que ocurre en personas susceptibles. (1) Durante un ataque de esclerosis múltiple, se produce inflamación en áreas de la sustancia blanca del sistema nervioso central en partes distribuidas al azar llamadas placas.

Es una área de desmielinización activa, las vainas de mielina se fragmenta y se desintegran .la vaina de mielina y el edema son los responsable del retraso de la conducción del impulso nervioso (2). Cuando hay daño a la mielina, la transmisión neurológica de los mensajes ocurre más lentamente o queda bloqueada totalmente, lo que conduce a una reducción o pérdida de función (hay menor celularidad y acentuada gliosis

Las características clínicas de la esclerosis múltiple son muy variadas y aparecerán en función del lugar, en el que se produzcan las lesiones y de la gravedad y la duración de la EM en relación con la localización del foco de desmielinización. Estas incluyen**:** trastornos sensitivos-motores en uno o más miembros (es la forma de presentación en alrededor del 80 % de los pacientes), neuritis óptica (síntoma inicial en el 25 % de los pacientes), diplopía, vejiga neurogénica, fatiga, disartria.

Síntomas paroxísticos, como neuralgia trigeminal (se presenta en menos del 10 %), nistagmo, vértigo, parestesias .Son más raros los signos corticales (afasia, apraxia, convulsiones, depresión) y los signos piramidales (temblor intencional, Ataxia, rigidez) [3].

La evolución de la esclerosis múltiple es imprevisible y varía de persona a persona. Lo más característicos de la enfermedad son los periodos de exacerbación o brotes, en los que aparecen nuevos síntomas o se agravan los existentes.

Las formas de evolución de la esclerosis múltiple son las siguientes:

Remitentes-recurrentes: Es las más frecuentes; se define por la presencia de exacerbaciones claras (brotes) con recuperación parcial o total de las secuelas. Pueden durar días, semanas e incluso meses, y variarán de un episodio a otro, según la zona del sistema nervioso central afectada.

Secundariamente progresiva: Inicialmente es una forma remitente-recurrente seguida de progresión, con o sin recaídas. Un 25% de las personas que padecen EM Remitente-Recurrente evolucionan con un empeoramiento neurológico progresivo que deriva, con los años, en este tipo de Esclerosis Múltiple.

Primariamente progresiva: Definida por la progresión continúa de déficit neurológico desde su inicio. Un 12% de los pacientes padece este tipo de EM. Especialmente relacionados con la habilidad de caminar y la fuerza motora.

Progresiva recurrente: Definida por la progresión del déficit neurológico desde su inicio con claras recaídas, con o sin recuperación completa. Esta clasificación la padece sólo un 5% de los pacientes con Esclerosis Múltiple y se caracteriza por una progresión constante de la enfermedad desde el principio y por exacerbaciones ocasionales en su evolución (1).

En el tratamiento médico, se ha demostrado en dos estudios con distribución aleatorizada y controlados con placebo ,se prescriben el tratamiento inmunomodula ,interferones y acetato glatiramer, reducen la frecuencia y gravedad de las recaídas y retrasan la aparición de la incapacidad en las personas con esclerosis múltiples recidivantes .el tratamiento inmunosupresor también ha recibido mucha atención(6).

El medico fisiatra realizará la evaluación de cada caso e indicará el tratamiento dependiendo del estadio y condiciones clínicas de cada paciente (espasticidad, parálisis, paresia, hipotonía, etc.), realizando el control y seguimiento con revaloración del paciente, por lo menos cada bloque de 10 sesiones indicadas, realizando escalas de medición funcional, como indicadores de evolución y mejoría respecto al inicio del tratamiento fisiátrico (7).

En el tratamiento fisioterapéuticos ,se deberá intervenir desde los signos más temprano hasta los estadios terminales de la enfermedad y necesita un consecuencia estar familiarizado con todas las técnicas apropiadas requeridas para tratar cualquier de las características clínicos posibles se suelen usar: vibraciones, masajes, estiramientos, ejercicios activos , programa de ejercicios, hidroterapia, , Tai Chi, movilizaciones pasivas, Mecanoterapia, Equinoterapia, FNP, Bobath, todo ello con el fin de reducir: el deterioro y mejorar la capacidad funcional y facilitar el movimiento y el equilibrio normal.[4].

Aunque no existe cura para la EM, los síntomas pueden ser tratados mediante ejercicio fisioterapéutico, pudiendo ayudar a mantener y mejorar el equilibrio, la movilidad y la calidad de vida de estas personas para continuar las tareas de su vida diaria. Como por ejemplo: reducir el deterioro de la función de la vejiga y la función intestinal en personas con EM. Afecta positivamente a la salud psicológica y la calidad de vida, retarda la reducción de la debilidad muscular, reduce potencialmente la fatiga sintomática, reduce los síntomas y puede disminuir los factores de riesgo cardiovascular y enfermedad metabólica[5].

Es por ello, que presentamos la siguiente revisión sistemática, para evidenciar el Efecto del Ejercicio fisioterapéutico en los pacientes con Esclerosis múltiple.

1.2. Formulación del problema

¿Cuál es el efecto del ejercicio terapéutico en pacientes con esclerosis múltiple?

1.3. Justificación

El presente estudio pretende conocer el efecto del ejercicio terapéutico en el equilibrio de pacientes con esclerosis múltiple, porque debido a los síntomas de la EM, esta población suele ser sedentaria, y la inactividad tiene consecuencias, como debilidad muscular, menor densidad ósea, menor forma cardiovascular y un aumento de la fatiga. Aunque no existe cura para la EM, los síntomas pueden ser tratados mediante ejercicio terapéutico, pudiendo ayudar a mantener y mejorar el equilibrio, y la calidad de vida de estas personas para continuar las tareas de su vida diaria[5].

Es así que la investigación se considera conveniente y útil, considerando que los estudios anteriores realizados con respecto al presente tema son pocos.

Así mismo, es factible y viable, en el sentido que se tienen los recursos metodológicos y herramientas para la identificación y análisis de la evidencia, la Universidad Privada Norbert Wiener cuenta con bases de datos a texto completo como la base EBSCO Host que permiten el acceso a la evidencia.

Este estudio se vincula a la universidad porque la revisión se encuentra dentro de las líneas de investigación de la carrera de terapia física como es la actividad física y el ejercicio físico.

1.4. Objetivos

Objetivo General

Determinar el efecto del ejercicio terapéutico en pacientes con esclerosis múltiple.

Objetivos específicos

Determinar el efecto de los ejercicios terapéuticos en el mejoramiento de la marcha en pacientes con esclerosis múltiple.

Determinar el efecto de los ejercicios terapéuticos en el mejoramiento del equilibrio en pacientes con esclerosis múltiple.

Determinar el efecto de los ejercicios terapéuticos en la disminución del riesgo de caídas en pacientes con esclerosis múltiple.

CAPÍTULO II: MÉTODOS

2.1. Criterios de Elegibilidad.

Se utilizaron como criterios de elegibilidad conforme a la estructura: Población, Intervención, Comparación y Outcome**(PICO):**

- **Población:** Pacientes con esclerosis múltiple
- **Intervención:** Ejercicio terapéutico
- **Comparación**: Tratamiento convencional
- **Outcome (resultados):** Equilibrio, marcha y riesgo de caídas

Además, se incluyeron otros criterios de elegibilidad:

- Publicaciones de los últimos 10 años para estimar la evidencia en este espacio de tiempo, porque nuestra investigación se basó en la búsqueda de la eficacia de nuevas modalidades fisioterapéuticas basado en la evidencia de los últimos avances.
- Publicaciones en inglés y español.

Criterios de Exclusión

- **Población:** Pacientes con otras enfermedades.
- **Intervención:** Intervenciones mediante asistencia robótica

Se buscaron estudios clínicos controlados, incluyendo también otros estudios, en los cuales se incluyó a pacientes con esclerosis múltiple en quienes se midió la efectividad del ejercicio terapéutico pretendiendo observar si ello les mejoraba su condición física y estilo de vida, y si al hacer ejercicio fisioterapéutico mejoraban su equilibrio, con fecha de publicación desde 2006 en adelante; estos artículos se hallaron en las bases de datos : PEDro,SciELO, PubMed, EBSCO; la información obtenida fue en todos los idiomas.

2.2. Fuentes de Información.

Para la elaboración de esta revisión sistemática fueron utilizadas las directrices propuestas por el PRISMA[8] y sus extensiones.

PRISMA es un conjunto mínimo de elementos basado en evidencia para escribir y publicar revisiones sistemáticas y metaanálisis, consta de 27 items terminología, formulación de la pregunta de investigación, identificación de los estudios y extracción de datos, calidad de los estudios y riesgo de sesgo, cuando combinar datos, metaanálisis y análisis de la consistencia, y sesgo de publicación selectiva de estudios o resultados.

Se realizó una revisión sistemática para verificar la efectividad del ejercicio terapéutico en pacientes con esclerosis múltiple. Se realizó la búsqueda de las bases de datos y buscadores especializados hasta el 08 de setiembre de 2017: PubMed, EBSCOhost, PEDroDatabase y SciELO-ScientificElectronic Library Online los cuales se muestran en la tabla 1.

Tabla N° 1

Estrategia de búsqueda

Fuente de Información	Enlace web	Tipo	Accesibilidad	Propietario/administrador
PUBMED	http://www.ncbi.nlm.nih.gov/pubmed	Motor de búsqueda y Base de Datos	Libre	Biblioteca Nacional de Medicina de los Estados Unidos
PEDRO Database	http://www.pedro.org.au/spanish/	Motor de búsqueda y Base de Datos especializada en fisioterapia	Libre	Centro de Fisioterapia Basada en la Evidencia en el George Institutefor Global Health
EBSCOhost	https://www.ebscohost.com/	Base de datos multidisciplinaria, académica y de investigación, contiene: SPORTDiscus MedicLatina Academic Search Premier	Suscripción	Elton B. Stephens COmpany
SciELO - Scientific Electronic Library Online	http://www.scielo.org/	Biblioteca electrónica publicación electrónica de ediciones completas de las revistas científicas	Libre	FAPESP (http://www.fapesp.br) - la Fundación de Apoyo a la Investigación del Estado de São Paulo, BIREME (http://www.bireme.br) - Centro Latinoamericano y del Caribe de Información en Ciencias de la Salud

2.3. Búsqueda.

La búsqueda inició con la determinación de las palabras claves ubicando sus sinónimos y terminología MESH o encabezados de términos médicos, encontrando que las cuatro palabras claves se encuentran en terminología Mesh.

Tabla N° 2

Términos Mesh y sinónimos en español e inglés

Búsqueda de Terminología Mesh/Desh				
	Término 1	**Término 2**	**Término 3**	**Término 4**
Término Español	Esclerosis Múltiple	Equilibrio	Terapia por Ejercicio	Anciano
DeCS	SI	NO	SI	SI
Término Ingles	MultipleSclerosis	Postural Balance	ExerciseTherapy	Aged
MESH	SI	SI	SI	SI
Sinónimos	Sclerosis, Multiple Sclerosis, Disseminated Disseminated Sclerosis MS (Multiple Sclerosis) Multiple Sclerosis, Acute Fulminating	Balance, Postural MusculoskeletalEquilibrium Equilibrium, Musculoskeletal Postural Equilibrium Equilibrium, Postural	Therapy, Exercise Exercise Therapies Therapies, Exercise Rehabilitation Exercise Exercise, Rehabilitation Exercises, Rehabilitation Rehabilitation Exercises Remedial Exercise Exercise, Remedial Exercises, Remedial Remedial Exercises	Elderly

Las estrategias de búsqueda variaron de acuerdo al buscador utilizado y sus características o filtros. Se realizó la estrategia de búsqueda en las bases de datos: PubMed (Tabla 3), PEDrodatabase (Tabla 4) EBSCOhost (Tabla 5), SciELO (ScientificElectronic Library Online) (Tabla 6).

Tabla N° 3

PUBMED

Estrategia	Buscados de constructor Mesh: aged, postural balance, multiplesclerosis, exercisetherapy con filtros de clinical trial y aged
Entradas	(("Aged"[Mesh] AND "Postural Balance"[Mesh]) AND "Multiple Sclerosis"[Mesh]) AND "Exercise Therapy"[Mesh] AND (Clinical Trial[ptyp] AND "aged"[MeSH Terms])

Tabla N° 4

PEDro

Estrategia	Busqueda avanzada : Multiplesclerosis and exercisetherapy balance: Clinical Trial
Entradas	multiple sclerosis and exercise therapy balance : Clinical trial

Tabla N° 5

EBSCO

Estrategia	Busquedasimple:Multiple sclerosis and exercise therapy balance
Entradas	Multiple sclerosis and exercise therapy balance

Tabla N° 6

SciELO

Estrategia	Ejercicio Esclerosis Múltiple
Entradas	Ejercicio sclerosis multiple

2.4. Selección de los estudios

El proceso de selección de estudios tuvo las siguientes etapas:

- **Fase de registro de salidas a las estrategias de búsqueda:** A las salidas (listado de estudios) determinadas por las estrategias de búsqueda establecidas en los buscadores y bases de datos consultadas, se incluyó el dato de fecha de búsqueda y número de estudios identificados. El tratamiento de este listado se realizó en una base de datos que consignaba a cada artículo según título, autor, journal, fecha, volumen y número.
- **Fase eliminación de duplicados:** se procedió a depurar los resultados, eliminando los estudios duplicados e integrándolos en una base de datos preladas alfabéticamente según el título.
- **Fase de análisis y selección:** Una vez obtenida la lista de estudios no duplicados se procedió a ordenar la base de datos según autor, año y título, se analizaron los artículos en base a sus títulos y resúmenes, finalmente las copias del texto completo para determinar la elegibilidad de acuerdo a los criterios de inclusión y exclusión. Se clasificaron según la elegibilidad de los estudios, en tres categorías: estudios incluidos, estudios eliminados por no cumplir algún criterio de inclusión y estudios eliminados por cumplir algún criterio de exclusión. Esta fase culmina cuando se obtuvo un listado de estudios seleccionados los cuales fueron ordenados por Autor (año) y título.

2.5. Riesgo de sesgo en los estudios individuales.

El riesgo de selección en los estudios individuales fue realizado analizando la calidad metodológica según la escala de PEDro que contiene 11 criterios de los

Cual es él Nº1 no se puntúa[9]..

La puntuación total va del 0 al 10, según los siguientes criterios

La escala PEDro considera dos aspectos de la calidad de los ensayos, a saber, la “credibilidad” (o “validez interna”) del ensayo y si el ensayo contiene suficiente información estadística para hacerlo interpretable. No mide la “relevancia” (o “generalización” o “validez externa”) del ensayo, o el tamaño del efecto del tratamiento [10].

La mayor parte de los criterios de la lista “se basan en la lista Delphi, desarrollada por Verhagen y sus colegas. La lista Delphi es una lista de características de ensayo que se consideran que están relacionadas con la “calidad” del ensayo por un grupo de expertos de ensayos clínicos. La escala PEDro contiene elementos adicionales sobre la adecuación del seguimiento y comparaciones estadísticas entre grupos. Un elemento presente en la lista Delphi (relativo a los criterios de elegibilidad) está relacionada con la validez externa, por lo que no se corresponde con las dimensiones de la calidad evaluada por la escala de PEDro. Este elemento no se emplea para calcular la puntuación del método que se muestra en los resultados de búsqueda (es por lo que una escala de 11 elementos tan solo ofrece una puntuación sobre 10). Este elemento, sin embargo, se ha conservado por lo que todos los elementos de la lista Delphi están presentes en la escala PEDro[11].

Tabla N° 7

Puntuaciones en la escala PEDro de Evaluación de la calidad - Ensayos Clínicos Controlados

N	ITEMS
1	Los criterios de elección fueron especificados
2	Los sujetos fueron asignados al azar a los grupos (en un estudio cruzado, los sujetos fueron distribuidos aleatoriamente a medida que recibían los tratamientos)
3	La asignación fue oculta
4	Los grupos fueron similares al inicio en relación a los indicadores de pronóstico más importantes
5	Todos los sujetos fueron cegados
6	Todos los terapeutas que administraron la terapia fueron cegados
7	Todos los evaluadores que midieron al menos un resultado clave fueron cegados
8	Las medidas de al menos uno de los resultados clave fueron obtenidas de más del 85% de los sujetos inicialmente asignados a los grupos
9	Se presentaron resultados de todos los sujetos que recibieron tratamiento o fueron asignados al grupo control, o cuando esto no pudo ser, los datos para al menos un resultado clave fueron analizados por “intención de tratar”
10	Los resultados de comparaciones estadísticas entre grupos fueron informados para al menos un resultado clave
11	El estudio proporciona medidas puntuales y de variabilidad para al menos un resultado clave

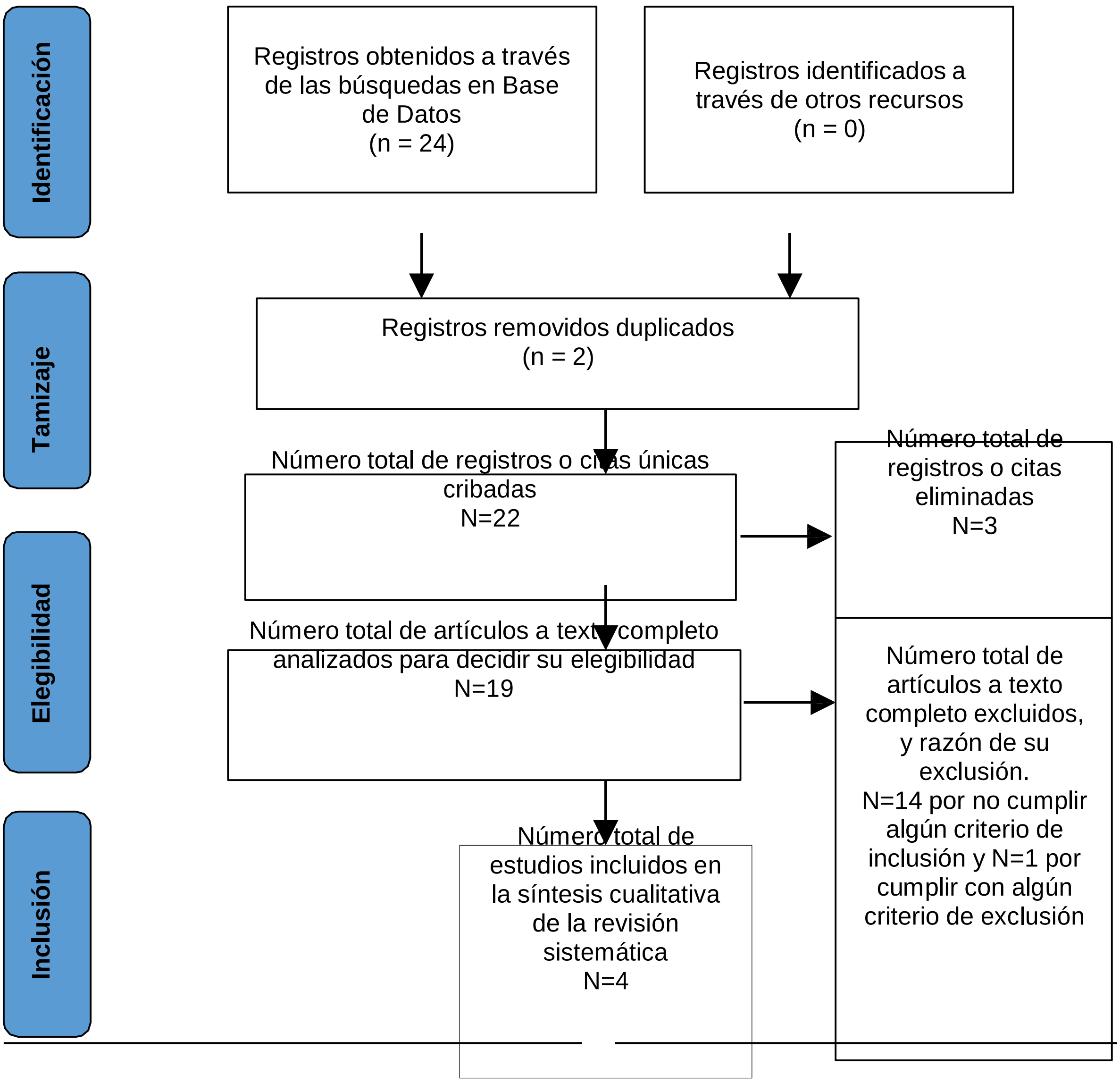
CAPÍTULO III: RESULTADOS

3.1. Selección de estudios

Los estudios identificados fueron 24: número de registros identificados en las búsquedas, N = **24:** En PEDrodataBase**= 8**, PubMed=**11**, EBSCOhost=**2,** SciELO-ScientificElectronic Library Online =**3** y revisiones sistemáticas N= **0.**

En el tamizaje se encontraron 2 estudios duplicados y en el proceso de elegibilidad fueron excluidos 15 estudios; por no cumplir criterio de inclusión =14 y presenta criterio de exclusión =1. Finalmente fueron incluidos 4 estudios.

Gráfico 1



Fuente: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoSMed 6(7): e1000097. doi:10.1371/journal.pmed1000097

3.2. Características de los estudios.

Los estudios seleccionados fueron en su totalidad estudios clínicos controlados y randomizados. 4 ensayos clínicos que cumplían los criterios de inclusión/exclusión y cuyo objetivo principal era determinar la efectividad del ejercicio terapéutico en pacientes con esclerosis múltiple. a nivel espacio fueron realizados en Italia, Estados Unidos y Australia. A nivel tiempo fueron publicados entre 2011 – 2016. La mayor población fue de 103 en un estudio realizado el 2015 y según PICO puede apreciarse las características de estos 4 estudios en relación a los participantes, intervenciones, criterios empleados para la comparación y variable de salida (medición) obtenidos que se recogen en la tabla 8.

Tabla N° 8

Sistematización de investigaciones identificadas

Autor y año	Propósito	Participantes	Intervención	Medición	Resultados
Brichetto G et. all 2015	Evaluar la eficacia de los tratamientos de rehabilitación a medida para los trastornos del equilibrio basados en deficiencias visuales, somatosensoriales y vestibulares frente a los ejercicios de rehabilitación tradicionales.	32 pacientes con esclerosis múltiple mayores de 18 años,	12 sesiones, tres Sesiones / semana, sesión de una hora por un mes.	Escala de Equilibrio de Berg (BBS), la puntuación compuesta (CS) obtenida mediante la posturografía dinámica computarizada (CDP) y la Escala de Impacto de Fatiga Modificada (MFIS).	La puntuación de BBS mostró una diferencia significativa entre las puntuaciones pre y post-tratamiento de 6.3 y 2.0 puntos respectivamente para PRG y TRG. CS mostró una diferencia significativa entre pre- y post-tratamiento de 16,6 y 7,6 puntos respectivamente para PRG y TRG. No se encontró ningún efecto de interacción para la puntuación de MFIS.

Autor y año	**Propósito**	**Participantes**	Intervención	Medición	**Resultados**
Davies BL et al. 2016	Evaluar las mejoras en la movilidad y el equilibrio postural que podrían lograrse en una cohorte de personas con esclerosis múltiple (EM) Que participaron en un protocolo de adaptación motora y una cohorte de personas con EM que participaron en un protocolo de ejercicio terapéutico.	Individuos (N = 42) con EM remitente-recidivante o secundaria progresiva (Escala de Estatus de Discapacidad Expandida [EDSS] puntajes, 3.0 - 6.5) fueron seleccionados inicialmente para la elegibilidad para la participación en el estudio, de los cuales los que cumplen los criterios de inclusión (n = 32) se inscribieron en el estudio. Los sujetos se asignaron de manera pseudoaleatoria a un grupo de tratamiento y se emparejaron según las puntuaciones de EDSS. Catorce individuos en la cohorte de adaptación motora (MAC) (edad media ± DE, 52,6 ± 9, puntuación media de EDSS ± SD, 5,5 ± 0,9) y 13 individuos en la cohorte de ejercicio terapéutico (TEC) (edad media ± DE, 54,0 ± 9y ; puntuación media EDSS ± SD, 5,3 ± 0,9) completaron la duración total de sus respectivos programas.	Dos veces al día, 5 días a la semana, durante 6 semanas.	Prueba de la organización sensorial, prueba de la caminata de 6 minutos y cinemática espaciotemporal de la marcha.	Colectivamente, ambos grupos de tratamiento tuvieron mejoras en el equilibrio postural (P=.001), resistencia al caminar (P=.002), velocidad de marcha (P=.004) y longitud del paso (P <.001) después de la terapia. Sin embargo, no hubo diferencias estadísticas entre los 2 grupos de tratamiento para ninguna de las variables de resultado (valores P> .01).

Autor y año	Propósito	Participantes	Intervención	Medición	Resultados
Sabapathy NM et al. 2011	El propósito de este estudio fue comparar las adaptaciones en las medidas funcionales y de calidad de vida después del entrenamiento de resistencia y ejercicio de resistencia en personas con esclerosis múltiple.	Los análisis se realizaron sobre los datos recogidos de 12 mujeres y 4 varones de 47-66 años. Los sujetos con esclerosis múltiple fueron incluidos en el estudio si podían ambular independientemente con o sin el uso de ayuda de caminar.	Los sujetos completaron un programa de entrenamiento de ocho semanas de resistencia y un programa de entrenamiento de resistencia de ocho semanas en un orden aleatorio. El entrenamiento de ejercicio comprendía programas progresivos individualizados que se completaron dos veces por semana en un grupo supervisado.	Fuerza de agarre, alcance funcional, cuadrado de cuatro pasos, cronometrado e ir y pruebas de caminata de seis minutos, Escala de Impacto de Esclerosis Múltiple y Escalas de Impacto de Fatiga Modificada, Inventario de Depresión de Becks y el Cuestionario de Estado de Salud Short Form-36.	Dieciséis de 21 (76%) sujetos completaron el estudio. Los sujetos asistieron a 13.2 ± 1.6 resistencia y 15.8 ± 1.9 sesiones de entrenamiento con ejercicios de resistencia. No se reportó ningún evento adverso. No se observaron diferencias significativas ($P<0.05$) en ninguna medida de resultado entre los dos programas de entrenamiento de ejercicio, ya sea al inicio del estudio o una vez completados ambos programas de entrenamiento.

Autor y año	Propósito	Participantes	Intervención	Medición	Resultados
Sosnoff JJ et al. 2015	Determinar la viabilidad de tres programas de prevención de caídas entregados a más de 12 semanas entre individuos con esclerosis múltiple: **(A)** un programa de ejercicios en el hogar dirigido a factores de riesgo fisiológicos; **(B)** un programa educativo dirigido a factores de riesgo conductuales; y **(C)** un programa combinado de ejercicio y educación dirigido a ambos factores.	Un total de 103 personas preguntaron sobre la investigación. Después de la selección, 37 personas con esclerosis múltiple que habían caído en el último año y con edades comprendidas entre 45 y 75 años se ofrecieron voluntariamente para la investigación. Un total de 34 participantes completaron la evaluación posterior después de la intervención de 12 semanas.	Los participantes fueron asignados aleatoriamente en una de cuatro condiciones: (1) control de lista de espera (n = 9); (2) ejercicio en el hogar (n = 11); (3) educación (n = 9); (4) un grupo combinado de ejercicios y educación (n = 8).	Antes y después de las intervenciones de 12 semanas, los participantes se sometieron a una evaluación del riesgo de caídas según lo determinado por la evaluación del perfil fisiológico y proporcionaron información sobre sus comportamientos de prevención de caídas según los índices de la Encuesta de Estrategia de Prevención de Caídas. Los participantes completaron los diarios de caídas durante los tres meses posteriores a la intervención.	Un total de 34 participantes completaron las pruebas post intervención. En general, las puntuaciones de riesgo de caída fueron inferiores en los grupos de ejercicio (1,15 SD 1,31) en comparación con los grupos sin ejercicio (2,04 SD 1,04) después de la intervención (p <0,01). No hubo diferencias de grupo en los comportamientos de prevención de caídas (p> 0,05).

3.3. Evaluación de calidad

La evaluación de la calidad según la escala de PEDro obtuvo en promedio un puntaje de 5/10, según se detalla en la siguiente tabla:

Tabla N° 9

Evaluación de la calidad - Ensayos Clínicos Controlados

Evaluación de la calidad - Ensayos Clínicos Controlados					
ITEMS		Brichetto G et al. 2015	Davies BL et al. 2016	Sabapathy NM et al. 2011	Sosnoff JJ et al. 2015
1	Los criterios de elección	SI	SI	SI	SI
2	Asignación aleatoria	SI	SI	SI	SI
3	La asignación fue oculta	SI	NO	NO	SI
4	Comparabilidad inicial	SI	SI	SI	SI
5	Todos los sujetos fueron cegados	NO	NO	NO	NO
6	todos los terapeutas fueron cegados	NO	NO	NO	NO
7	todos los evaluadores fueron cegados	SI	NO	NO	SI
8	Seguimiento adecuado	NO	SI	SI	SI
9	Por intensión de tratar el análisis	NO	NO	NO	NO
10	Entre el grupo de las comparaciones	SI	SI	SI	NO
11	Apunte estimaciones y variabilidad	SI	SI	SI	NO
		6	**5**	**5**	**5**

3.4. Síntesis de los resultados.

Se analizaron 4 ensayos controlados aleatorios en donde la tabla 9 muestra los resultados y las características más relevantes de los estudios analizados. La esclerosis múltiple es un trastorno neurológico progresivo o recidivante del sistema nervioso central.

Los síntomas físicos, que incluyen fatiga y problemas de movilidad, pueden contribuir a la reducción de la capacidad funcional e interferir con la capacidad de realizar actividades de la vida diaria. Las actividades de la vida diaria más afectadas en personas con esclerosis múltiple son aquellas tareas que podrían clasificarse como relacionadas con la movilidad y físicamente exigentes (por ejemplo, tareas domésticas, jardinería)[12].

Según los resultados obtenidos en los diferentes estudios realizados por indican que los participantes de los estudios demostraron una mejoría significativa en el balance y movilidad de los pacientes [13-16].

CAPÍTULO IV: DISCUSIÓN

4.1. Análisis e Interpretación

Los hallazgos del estudio de Brichetto et al. 2015 demuestran la viabilidad de un enfoque de rehabilitación personalizado y su efectividad para mejorar el equilibrio (puntaje BBS) y el control postural vertical (puntaje compuesto). Notablemente, las mejoras fueron significativamente mayores para el PRG que el TRG[13], esto coincide con lo encontrado por Davies BL et al. 2016 pero este último no encontró diferencias entre aplicar un programa de adaptación motora frente a un protocolo de ejercicios terapéuticos, probablemente porque ambos tienen efectos sobre el equilibrio.

En ese sentido, Davies BL et al. 2016 comparó los resultados de una cohorte de personas con EM que participaron en el protocolo MAC con una cohorte de personas con EM que participaron en el protocolo TEC, que después de completar los respectivos programas, ambos grupos tuvieron mejoras en su resistencia al caminar y velocidades de marcha más rápidas, lo que se logró mediante el uso de una longitud de paso más larga [14]. Sin embargo, los resultados terapéuticos de los respectivos grupos fueron equívocos, lo que indica que ambos enfoques de tratamiento pueden tener el mismo efecto en la movilidad. Estas mejoras de movilidad podrían estar relacionadas con la alta frecuencia de actividades para caminar que ambos grupos completaron. Los protocolos de entrenamiento en tapiz rodante utilizados en otras investigaciones que evaluaron la velocidad de marcha preferida consistieron en 30 minutos de caminatas en cinta ergométrica que se realizaron 3 veces por semana durante un período de 4 semanas. Los resultados de estos estudios han sido bastante variables con una mejora del 3% al 12% en la velocidad de marcha. Nuestros resultados están en el techo de estos resultados previos, lo que sugiere que una mayor frecuencia de actividades para caminar puede ser beneficiosa para mejorar la movilidad de las personas con EM. En general, los resultados positivos observados en ambos grupos sugieren que la fisioterapia de alta frecuencia puede promover mejoras en el equilibrio postural y la movilidad de las personas con EM. La frecuencia de la terapia física utilizada en esta investigación fue mucho más alta que la mayoría de los programas que se han evaluado para personas con EM[14].

En el artículo Brichetto et al. [13] y el artículo Davies BL et al [14] se evidencia que ambos tienen como objetivo en común el mejorar el equilibrio pero solamente en el de Davies BL et al [14] se adiciona el mejoramiento de la marcha como objetivo aparte del mejoramiento del equilibrio.

Considerando lo anterior, en el posterior estudio de Sabapathy et al. 2011no se encontraron diferencias entre los modos de entrenamiento (entrenamiento de resistencia versus ejercicio de resistencia) para ninguna de las medidas de la capacidad física. Sin embargo, con la excepción de la fuerza de agarre, el análisis de los datos encontró que todas las medidas de la capacidad física mejoraron significativamente con ocho semanas de entrenamiento físico[15].

Dentro del efecto en el equilibrio solo el estudio de Sosnofet al. 2015 evaluaron el riesgo de caídas, si bien es cierto el equilibrio es una variable importante de ser medida son las caídas y el riesgo de caer, el estándar más robusto de medición en ese sentido un programa de ejercicios en el hogar dirigido a factores de riesgo fisiológicos comparado con un programa educativo dirigido a factores de riesgo conductuales y un programa combinado de ejercicio y educación dirigido a ambos factores. Se encontró que los programas que incluyen ejercicios disminuyen los riesgos de caídas.(16)

4.2. Limitaciones.

Se encontraron pocos artículos de investigación adecuados con las características requeridas.

La búsqueda se limitó a los buscadores más importantes, aun así es posible que se encuentre alguna evidencia no identificada en otros buscadores.

4.3. Conclusiones.

- Se determina que existe un efecto positivo del ejercicio terapéutico en pacientes con esclerosis múltiple.

- Se determina que el ejercicio terapéutico tiene efecto en el mejoramiento del equilibrio en los dos estudios que se evaluó el equilibrio, sin embargo, solo en uno de los dos estudios el resultado fue estadísticamente significativo y en el otro no.

- En base a las investigaciones realizadas solo en una se evaluó el mejoramiento de la marcha y en esta se determina que el ejercicio terapéutico tuvo efecto en el mejoramiento de la marcha, pero el resultado no fue estadísticamente significativo.

- De los cuatro estudios realizados solo en uno se evaluó el riesgo de caídas y se determinó que el ejercicio terapéutico disminuyó el riesgo de caídas, pero el resultado no fue estadísticamente significativa

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ANEXOS

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Tailored balance exercises on people with multiple sclerosis: A pilot randomized, controlled study

Giampaolo Brichetto, Elisa Piccardo, Ludovico Pedullà, Mario Alberto Battaglia and Andrea Tacchino

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Tailored balance exercises on people with multiple sclerosis: A pilot randomized, controlled study

Giampaolo Brichetto, Elisa Piccardo, Ludovico Pedullà, Mario Alberto Battaglia and Andrea Tacchino

Abstract

Background: Altered integration of signals from visual (VIS), somatosensory (PROP) and vestibular system (VEST) lead to balance control impairments affecting the daily living activities of patients with multiple sclerosis (PwMS). As a consequence, tailored interventions could be crucial in improving efficacy of balance rehabilitation treatments.

Objective: The objective of this paper is to assess the efficacy of tailored rehabilitation treatments for balance disorders based on visual, somatosensory and vestibular deficits versus traditional rehabilitation exercises.

Methods: Thirty-two PwMS were assessed with the Berg Balance Scale (BBS), the composite score (CS) obtained by computerized dynamic posturography (CDP) test and the Modified Fatigue Impact Scale (MFIS). Based on CDP analysis, prevalent VIS, PROP or VEST deficits were identified and patients randomly allocated to a personalized (PRG) or traditional (TRG) rehabilitation group.

Results: BBS score showed a significant difference between pre- and post-treatment scores of 6.3 and 2.0 points respectively for PRG and TRG. CS showed a significant difference between pre- and post-treatment scores of 16.6 and 7.6 points respectively for PRG and TRG. No interaction effect was found for MFIS score.

Conclusions: BBS and CS showed changes in the PRG group that met clinical relevant difference, underlining that tailored rehabilitation interventions based on patient-specific sensory system impairment could improve balance and postural control in PwMS.

Keywords: Balance disorders, rehabilitation, tailored interventions, multiple sclerosis, computerized dynamic posturography, sensory analysis

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Introduction

Balance control impairments are common in patients with multiple sclerosis (PwMS) and may affect about three-quarters of patients during the course of the disease.[1,2] Central nervous system damage, observed in PwMS, leads to an altered central sensory integration of signals from muscle, tendon, joint proprioceptors, skin exteroceptors, vestibular and visual inputs affecting postural response in maintaining correct balance.[3] These abnormalities, together with other impairments and disabilities, often prevent people from performing their daily living activities and are also risk factors for falls in PwMS.[4] Mainly for these reasons, the assessment[5,6] and the treatment[7–9] of balance and gait impairments have gained more interest within the scientific community.

Balance is an essential component in assessing the efficacy of interventions for improving postural stability.[10] Clinicians have available a growing number of clinical tests to quantify balance, such as the Berg Balance Scale (BBS) and Timed-get-up-and-go-test (TUG).[11,12] However, computerized dynamic posturography (CDP) has become an important tool for assessing balance in clinical settings, in particular in stroke patients and older adults.[13–17] Furthermore, a CDP training program could also reduce risk of fall in chronic stroke patients.[18] A key CDP test is the Sensory Organization Test (SOT), which provides information about the integration of visual, proprioceptive, and vestibular components of balance that leads to an outcome measure called the Composite score, reflecting the overall coordination of these systems to maintain standing posture.[19]

Since MS' multifaceted characteristics often lead to heterogeneous deficits and that impairment of visual (VIS),[20] proprioceptive (PROP)[21] and vestibular (VEST)[22] systems are very common in PwMS, task-specific rehabilitation of VIS, PROP and VEST deficits, evaluated with CDP, could have a key role in improving efficacy of balance rehabilitation interventions and stimulate patients' attention,[23,24] preventing injuries and falls in PwMS.[9,25]

This study aimed to assess the efficacy of tailored rehabilitation treatments for balance disorders based on VIS, PROP and VEST deficits evaluated by means of CDP versus traditional rehabilitation exercises.

Methods

Subjects

PwMS according to the McDonald criteria[26] and followed as outpatients at the Italian MS Society Rehabilitation Service, Genoa, Italy, were asked to participate in this study. Individuals who met the following inclusion criteria were enrolled in this study: an age older than 18 years, stable phase of the disease without relapses or worsening in the last three months, referring fear of falling or a history of falls (at least one fall in the last year). In order to not include individuals with a high level of balance, a composite score less than 72[27] and a maximum score of 50 on the BBS[9,27,28] were considered. Furthermore, in order to avoid an effect of severe motor strength impairment, we included patients evaluated with the Medical Research Council (MRC) scale[29] (0 to 5 grades) at the proximal and distal lower limb segments (hip, knee and ankle), with at least grade 4 in all muscle groups or grade 3 in no more than one joint. We excluded individuals with psychiatric disorders, blurred vision, severe cognitive impairment, severely impaired upright postural control or limited participation in a rehabilitation program; or cardiovascular and respiratory disorders. The study was approved by the local ethics committee, and before any study related-procedure each patient was asked to provide a written informed consent.

Sample size

Sample size was determined by comparing means of BBS from a previous work on PwMS.[23] The criterion for significance (α) was set at 0.05 (two tailed) and the statistical power was at least 80%. The proposed sample size would be 30.28 participants for both groups.

Instrumental evaluation

Postural assessment was quantified by a blinded physician, not involved in the study, with a computerized dynamic stabilometric platform (EquiTest, Neurocom, Clackamas, OR, USA). Subjects were evaluated barefooted with CDP, placed at the center of a sound-attenuated room, approximately three meters from the walls,[23] during three replicate 20-second runs under each of the following six sensory conditions: sensory organization test (SOT) 1, immobile surface, immobile visual surround, eyes open; SOT 2, immobile surface, eyes closed; SOT 3, immobile surface, mobile visual surround, eyes open; SOT 4, mobile surface, immobile visual surround, eyes open; SOT 5, mobile surface, eyes closed; SOT 6, mobile surface, mobile visual surround, eyes open. By independently averaging the scores achieved under conditions SOT 1 and SOT 2, adding these two values to the sum of all three scores under sensory conditions SOT 3, 4, 5 and 6 and then dividing the sum by the total number of trials, the Composite score, a mathematical-analytic indicator of balance, was calculated.[30] Furthermore, an algorithm for calculating individual component of balance was used. In particular, the VIS system individual component was calculated by a quotient $\frac{SOT4}{SOT1}$ and defined the patient's ability to use input from the *visual system* (VIS) to maintain balance; the PROP system individual component was calculated by a quotient $\frac{SOT2}{SOT1}$ and defined the patient's ability to use input from the *proprioceptive system* (PROP) to maintain balance; the VEST system individual component was calculated by a quotient $\frac{SOT5}{SOT1}$ and defined the patient's ability to use input from the *vestibular system* (VEST) to maintain balance.[30]

Randomization

Based on CDP sensory analysis, three strata of participants with prevalent VIS or PROP or VEST deficits, defined as a deviation of at least 15% from normal values based on healthy individual reference data,[19,31,32] were formed. Block sizes of two were randomly selected for each strata and a blinded physician, not involved in

the study, concealed the block sequences and provided the random group assignments. Participants were then randomly allocated to one of two intervention groups (personalized rehabilitation group – PRG and traditional rehabilitation group – TRG).

Outcome measures

Individuals were evaluated by a blinded physician at T0 (start of treatments) and, after one month, at T1 (end of treatments). The BBS score[28] was considered as primary outcome, Composite score and Modified Fatigue Impact Scale (MFIS)[33] as secondary outcomes.

The BBS is a 14-item scale exploring the ability to sit, stand, lean, turn, and maintain the upright position on one leg. Composite score of equilibrium is based on the weighted average of the percentage of equilibrium scores for each of the six conditions performed with the CDP. Moreover, based on previous results from literature on the effect of vestibular rehabilitation on fatigue[27] and on the association between balance and MS-related fatigue as a function of central sensory integration, symptomatic fatigue was measured using a related clinical scale.[34] The MFIS is a fatigue-related scale for PwMS that ranges from 0 to 84.

On the basis of previous studies, a clinically significant improvement was set at 4.0 points for the BBS,[9] at 7.0 points for the Composite score[35] and at 15.0 points for the MFIS.[36]

Interventions

PRG participants were submitted to a personalized rehabilitation treatment tailored to the prevalent sensory system impairment while TRG was submitted to a standardized rehabilitation treatment for balance disorders (for both PRG and TRG: 12 sessions, three sessions/week, one-hour session for one month). The treating therapist was preliminary trained on PRG and TRG protocols.

PRG intervention

Individuals with a prevalent VIS deficit received visual rehabilitation treatment for balance disorders in the open-eyes condition and with visual feedback. Intervention included: exercises for body stability in different positions (bridge, sitting, quadrupedal, half-kneeling, kneeling, standing, monopodalic) performed with visual biofeedback; transfers training performed in front of a mirror; ambulation training with courses drawn on the ground in a straight line and with more complex tracks with visual control; exercises with a biofeedback platform (Balance Master, Neurocom) and in particular using the protocols seated balance/strength training, standing balance/weight-bearing training, mobility training and closed-chain training; and visuo-proprioceptive exercises with a Wii® balance board according to a previous study.[23]

Patients with prevalent PROP deficit received PROP rehabilitation treatment for balance disorders in the open-eyes and closed-eyes conditions with balance and gait-training exercises. Exercises included progressive restriction of support base and use of unstable surfaces like wobble boards, balance pads or stability balls in different positions (bridge, sitting, quadrupedal, half-kneeling, kneeling, standing, one-leg standing), stimulation of deep sensitivity with air splints, taping, vibration; exercises for dynamic balance during transfers and ambulation using unstable surfaces and stimuli performed without visual control and ambulation with closed eyes.[25]

Participants with prevalent VEST deficit received VEST rehabilitation treatment for balance disorders with specific interventions for enhancing gaze stability, postural stability and improving vertigo. Exercises included balance training using variable or moving surfaces, movement of the head (when the body is stationary or moving), decreasing visual inputs, as well as moving the head and/or eyes; exercises for slow and fast ocular motility in different head positions sit- ting and standing on stable and unstable surfaces; gaze exercises with head movements in sitting pos- ture; standing and transfers in stable and unstable sur- faces; ambulation with head in different positions and with head movements in different directions with open and closed eyes.[27]

TRG intervention

TRG exercises consisted of static and dynamic exercises in single-leg and double-leg stance, half-kneeling exercises with increasing difficulty, gait and treadmill training tailored to the ability level of each participant.[9]

Data analysis

Analysis was performed in order to assess the overall efficacy of rehabilitation treatments and to identify possible changes induced by personalized rehabilitation treatments. Statistical analysis was performed at three separated steps.

First, Shapiro-Wilks and Levene tests were used to check the normality of distribution and the

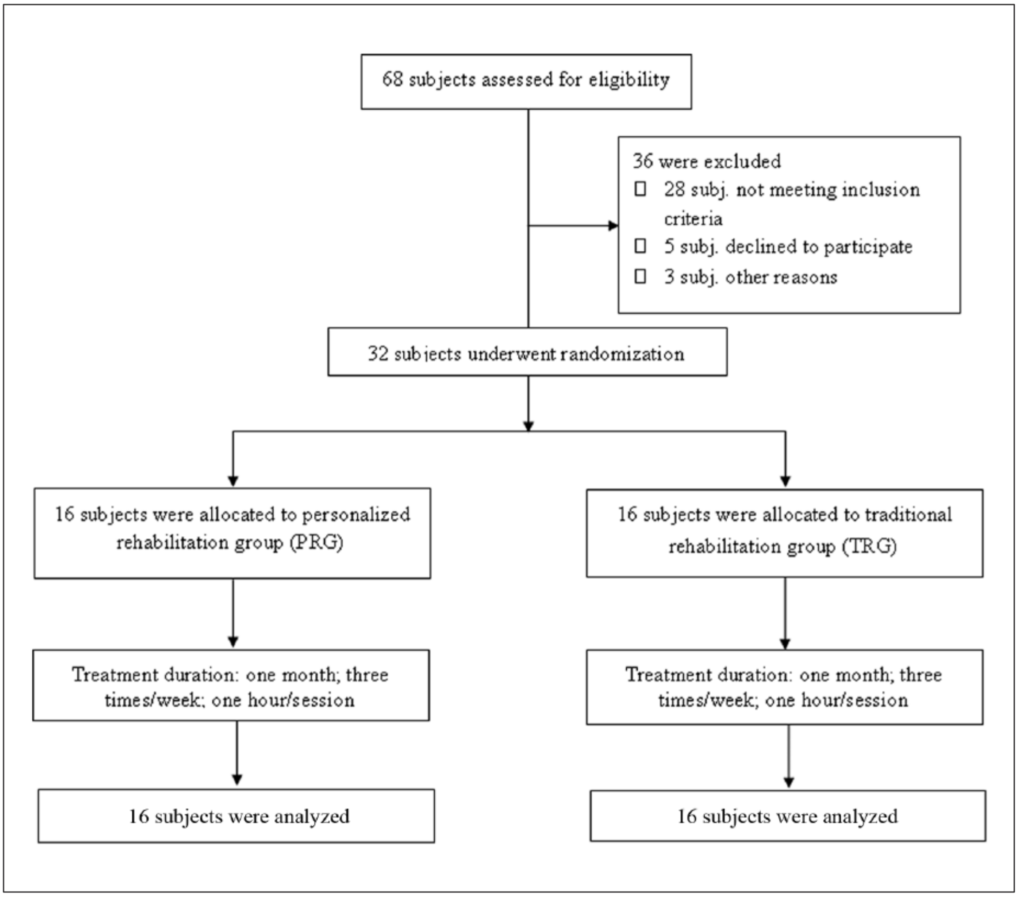

Figure 1. Flow diagram of participant recruitment and participation in the study. PRG: personalized rehabilitation group; TRG: traditional rehabilitation group.

homogeneity of variances. Second, in order to evaluate baseline characteristics and change scores of the study participants, the two groups were compared using a one-way analysis of variance (ANOVA). Finally, a repeated-measurements ANOVA analysis on the primary and secondary outcomes was carried out for the *group* (PGR, TGR) and *time* (T0–T1) factors. Furthermore, an explorative analysis was carried out in order to show improvements per subgroups. Statistical analysis was performed using SPSS for Windows Version 21.

Results

Participants

From January 2, 2011 to March 30, 2012, a total of 68 PwMS followed as outpatients at AISM Rehabilitation Service, Genoa, Italy, were assessed for eligibility; out of these 32 PwMS (nine male, 23 female; mean age 50.5 ± 11.6 years; mean disease duration: 10.5 ± 6.4 years; mean Expanded Disability Status Scale (EDSS) 3.7 ± 1.2; 19 individuals were relapsing–remitting, nine secondary progressive and four primary progres- sive) were recruited for the present study (see Figure 1 and Table 1). Based on CDP, 10 patients with prevalent VIS deficit (minus 19.7 ± 4.2% for VIS, minus 5.4 ± 1.2% for PROP and minus 6.3 ± 1.3% for VEST from normal values based on healthy individuals' reference data), 11 participants with prevalent PROP deficit (minus 23.4 ± 6.7% for PROP, minus 7.5 ± 3.4% for VIS and minus 4.2 ± 0.9% for VEST from normal values for healthy individuals) and 11 patients with prevalent vestibular deficit (minus 21.2 ± 5.4% for VEST, minus 8.1 ± 3.2% for PROP and minus 2.7 ± 0.9% for VEST from normal values for healthy individuals) were identified. Then, following a randomization procedure, 16 patients (five VIS patients, six PROP patients and five VEST patients) were assigned to PRG, while 16 individuals (five VIS, five PROP and six VEST individuals) were assigned to TRG (see Table 1 for further details).

No significant differences between groups were found in the baseline characteristics for age, EDSS,

Table 1. Demographical and clinical data of the study participants.

	All (*N* = 32)	PRG (16)	TRG (16)
Age	50.5 ± 11.6	50.1 ± 13.5	51.0 ± 8.9
Gender (male/female)	9/23	4/11	5/12
Disease duration (years)	10.5 ± 6.4	9.5 ± 6.6	12 ± 6.2
Relapsing–remitting *n*. (%)	19 (59.4)	9 (56.3)	10 (62.5)
Secondary progressive (%)	9 (28.2)	5 (31.2)	4 (25.0)
Primary progressive (%)	4 (12.5)	2 (12.5)	2 (12.5)
EDSS	3.7 ± 1.2	3.7 ± 1.1	3.7 ± 1.4
MRC hip	4.6 ± 0.5	4.5 ± 0.6	4.6 ± 0.4
MRC knee	4.4 ± 0.5	4.4 ± 0.4	4.3 ± 0.6
MRC ankle	4.1 ± 0.7	4.2 ± 1.1	4.1 ± 0.5
BBS	46.6 ± 5.5	46.5 ± 3.6	46.8 ± 7.5
Composite	57.6 ± 11.5	57.8 ± 11.2	57.4 ± 12.6
MFIS	35.1 ± 17.62	36.5 ± 17.5	33.4 ± 18.4

Values are means ± standard deviation for age, disease duration and Expanded Disability Status Scale (EDSS); disease course in percentage; MRC: Medical Research Council scale; BERG: Berg Balance Scale; MFIS: modified fatigue impact scale; Composite: composite score of Sensory Organization Test; PRG: personalized rehabilitation group; TRG: traditional rehabilitation group. No significant differences occurred between groups in baseline characteristics.

Table 2. Effect of tailored and traditional intervention in PwMS.

		T0	T1	RM-ANOVA
BBS (score)	ALL	46.2 ± 4.9	50.7 ± 5.1	TIME *p* < 0.001 TIME*GROUP *p* < 0.001
	PRG	46.5 ± 3.6	52.8 ± 2.8	
	TRG	45.8 ± 6.6	47.8 ± 6.1	
Composite (%)	ALL	57.6 ± 11.5	70.4 ± 8.7	TIME *p* < 0.001 TIME*GROUP *p* < 0.05
	PRG	57.8 ± 11.2	74.4 ± 6.4	
	TRG	57.4 ± 12.6	65.0 ± 8.6	
MFIS (score)	ALL	35.2 ± 17.6	24.1 ± 13.2	TIME *p* < 0.001 TIME*GROUP *p* > 0.05
	PRG	36.5 ± 17.5	27.7 ± 14.0	
	TRG	33.4 ± 18.5	19.1 ± 10.7	

Values are means ± standard deviation for BBS: Berg Balance Scale; Composite: composite score of Sensory Organization Test; MFIS: Modified Fatigue Impact Scale; ALL: all patients with multiple sclerosis (PwMS); PRG: personalized rehabilitation group; TRG: traditional rehabilitation group; RM-ANOVA: repeated measurements analysis of variance.

disease duration, BBS, Composite score and MFIS (see Table 1).

Interventions effect on primary and secondary outcomes. We examined differences among groups in the primary and secondary outcomes following the four-week intervention program. Table 2 shows the main findings of our study, namely the average BBS score (± SD), Composite score (± SD) and MFIS score (± SD) for the two groups and for the whole group of PwMS. Noticeably, whatever the *group*, BBS, Composite and MFIS scores, taking into account the *time* factor, revealed a significant differences between T0 and T1.

Further exploring our findings, the BBS showed a difference between pre-treatment and post-treatment scores of 6.3 and 2.0 points respectively for PRG and TRG. ANOVA showed an interaction effect between *group* and *time* ($p < 0.001$; see Figure 2).

The Composite score showed a difference between pre-treatment and post-treatment scores of 16.6 and 7.6 points respectively for PRG and TRG. ANOVA showed an interaction effect between *group* and *time* ($p < 0.05$; see Figure 3).

The MFIS score showed a difference between pre-treatment and post-treatment scores of 8.8 and 14.2

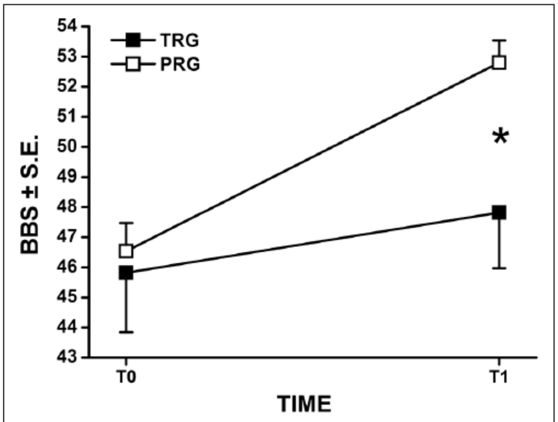

Figure 2. Group*Time interaction effect on the Berg Balance Scale. After interventions, PRG showed a significant increase in BBS score with respect to TRG that exceeded 4.0 points set as minimal clinically relevant difference. BBS: Berg Balance Scale; PRG: personalized rehabilitation group; TRG: traditional rehabilitation group.

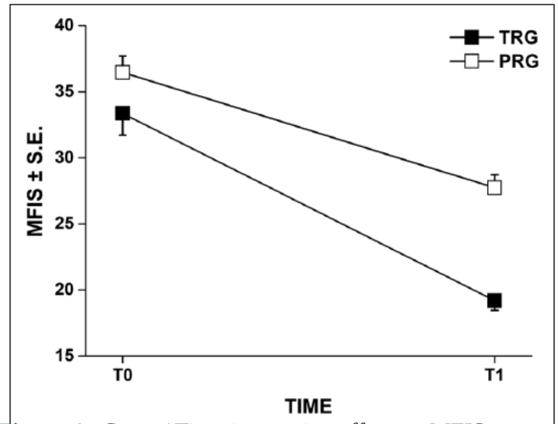

Figure 4. Group*Time interaction effect on MFIS score. After interventions, no significant interaction effect between group and time was found. MFIS: Modified Fatigue Impact Scale; PRG: personalized rehabilitation group; TRG: traditional rehabilitation group.

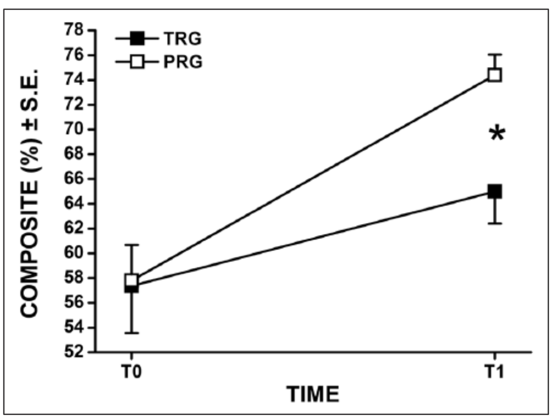

Figure 3. Group*Time interaction effect on Composite score. After interventions, PRG showed a significant increase in Composite score with respect to TRG that exceeded 7.0 points set as minimal clinically relevant difference. PRG: personalized rehabilitation group; TRG: traditional rehabilitation group.

points respectively for PRG and TRG. ANOVA did not show an interaction effect between *group* and *time* ($p = 0.22$; see Figure 4).

Explorative analyses on sub-groups (VIS, PROP, VEST) in PRG patients showed, for the BBS, an improvement (percentage) of 13.2% for VIS, 9.7% for PROP and 12.7% for VEST. Composite score improved 25.7% for VIS, 10.6% for PROP and 30.3% for VEST. Furthermore, from normal values based on a healthy population, PRG patients at T1 with a prevalent VIS deficit showed minus 4.3 ± 2.1% for VIS sub-scores, individuals with a prevalent PROP deficit showed minus 5.4 ± 1.8% for PROP and patients with a prevalent VEST deficit showed 7.4 ± 3.2% for VEST.

Discussion

In the present study we investigated the effect of tailored rehabilitation treatments in improving balance in a group of PwMS. Findings from this study demonstrate the feasibility of a personalized rehabilitation approach and its effectiveness in improving balance (BBS score) and upright postural control (Composite score). Noticeably, the improvements were significantly greater for the PRG than the TRG.

Effects on balance, upright postural control and fatigue in MS

The main outcome of the study was related to balance, and the BBS has been already assessed for PwMS in previous studies, showing an excellent validity and reliability.[11,28] The first interesting finding is that the PRG members had an improvement of 6.3 points on the BBS and exceeded the improvement of 2.0 points of the TRG group. The improvement in the BBS has already been shown in previously published papers on the effect of balance rehabilitation in PwMS;[9,23,37] however, in the present study the PRG showed an improvement that met the clinically relevant difference of 4.0 points.[9] This result could have an impact in improving static and dynamic balance, reducing fear of falling and risk of fall and in improving quality of life in PwMS.

The second major finding of this study was that the PRG members improved significantly in upright postural control (16.6 points for Composite score). The Composite score, considered as a secondary outcome in this study, showed a significant improvement in the experimental group (PRG) that is greater than the clinically relevant difference of 7.0 points reported in a previous study[35] and also above the known learning effect (8.0 points) found in a population of healthy individuals.[38]

The third finding is that changes in the MFIS total score for both groups, despite treatment type, were significant for the *time* factor ($p < 0.001$), but did not show an interaction effect between *group* and *time* ($p > 0.05$). However, while differences between T0 and T1 did not meet the clinically relevant difference of 15.0 points[36] for the PRG group as shown in a previous study,[29] results for the TRG group showed an MFIS improvement that could be considered as clinical meaningful. We could speculate that the design of TRG intervention, in which individuals were treated with gait and treadmill training, showed a greater impact on fatigue with respect to the PRG intervention. MFIS findings contrast with those published by Hebert et al.[27] in which a six-week vestibular rehabilitation program demonstrated both statistically significant and clinically relevant change in fatigue in the group treated with vestibular rehabilitation. Contrasting results could be due to a different level of fatigue in PwMS recruited respectively in the present study and in the Hebert et al. study (mean baseline MFIS score: 35.2 ± 17.6 in the present study; mean MFIS score > 38.0 in the Hebert et al. study).

The study was not designed to test the neurophysiological basis for improvements in balance and upright postural controls; however, the conceptual framework of our study could provide insight into theoretical reasoning. Impaired motor control that is usually found in PwMS is a result of demyelination and axonal degeneration but there is evidence of spontaneous partial neural repair, with axonal and dendritic collateral sprouting.[39–41] Furthermore, several studies showed that clinical recovery in PwMS is facilitated by adaptive functional reorganization[42–44] enhanced by task-specific rehabilitation training.[44–46] With this knowledge, it can be argued that tailored balance rehabilitation training could provide the necessary task-specific trigger for reorganization of neural networks, promoting central sensory integration and, as consequence, improving balance and upright postural control.

Limitations

Limitations of the present study should be acknowledged. The sample size was too small to evaluate in the three subgroups of PRG participants interactions among PROP, VIS and VEST interventions. However, exploratory analyses showed a greater percentage improvement in VIS and VEST subgroups, suggesting that these dysfunctions seem to be more trainable than the PROP. Furthermore, explorative analyses results at T1 could suggest that PRG individuals superiorly improved because of reduced impairment rather than because of compensation strategies. In addition, no follow-up evaluation on the maintenance of the exercises' effect over time was taken into consideration. We also must acknowledge that traditional rehabilitation exercises that comprise, as part of clinical routine practice, techniques such as variety of ground surfaces and eyes-open/-closed exercises, could have an impact on PROP and VIS subgroups among TRG participants. As previously discussed, the study lacks neurophysiological measures that could help shed further light on functional reorganization of neural networks in PwMS treated with highly tailored rehabilitation interventions. Finally, the study lacks walking and number-of-falls measures that could have provided meaningful ecological data of balance improvement.

Conclusions

The study showed a large treatment effect for primary and secondary outcome occurring after four weeks of tailored interventions with respect to traditional rehabilitation intervention. Our results provide evidence that a multimodal approach training sensory impairments is more effective than static and dynamic training in improving balance and upright postural control in PwMS. We feel that the theoretical concept presented in the current study, i.e. assessing sensory system impairment that impact balance control in PwMS and providing tai- lored interventions, could serve as the basis for further investigations on the designing of personal- ized balance disorders rehabilitation treatment for PwMS.

Conflict of interest

None declared.

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ORIGINAL RESEARCH

Two Different Types of High-Frequency Physical Therapy Promote Improvements in the Balance and Mobility of Persons With Multiple Sclerosis

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Abstract

Objective: To evaluate the mobility and postural balance improvements that could be achieved in a cohort of persons with multiple sclerosis (MS) who participated in a motor adaptation protocol and a cohort of persons with MS who participated in a therapeutic exercise protocol.

Design: A cohort design, where subjects were evaluated before and after a 6-week intervention period.

Setting: Clinical laboratory setting.

Participants: Individuals (NZ42) with relapsing-remitting or secondary progressive MS (Expanded Disability Status Scale [EDSS] scores, 3.0e6.5) were initially screened for eligibility for participation in the study, from which those who fit the inclusion criteria (nZ32) were enrolled in the study. Subjects were pseudorandomly assigned to a treatment group and matched based on EDSS scores. Fourteen individuals in the motor adaptation cohort (MAC) (mean age SD, 52.6 9y; mean EDSS score SD, 5.5 0.9) and 13 individuals in the therapeutic exercise cohort (TEC) (mean age SD, 54.0 9y; mean EDSS score SD, 5.3 0.9) completed the entire duration of their respective programs.

Interventions: Both cohorts completed their therapy twice a day, 5 days each week, for 6 weeks. Each session of the MAC program consisted of balance and gait training that encouraged new ways to adapt to challenging task demands. The TEC program was similar to a traditional exercise program.

Main Outcome Measures: The Sensory Organization Test, 6-minute walk test, and gait spatiotemporal kinematics.

Results: Collectively, both treatment groups had improvements in postural balance (PZ.001), walking endurance (PZ.002), walking speed (PZ.004), and step length ($P<.001$) after therapy. However, there were no statistical differences between the 2 treatment groups for any of the outcome variables (P values $>.01$).

Conclusions: Our exploratory results suggest that a high frequency of physical therapy rather than a specific activity focus might be an important parameter for persons with MS.

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Multiple sclerosis (MS) affects approximately 570,000 individuals in the United States and is one of the most common neurologic disabilities in young and middle-aged adults.[1,2] Persons with MS often face motor impairments that may instigate postural balance and walking dysfunction.[3-12] Since postural balance and mobility are vital for daily living, they are often the primary focus of therapeutic goals. Traditionally, clinicians have discouraged persons with MS from participating in intensive physical therapy programs because it was thought that these programs would exacerbate the MS symptoms.[13,14] However, the current therapeutic trends have been redirected toward identifying the optimal treatment parameters that promote improvements in mobility and postural balance.

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Several investigations[15-26] have attempted to address this current knowledge gap by evaluating the effectiveness of various types of programs for persons with MS. Many of these investigations have reported improvements in postural balance and mobility. However, the therapeutic approaches used in these programs have been highly variable in terms of frequency, intensity, and type. For example, aerobic or strength training sessions have historically been conducted for 30 minutes, 2 to 3 times per week, while the balance training programs have been 45 to 60 minutes in length and performed 2 to 4 times per week. Although optimal training parameters may be different for the various activities, the lack of a systematic evaluation of the respective treatment parameters has blurred our understanding of the optimal parameters that promote mobility and postural balance improvements in persons with MS.

We recently completed an exploratory investigation[27] that evaluated whether a novel, high-frequency physical therapy protocol could augment clinically relevant improvements in the postural balance and mobility of persons with MS. This protocol was unique because it was directed at improving the individual's motor adaptability by constantly challenging the patient's postural balance and mobility. Our exploratory results showed vast improvements in postural balance, walking speed, and control of the ankle musculature. We suspected that the motor adaptation exercises were responsible for these outcomes because the subjects focused on the awareness of their motor strategies, and learning how to meet the task demands. We suggest that this treatment approach was optimal because it promoted a greater amount of variability in the practiced motor tasks, which has been shown to potentially augment beneficial neuroplastic changes in the brain.[28,29] Based on these premises, we anticipate that a high-frequency therapeutic protocol that uses traditional exercises may achieve less favorable results in persons with MS.

The purpose of this exploratory investigation was to test this notion by evaluating the mobility and postural balance improvements achieved in a cohort of persons with MS who participated in a therapeutic exercise protocol, and a cohort of persons with MS who participated in our motor adaptation protocol. We hypothesized that the cohort that completed the motor adaptation therapeutic protocol would have greater improvements in postural balance, preferred walking speed, and walking endurance than the cohort who completed the therapeutic exercise protocol.

Methods

Based on our initial investigation, 12 persons with MS would provide >80% power to detect the pre/post therapy differences in the Sensory Organization Test[a] (SOT) at a .05 alpha level. Assuming a 20% dropout rate, we aimed to recruit at least 14 persons to participate in each group. Inclusion criteria were as follows: (1) between 30 and 70 years of age; (2) a Kurtzke Expanded Disability Status Scale (EDSS) score of 3.0 to 6.5; (3) a definitive diagnosis of MS; (4) able to walk on a treadmill at 0.5 miles per hour while holding onto handrails; (5) cognitively competent; and (6) a Mini-Mental State Examination score of >21. The exclusion criteria were as follows: (1) documented relapse in the previous 6 months; (2) major MS-specific medication changes in the previous 3 months; and (3) the presence of another major comorbidity such as a neurologic disorder or uncontrolled pain. The study was reviewed and approved by the University of Nebraska Medical Center Institutional Review Board, and all participants provided written consent. The enrolled participants were pseudorandomly assigned to either a motor adaptation cohort (MAC) or a therapeutic exercise cohort (TEC). The assignments were performed such that a participant meeting the inclusion criteria was randomly assigned to 1 of the treatment groups, and a second participant with a similar EDSS score was placed in the other group. The enrolled subjects completed all outcome measures before and after their respective therapeutic programs.

List of abbreviations:

EDSS	Expanded Disability Status Scale
MAC	motor adaptation cohort
MS	multiple sclerosis
SOT	Sensory Organization Test
TEC	therapeutic exercise cohort

Interventions

The total intervention period for both cohorts was 6 weeks. The therapy was performed twice a day for approximately 60 minutes each session on 5 consecutive days each week. The initial 2 weeks were conducted under supervision of a physical therapist, while the remaining 4 weeks were performed by the patients at their homes and were monitored weekly via teleconferences with the therapist. Subjects completed the same activities at home as they did during the initial 2 weeks and kept a log book to track their activity. A more complete description of the respective therapeutic programs can be found in supplemental appendix S1 (available online only at http://www.archives-pmr.org/).

Motor adaptation cohort

Each session began with a 5-minute warmup of trunk and limb movements. Next, the subjects completed a 20-minute balance training program that consisted of tasks such as standing in the corner with their feet on a piece of foam with eyes closed. Each training session concluded with 20 minutes of treadmill and overground walking. The treadmill training consisted of activities such as walking backward or sideways. The overground training activities varied in walking direction, speed, and/or use of an assistive device. Difficulty level was steadily increased both within and between sessions for all activities. The therapist provided verbal feedback to direct the patients' attention toward monitoring the outcomes of their motor performance and exploring new ways to adapt to the challenging tasks.

Therapeutic exercise cohort

The activities in the TEC program were similar to those that would be performed in a traditional group exercise program. Each session consisted of 15 minutes of strength and flexibility exercises, 15 minutes of postural balance exercises, and 15 minutes of treadmill walking. Strength exercises included activities such as forward/backward lunges. The flexibility training focused specifically on the lower extremities. Balance activities consisted of both static (ie, standing on 1 leg as long as possible with support) and dynamic balance exercises (ie, kicking a ball). Speed on the treadmill was adjusted as needed to accomplish the total time, and subjects were encouraged to remove 1 or both hands from the handrails. Compensatory strategies (ie, widening the base of support) for completing the assigned exercises were demonstrated when subjects were having difficulty completing the tasks.

Postural control measures

Postural control was assessed using the composite score on the SOT, which consists of 6 conditions that measure a person's ability to integrate visual, somatosensory, and vestibular feedback to reduce the overall amount of postural sway. The composite score was calculated by the NeuroCom software[b] based on the subject's overall amount of postural sway, which was measured with a forceplate integrated into the system's platform.

Mobility measures

Subjects were allowed to use their regular assistive devices (ie, canes, wheeled walkers, ankle-foot orthoses) for all mobility measures.

Walking endurance was measured using the 6-minute walk test. Subjects walked around cones placed at the ends of an approximately 40-m hallway and were instructed to try to walk as far as possible within the 6-minute time limit. No verbal encouragement was provided during the test, and the subjects were allowed to stop for rest during the test, but the time was not paused.

The spatiotemporal kinematics of gait were measured with a 5.75-m digital mat (GAITRite[c]). The participants completed 2 self-paced walking trials, which were averaged together for the final analyses. The variables of interest were gait velocity (m/s), step width (m), step length (m), and cadence (steps/min).

Statistical analysis

Separate mixed repeated-measures analyses of variance (group pre/post assessment) were used to compare the differences of the variables of interest between therapeutic groups and before/after the therapeutic protocols. The false discovery rate algorithm was used to adjust the alpha level to control the potential familywise error rate that may occur when conducting multiple tests.[30] Cohen's d was calculated to determine the effect sizes of the respective changes. The following guidelines were used to interpret the effect sizes: 0.2 is a small effect size; 0.5, a moderate effect size; and 0.8, a large effect size.[31] Results are displayed as means SE of means, and P values equal to or less than the corrected .01 alpha level were considered significant.

Results

Forty-two individuals were initially screened for eligibility to participate in the study (fig 1), from which 32 persons with relapsing-remitting or secondary progressive MS fit the inclusion criteria and were assigned to either group. The subjects' baseline demographic and clinical characteristics are presented in table 1. All subjects were blinded as to which therapeutic intervention cohort that they were assigned. Fourteen individuals in the MAC (mean age SD, 52.6 9y; 9 women; mean EDSS score SD, 5.5 0.9) and 13 individuals in the TEC (mean age SD, 54.0 9y; 6 women; mean EDSS score SD, 5.3 0.9) completed the entire 6 weeks of their respective programs and were included in the analyses. There were no between-group differences for any variables at baseline. No adverse MS-related events occurred for any subject during the intervention period. Based on the available home log information, subjects from both groups had a compliance rate of 92%. Individual results for all outcome variables are shown in supplemental table S1 (available online only at http://www.archives-pmr.org/).

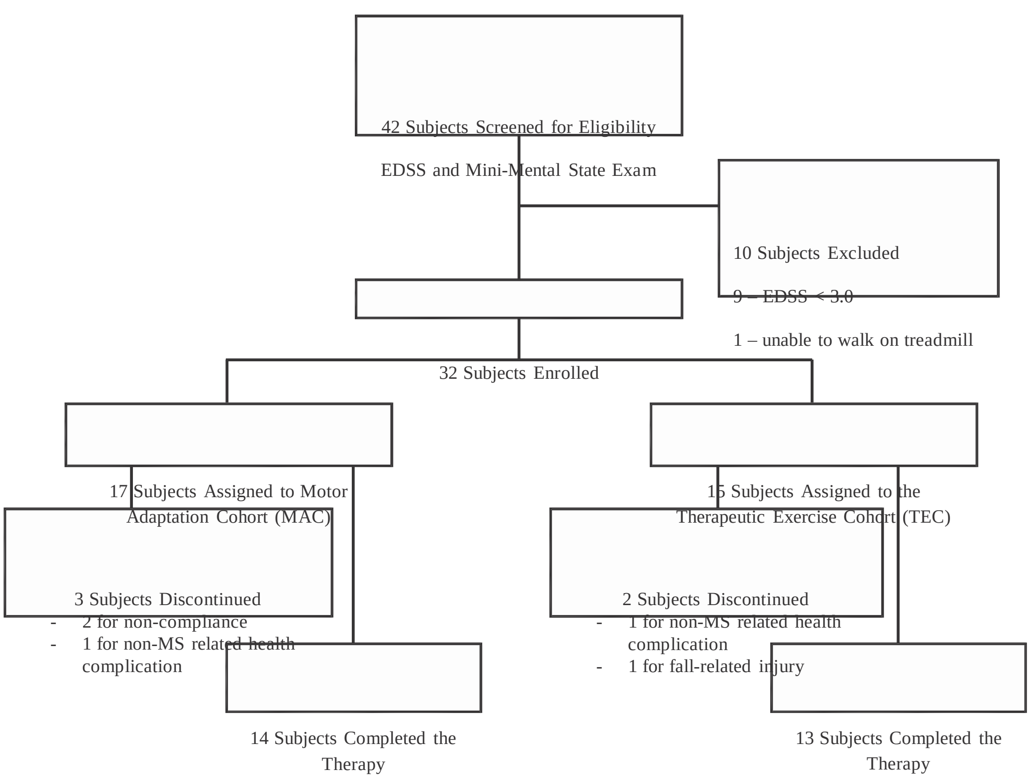

Fig 1 Flow diagram of participant recruitment and participation in the study.

Table 1 Baseline demographic and clinical characteristics of the participants

TEC Subject No.	Sex	Age (y)	MS Type	MS Duration (y)	EDSS Score	Assistive Device
1	M	69	RR	24	5.0	Cane/AFO
2	M	48	SP	12	5.5	Cane
3	F	57	RR	12	5.5	Three-foot cane
4	F	57	RR	12	4.0	None
5	F	36	SP	14	6.5	Walker
6	M	55	SP	4	4.5	AFO
7	M	59	RR	5	6.0	AFO
8	M	65	SP	7	6.5	Walker
9	F	50	RR	15	4.5	Cane
10	F	50	RR	12	3.5	None
11	F	60	RR	15	5.0	Cane
12	M	64	RR	10	6.0	Cane
13	M	56	RR	19	6.0	Foot drop electrical stimulator and cane
14	M	40	RR	8	6.0	Cane/AFO
15	F	56	RR	9	5.0	None
Average	7 F/8 M	54.8 9	11 RR/4 SP	11.9 5	5.3 0.2	

MAC Subject No.	Sex	Age (y)	MS Type	MS Duration (y)	EDSS Score	Assistive Device
1	F	44	RR	17	4.0	None
2	F	43	RR	11	6.0	Cane
3	F	55	RR	30	4.0	None
4	M	68	SP	9	6.0	Cane/AFO
5	F	59	SP	21	3.5	Cane
6	F	62	SP	12	4.0	None
7	M	49	RR	12	5.5	AFO
8	M	54	SP	18	5.5	None
9	F	43	RR	12	6.0	Cane
10	F	47	RR	17	6.5	Forearm crutches
11	F	59	RR	21	6.5	Walker
12	M	61	RR	15	5.5	Cane/AFO
13	F	66	RR	10	6.0	Cane
14	F	45	RR	8	4.0	None
15	M	59	SP	13	6.0	Cane/AFO
16	F	42	RR	27	6.5	Walker/AFO
17	F	60	SP	18	6.0	Cane
Average	12 F/5 M	53.9 8	11 RR/6 SP	15.9 6	5.4 0.2	

NOTE. Values are mean SD or as otherwise indicated.
Abbreviations: AFO, ankle-foot orthosis; F, female; M, male; RR, relapsing-remitting; SP, secondary progressive.

Postural control measures

There was a significant pre/post main effect for the SOT composite score (PZ.001; Cohen's dZ.88) (fig 2A), indicating that there was an improvement in the postural balance of both groups. The average percent improvement in postural balance across subjects in both groups was 45.8% 19%. The MAC subjects improved their postural balance by 53.9% 33.6%, and the TEC subjects improved their postural balance by 37.1% 15.9%. However, there was not a significant interaction or group main effect (P values >.01), suggesting that both groups improved their postural balance similarly.

Mobility measures

There was a significant pre/post main effect for the 6-minute walk test (PZ.002; Cohen's dZ.39) (fig 2B), indicating that both groups improved their walking endurance. Collectively, the average percent increase in walking endurance across individuals in both groups was 14.5% 4.2%. The MAC subjects improved their walking endurance by 21.3% 7.3%, and the TEC subjects improved their walking endurance by 7.2% 3.0%. There was not a significant interaction or group main effect (P values >.01), indicating that both groups improved their walking endurance equally.

There was a significant pre/post main effect for the walking velocity (PZ.004; Cohen's dZ.42) (fig 3A), demonstrating that both groups improved their preferred walking speed. Overall, the individuals in both groups had an average percent increase of 14.6% 4.5% in their walking velocity. The MAC subjects improved their walking velocity by 18.7% 7.7%, and the TEC subjects improved their walking velocity by 10.1% 4.4%. There was not a significant interaction or group main effect (P values

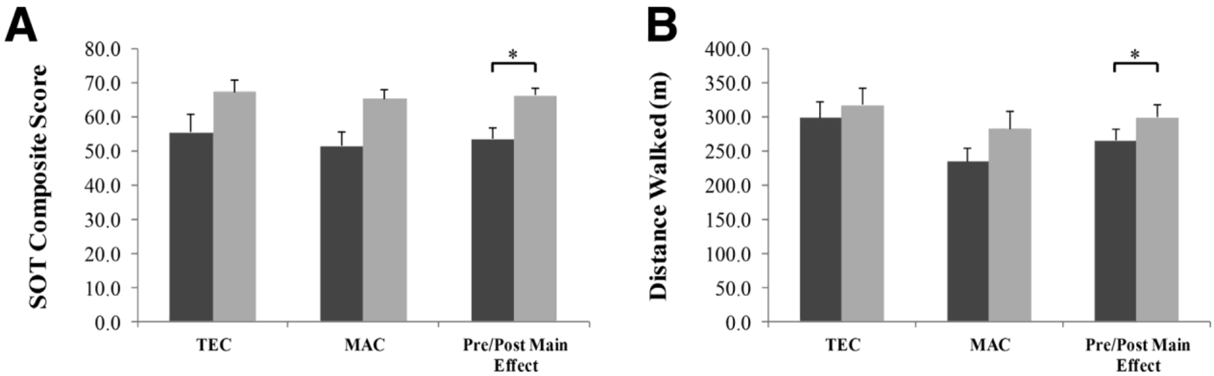

Fig 2 (A) Pre/post values for the respective groups and the pre/post assessment main effect for the SOT composite score. (B) Pre/post values for the respective groups and the pre/post assessment main effect for the 6-minute walk test. *P<.01.

>.01), which indicated that both groups had similar improvements in their walking speed.

There was a significant pre/post main effect for the step length (P<.001; Cohen's dZ.55) (fig 3B), signifying that both groups used a longer step length after completing the respective therapeutic protocols. Overall, the average percent change in the step length across individuals in both groups was 11.4% 2.5%. The MAC subjects improved their step lengths by 16.4% 3.9%, and the TEC subjects improved their step lengths by 6.0% 2.4%. There was no group main effect or significant interaction (P values >.01), indicating that both groups had similar improvements in step length. There were also no significant main effects or in- teractions for step width and cadence, suggesting that neither protocol influenced these variables (P values >.01).

Discussion

This investigation compared the results from a cohort of persons with MS who participated in our MAC protocol with a cohort of persons with MS who participated in our TEC protocol. We hypothesized that the participants in the MAC would have greater improvements in their balance and mobility than the participants in the TEC. Our results showed that both groups made significant improvements in their postural balance and mobility. However, there were no differences in the extent of the improvements seen between the respective treatment groups. Since both groups completed different activities at the same frequency, a high-frequency physical therapy protocol might be an essential dosage variable for promoting improvements in persons with MS.

Both groups had a 13-point improvement in their SOT scores, which was well above the 8.0-point criterion for a clinically meaningful change but is somewhat lower than what has been reported from prior investigations (16e18 points).[22,23,32] These other studies used 12 one-hour balance treatment sessions performed over a 4- to 6-week period, which was considerably different than the dosage used in the current investigation. We suspect that the hour of focusing on task-specific postural balance training used in the prior studies may have augmented the larger postural balance improvements. Secondarily, we suspect that larger balance improvements may have been achieved if our subjects would have continued to work one-on-one with the physical therapist for all of the treatment sessions. However, the balance improvements of the current investigation are similar to or greater than those previously reported after the completion of home exercise programs.[33-35]

Surprisingly, the postural balance improvements were comparable between the respective groups. These outcomes were contradictory to our original hypothesis and imply that similar outcomes can occur when the program is less focused on learning how to adapt to challenging postural conditions. Perhaps the balance exercises used in the TEC provided enough challenge to

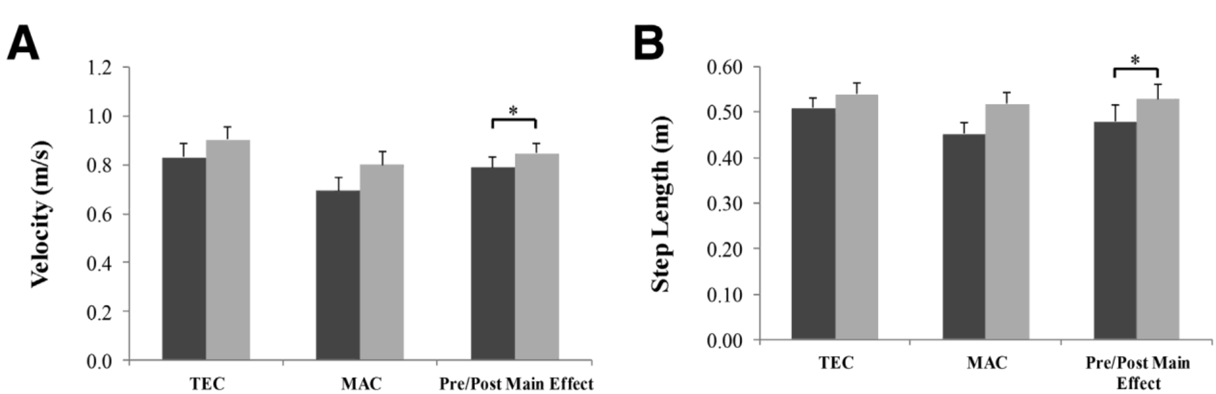

Fig 3 (A) Pre/post values for the respective groups and the pre/post assessment main effect for the velocity at the self-selected preferred walking pace. (B) Pre/post values for the respective groups and the pre/post assessment main effect for the step length at the self-selected preferred walking pace. *P<.01.

direct the participants' attention toward relearning how to maintain their balance. Also, the outcomes were possibly equivocal because the exercises assigned to the TEC were more feasible for them to complete at home, whereas the MAC may have had greater difficulty in properly adjusting the difficulty level of the exercises without the one-on-one interaction with the therapist. This may have resulted in both groups completing similar home balance protocols.

After completing the respective programs, both groups had improvements in their walking endurance and faster walking speeds, which was accomplished by using a longer step length. However, the therapeutic outcomes of the respective groups were equivocal, indicating that both treatment approaches may have the same effect on mobility. These mobility improvements could be related to the high frequency of walking activities both groups completed. The treadmill training protocols used in other investigations[20,21] that have evaluated preferred walking speed consisted of 30 minutes of treadmill walking that was performed 3 times a week over a 4-week period. The outcomes from these studies have been quite variable with a 3% to 12% improvement in walking speed. Our results are at the ceiling of these previous outcomes, which suggests that a higher frequency of walking activities may be beneficial for improving the mobility of persons with MS.

Overall, the positive results observed in both groups suggest that high-frequency physical therapy may promote improvements in the postural balance and mobility of persons with MS. The frequency of physical therapy used in this investigation was much higher than most programs that have been evaluated for persons with MS.[16-23,26] A recent investigation by Kalron et al[25] consisted of a 3-week rehabilitation program that comprised many different exercise types that were performed 5 days a week. Their results demonstrated that a high amount of activity can result in improved mobility in persons with MS.[25] However, unlike the current outcomes, most of these mobility improvements were relatively small and below the minimal clinical difference threshold. Nevertheless, the results from this investigation further support the notion that a high frequency of physical therapy may be an important parameter for promoting improvements in the mobility. This conjecture should be challenged by future studies directed at identifying the optimal treatment parameters.

Study limitations

The small sample size in the study may have contributed to the lack of differences between groups. However, our post hoc power analysis on the smallest observed difference between groups (Cohen's dZ.15) indicated that a substantially larger sample size (n>500) would be needed to find differences between the 2 groups. Potentially, individuals with different diagnoses may have also responded differently to the respective interventions; how- ever, our sample size was too small to address this question. This notion should be further explored to better identify treatment parameters that can be used to individualize a patient's treatment. Moreover, the use of a simple gain score to measure outcomes could potentially lead to a ceiling effect since those who have lower scores at baseline have the potential to improve more than those who scored high at baseline. We also did not quantify each subject's baseline fitness level using maximum oxygen consumption. However, since there were no differences between the 2 groups in the distance walked during the baseline 6-minute walk test, the 2 groups likely had equivocal baseline fitness levels. Therefore, we do not believe that our results were due to 1 group having a higher initial fitness level. Another limitation to this investigation was that the gait training components of the interventions were primarily completed on a treadmill rather than overground walking; therefore, it is currently unknown whether the treatment outcomes would extend to other types of gait training. Finally, the study lacked a group of individuals who completed a physical therapy program conducted at a more normal dosage level (ie, 30- to 60-min sessions conducted 2 to 3 times per week). This would allow for better insight as to whether the frequency of the therapy is an important parameter for pro- moting the clinically relevant improvements seen in the cur- rent study.

Conclusions

Our exploratory results suggest that the focus of the physical therapy may not be the key factor for promoting improvements in the postural balance and mobility of persons with MS. Rather a high-frequency physical therapy may be an important parameter for improving the postural balance and mobility of persons with MS. These preliminary outcomes should be further explored and taken into consideration when deciding on dosage parameters that will likely meet the therapeutic goals of persons with MS.

Suppliers

a. Sensory Organization Test; NeuroCom International.
b. Natus Medical Inc.
c. GAITRite; CIR Systems, Inc.

Keywords

Exercise; Gait; Posture; Rehabilitation; Walking

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Supplemental Appendix S1 Therapeutic Protocols

Most of the participants had a treadmill inside their homes and completed the entire home exercise program at their houses. The participants who did not have a treadmill visited a fitness center to complete their treadmill walking. In addition, because the training focused on overground activities, participants were encouraged to complete overground walks outside throughout their neighborhood or at an indoor track. In the home exercise program log, subjects were instructed to make note of whether the training was being done on a treadmill or overground. All participants were provided with pieces of foam to complete some of the balance training exercises. To ensure safety during the balance exercises at home, participants were encouraged to complete the balance training activities standing next to a wall, chair, or bed so that they were equipped with adequate support against falls.

Motor adaptation cohort

The 5-minute standardized warmup consisted of several repetitions of trunk and limb movements, as well as participant-specific stretches and coordination activities for the limbs. After the warmup, the therapist prescribed a 20-minute balance training program based on an initial assessment. After the balance training, the participants completed 20 minutes of challenging treadmill and overground walking training based on each subject's assessed ability and need for an assistive device.

The balance training program consisted of a challenging sitting/standing balance task such as sitting on an exercise ball or standing in a corner with the feet either on the floor or on a piece of foam with eyes closed. The objective of this training was to challenge and progress the participant's balance incrementally within the session to maintain upright control despite altered visual and somatosensory inputs. For example, participants might begin in a less challenging position for the first 5 minutes on foam with their feet 10in apart, progressing to more challenging positions during subsequent 5-minute periods, and returning to a less challenging position for the final 5 minutes. During this training, the therapist provided verbal and tactile cues for upright posture and relaxation of tense body parts, verbal cues to increase sensory awareness (ie, location of pressure on the soles of feet), and observed the participant for the ability to meet the task's demand (ie, the number of touches to the wall). Based on these observations and standardized guidelines, the therapist would increase the demands of the postural training. Generally, no rest periods occurred during the balance sessions. During all balance exercises, participants were supplied with a table or chair in front of them so that they could reach out for temporary support as needed, and each participant wore a gait belt so that the therapist was able to provide balance assistance as needed.

The walking training included tasks such as forward, backward, or sideways walking on the treadmill with a harness used as needed for safety. The use of handrails, the degree of ramp incline, and the treadmill speed were varied throughout the training to provide an appropriate level of intensity for each subject. Additionally, the therapist provided overground training indoors while varying walking direction, speed, using a less-supportive assistive device, and/or increasing dynamic balance activities. The therapist provided verbal and manual cues to assist participants to achieve a more normal gait pattern, and visual feedback was provided to all participants by training in front of a mirror. A protocol similar to that described above for the balance task was used to progress each 5-minute training period. Participants were provided with short sitting rest periods as needed. The intensity of the activities was increased as tolerated and recorded. Generally, the increase in intensity was based on each subject's level of performance and fatigue during the previous session.

MAC home program

The following is an example of the home program provided to the MAC subjects:

1. Warmup exercises (about 5min)
   All exercises begin from a relaxed neutral posture with good alignment in sitting or standing.
   Movements are circles or figure 8s.
   Perform exercises in both directions.
   The goal for each exercise is 5 repetitions in each direction.
   Start slowly and increase speed to make it harder but without losing the quality of the movement.
   Using a mirror when performing exercises provides visual feedback.

   The warmup exercises are:
   a. Halos (head circles)
   b. Tornados (rib cage circles)
   c. Shoulder circles with arms relaxed
   d. Lead the orchestra (arm circles or figure 8s)
   e. Finger waves (both directions: begin from thumb and begin from little finger)
   f. Belly dance (pelvic tilts or figure 8s)
   g. Standing flamingos (single leg circles or figure 8s with arm support as needed)
2. Balance exercises with eyes closed
   Stand on floor with shoes, feet apart 12in, 5 minutes
   Stand on floor with shoes, feet apart 8in, 5 minutes
   Stand on floor with shoes, feet apart 6in, 5 minutes
   Stand on floor with shoes, feet apart 10in, 5 minutes
3. Walking training for 20 minutes on the treadmill or 20 minutes overground walking or a combination:
   A. Treadmill walking training
      Walk with 2 handrails, 1.0mph, 5 minutes, work on step length
      Walk with 2 handrails, 1.2 to 1.4mph, 5 minutes, work on step length and heel strike, forward direction
      Walk with 1 handrail, 1.2 to 1.4mph, 5 minutes, work on step length and arm swing
      Walk with 1 to 2 handrails, 1.2mph, 5 minutes, work on optimal pattern
   B. Overground walking exercises
      Practice forward walking on level surface with optimal posture and gait pattern
      Side-stepping
      Backward stepping
      Stepping over an object
      Walking and turning
      Stepping up on 4- to 8-in step, leading with each leg

Therapeutic exercise cohort

Each therapy session consisted of 15 minutes of strength and flexibility exercises, 15 minutes of postural balance exercises, and 15 minutes of treadmill walking. The activities selected for the therapeutic program were similar to those that would be performed in a group exercise program. Subjects were instructed to complete each activity at their own pace for 3 minutes. Strength exercises included activities such as forward/backward lunges, stepping up/down a step, and squats. Flexibility training was completed both standing up and lying on a mat. Subjects were shown how to stretch the lower extremity muscles, especially any muscle that was specifically problematic to them. Both static and dynamic balance exercises were completed in each session. Static balance exercises included standing on a piece of foam with eyes open and feet wide apart, or standing on 1 leg as long as possible with support. Dynamic balance exercises included stepping over small obstacles, walking sideways, or walking heel to toe. While walking on the treadmill, the subjects were encouraged to remove 1 or both hands from the handrails if possible. The subjects were allowed to increase and decrease their speed as needed to accomplish the total time. All subjects reported their rate of perceived exertion based on the Borg scale, and were instructed to attempt to work at a score of 12 or 13, which suggests that the exercise was somewhat hard. Rest was given as needed throughout the entire TEC program.

TEC home program

1. Warmup exercises (about 5min)
   All exercises are to be done for 3 to 5 repetitions to warmup the muscles.
   Exercises are done as demonstrated by your therapist in standing, sitting, or lying down.

   The warmup exercises are:
   a. Chin tucks
   b. Arm circles
   c. Shoulder shrugs
   d. Marching in place
   e. Hamstring stretch
   f. Heel cord stretch
   g. Knee to chest
   h. Heel raises/toe raises
   i. Mini-squats
2. Strengthening activities: Choose 5 exercises, spend 3 minutes on each one
   Bridges with 1 leg or 2 legs
   Table tops in all fours position
   Planks
   Squats
   Lunges
   Reverse lunges
   Hip abduction standing at a counter: lift one leg out to the side
   Warrior pose
   Step ups/step downs
   Skip jumps
3. Balance exercises with eyes closed: Choose 5 exercises, spend 3 minutes on each one
   Stand on floor or foam: feet shoulder width apart–eyes open/eyes closed
   Stand on floor or foam: feet in tandem, right foot leading–eyes open/eyes closed
   Stand on floor or foam: feet in tandem, left foot leading–eyes open/eyes closed
   Walk on a line, heel to toe
   Side stepping
   Walk backward
   Walks with stops, turns, change of speed
   Four-square stepping
   Grapevine stepping
   Step over a small obstacle (2–4in)
   Trap and kick a ball
   Play catch
   Bounce, dribble a ball
   Stand on 1 leg
   Sway from the ankles without stepping
4. Walking training for 15 minutes on the treadmill or overground or a combination. Log your rating of perceived exertion for all your walking training.
   A. Treadmill walking training
      Walk with or without handrails at a comfortable speed as practiced with the therapist.
      Log your time, speed, and number of handrails.
   B. Overground walking training
      Practice forward walking on a level surface with or without your assistive device.
      Log your time.

Supplemental Table S1 Individual pre/post results for both groups

TEC

Subject No.	SOT Pre	SOT Post	SOT % Change	6-Min Walk (m) Pre	6-Min Walk (m) Post	6-Min Walk (m) % Change	Velocity (m/s) Pre	Velocity (m/s) Post	Velocity (m/s) % Change	Step Length (m) Pre	Step Length (m) Post	Step Length (m) % Change	Step Width (m) Pre	Step Width (m) Post	Step Width (m) % Change	Cadence (steps/min) Pre	Cadence (steps/min) Post	Cadence (steps/min) % Change
1	73	77	5.5	370.1	354.2	4.3	1.04	1.02	1.3	.62	.61	1.3	.18	.16	12.3	100.3	100.6	0.3
2	42	53	26.2	314.6	305.0	3.0	0.92	0.90	2.3	.54	.54	0.1	.12	.11	9.3	102.9	100.5	2.3
3	66	71	7.6	211.4	262.2	24.1	0.54	0.58	7.0	.37	.36	3.2	.26	.29	11.6	87.9	96.4	9.7
4	64	80	25.0	330.8	365.1	10.4	0.90	1.08	20.7	.44	.50	14.0	.14	.17	24.2	122.9	129.9	5.7
5	35	58	65.7	257.3	293.8	14.2	0.67	0.99	46.5	.51	.62	22.4	.10	.09	15.1	79.6	95.3	19.7
6	68	77	13.2	298.8	330.7	10.7	0.78	0.89	15.3	.52	.59	12.9	.19	.17	12.5	89.4	91.0	1.7
7	78	79	1.3	481.0	499.5	3.9	1.27	1.18	7.3	.66	.65	1.9	.11	.11	0.8	115.8	109.5	5.5
8	50	68	36.0	137.3	157.6	14.8	0.42	0.44	3.1	.40	.39	2.7	.09	.09	5.8	64.0	67.6	5.7
9	78	81	3.8	305.0	300.1	1.6	0.87	0.88	1.5	.54	.55	2.9	.08	.11	37.5	96.6	95.3	1.4
10	11	35	218.2	367.6	437.5	19.0	0.92	1.08	16.4	.54	.58	6.2	.11	.10	3.1	102.4	112.0	9.4
11	52	60	15.4	285.5	251.6	11.9	0.86	0.85	2.0	.53	.53	1.1	.11	.12	8.8	98.1	95.2	3.0
15	53	68	28.3	237.8	237.7	0.0	0.89	0.90	1.2	.46	.50	8.2	.16	.16	2.1	116.0	108.0	6.9
16	50	68	36.0	286.8	338.3	18.0	0.71	0.94	33.3	.50	.60	19.3	.16	.18	13.8	84.2	93.8	11.3
Average	55.4	67.3	37.1	298.8	318.0	7.2	0.83	0.90	10.1	.51	.54	6.0	.14	.14	3.1	96.9	99.6	3.4
SEM	5.3	3.6	15.9	23.2	24.3	3.0	0.06	0.06	4.4	.02	.02	2.4	.01	.02	4.3	4.5	4.0	2.1

MAC

Subject No.	SOT Pre	SOT Post	SOT % Change	6-Min Walk (m) Pre	6-Min Walk (m) Post	6-Min Walk (m) % Change	Velocity (m/s) Pre	Velocity (m/s) Post	Velocity (m/s) % Change	Step Length (m) Pre	Step Length (m) Post	Step Length (m) % Change	Step Width (m) Pre	Step Width (m) Post	Step Width (m) % Change	Cadence (steps/min) Pre	Cadence (steps/min) Post	Cadence (steps/min) % Change
1	59	60	1.7	299.6	368.1	22.9	0.87	0.92	5.9	.47	.49	3.6	.14	.14	4.4	110.9	113.2	2.1
2	66	67	1.5	191.0	210.4	10.1	0.71	0.66	6.4	.42	.47	12.6	.15	.20	30.1	104.1	85.1	18.3
3	13	76	484.6	243.6	395.6	62.4	0.71	0.79	10.3	.38	.47	23.9	.10	.09	16.6	113.5	100.2	11.9
4	46	50	8.7	159.1	185.0	16.3	0.41	0.53	29.0	.44	.48	10.8	.05	.05	0.4	56.6	66.0	16.6
7	63	74	17.5	352.5	397.2	12.7	0.97	1.25	29.2	.53	.71	32.6	.12	.14	15.9	110.1	104.9	4.7
8	63	67	6.3	243.2	274.4	12.8	0.85	1.03	21.0	.51	.61	20.0	.20	.14	31.1	99.9	100.5	0.6
9	38	60	57.9	159.5	249.4	56.3	0.40	0.78	95.4	.29	.41	44.2	.11	.08	24.6	83.6	113.3	35.6
10	66	80	21.2	255.2	260.5	2.1	0.63	0.69	10.0	.47	.51	8.4	.11	.09	15.9	80.7	81.8	1.4
12	48	77	60.4	194.8	351.7	80.6	0.80	0.88	10.4	.35	.46	30.2	.20	.24	24.3	136.9	114.6	16.3
13	41	52	26.8	222.7	256.0	15.0	0.52	0.70	33.9	.41	.48	16.9	.12	.09	26.9	77.2	88.4	14.6
14	64	65	1.6	386.9	430.2	11.2	0.73	1.06	45.3	.49	.63	29.4	.15	.09	38.1	89.5	100.7	12.5
15	44	61	38.6	166.2	173.8	4.6	1.02	0.77	24.0	.68	.60	11.1	.12	.14	16.9	91.2	77.7	14.8
16	53	68	28.3	173.2	129.8	25.0	0.54	0.47	13.3	.51	.52	2.2	.14	.09	32.1	64.0	54.4	14.9
17	58	58	0.0	239.3	278.3	16.3	0.56	0.65	15.8	.39	.41	5.5	.11	.11	0.7	85.8	94.1	9.6
Average	51.6	65.4	53.9	234.8	282.9	21.3	0.69	0.80	18.7	.45	.52	16.4	.13	.12	6.7	93.1	92.5	0.87
SEM	3.9	2.5	33.6	18.9	24.8	7.3	0.05	0.06	7.7	.03	.02	3.9	.01	.01	6.1	5.7	4.8	4.2

Abbreviation: SEM, standard error of the mean.

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Comparing endurance- and resistance-exercise training in people with multiple sclerosis: a randomized pilot study

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Objective: The purpose of this study was to compare adaptations in functional and quality of life measures following endurance- and resistance-exercise training in people with multiple sclerosis.
Design: Cross-over design with an eight-week washout period.
Setting: Community health centre.
Subjects: Sixteen individuals with multiple sclerosis.
Intervention: Subjects completed both an eight-week endurance- and an eight-week resistance-exercise training programme in a randomized order. The exercise training comprised individualized progressive programmes that were completed twice weekly in a supervised group setting.
Main measures: Grip strength, functional reach, four step square, timed up and go and six-minute walk tests, Multiple Sclerosis Impact and Modified Fatigue Impact Scales, Becks Depression Inventory and the Health Status Questionnaire Short Form-36.
Results: Sixteen of 21 (76%) subjects completed the study. Subjects attended 13.2 1.6 endurance- and 15.8 1.9 resistance-exercise training sessions. No adverse events were reported. No significant differences (P50.05) in any outcome measures were observed between the two exercise training programmes either at baseline or following the completion of both training programmes.
Conclusion: Both endurance- and resistance-exercise training were well tolerated and appear to provide similar effects for people with multiple sclerosis, but larger studies are required to confirm these findings.

Introduction

Multiple sclerosis is a progressive or relapsing neurological disorder of the central nervous system. Physical symptoms, including fatigue and mobility impairments, can contribute to a reduction in functional capacity and interfere with the patient's ability to perform activities of daily living. The activities of daily living that are most affected in people with multiple sclerosis are those tasks that could be classified as mobility-related and physically demanding (e.g. housework, gardening).[1] In people with multiple sclerosis a reduced ability to complete activities of daily living is associated with higher depression scores and decreased quality of life.[2] Currently, multiple sclerosis has no cure and pharmacological interventions are limited in their

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ability to slow/prevent the progression of physical disability.[3] Therefore, alternative evidence-based interventions that can improve functional capacity, as well as increase quality of life in people with multiple sclerosis must be explored.

Research examining adaptations to exercise in people with multiple sclerosis have predominately focused on endurance-exercise training programmes (see Dalgas et al. for review[4]). Endurance exercise can be described as moderate-intensity continuous exercise that involves the use of large skeletal muscle groups and predominantly uses aerobic metabolism to sustain the activity.[5] Examples of such activity are exercises such as treadmill walking, or stationary cycling. While there is some evidence to suggest that endurance-exercise training may improve mobility and cardiorespiratory fitness in people with multiple sclerosis,[6,7] endurance-exercise training may have little impact on muscular strength[8,9] or balance.[6] Thus, exercise training adaptations from endurance-exercise training may not translate to the greatest improvements in functional capacity in people with multiple sclerosis.

The primary aim of resistance-exercise training is to improve muscular strength and/or muscle endurance. Adaptations vary depending upon the workout protocols used.[5] Few studies have investigated the effect of resistance-exercise training on people with multiple sclerosis (see Dalgas et al. for review[4]). While previous studies suggest that resistance-exercise training may improve strength, the impact of resistance-exercise training on functional capacity in people with multiple sclerosis is still inconclusive.[4] A recent study which specifically investigated the impact of progressive resistance-exercise training on muscular strength and functional capacity in people with multiple sclerosis found that progressive resistance training improved muscular strength and functional capacity.[10] Dalgas et al. reported a 21.5% increase in functional capacity in 19 people with multiple sclerosis.[10] Participants in the Dalgas et al. study improved their performance on the following functional capacity tasks: chair stand, ascending stair climbing, 10-metre walk and six-minute walk tests.[10] Further investigation is required to confirm the impact of resistance training on functional capacity in people with multiple sclerosis.

The impact of exercise training on quality of life in people with multiple sclerosis is inconclusive. A meta-analysis examining the impact of exercise training on quality of life in people with multiple sclerosis concluded that although endurance-exercise training significantly improved quality of life, there was insufficient evidence to draw conclusions on the effect of non-endurance-exercise training (such as resistance-exercise training) on quality of life in people with multiple sclerosis.[11]

No previous study has directly compared endurance- and resistance-exercise training in the same cohort of people with multiple sclerosis. Thus, it remains unclear as to which mode of exercise training will elicit optimal physical and psychological improvements in this clinical population. The aim of this pilot study was to compare adaptations in grip strength, balance, mobility, fatigue, depression and quality of life following endurance and resistance-exercise training in people with multiple sclerosis.

Methods

Experimental design

The present study was a cross-over design in which 16 subjects completed eight weeks of endurance-exercise training and eight weeks of resistance-exercise training (Figure 1). Participation in the two programmes was separated by an eight-week interval. Programme order was randomized using a coin toss. Eleven subjects performed resistance-exercise training first. Outcome measures were assessed before and after the endurance- and resistance-exercise training programmes. The primary outcomes in this study were mobility, fatigue and quality of life. The secondary outcomes were grip strength, balance, disease impact and depression. Two of the four assessors were blinded to the order in which subjects completed the training programme. This study was approved by the Griffith University Human Research Ethics Committee and the Queensland Health Research Ethics Committee.

Subjects

Twenty-one individuals with multiple sclerosis responded to a ‘call for volunteers’ flyer displayed

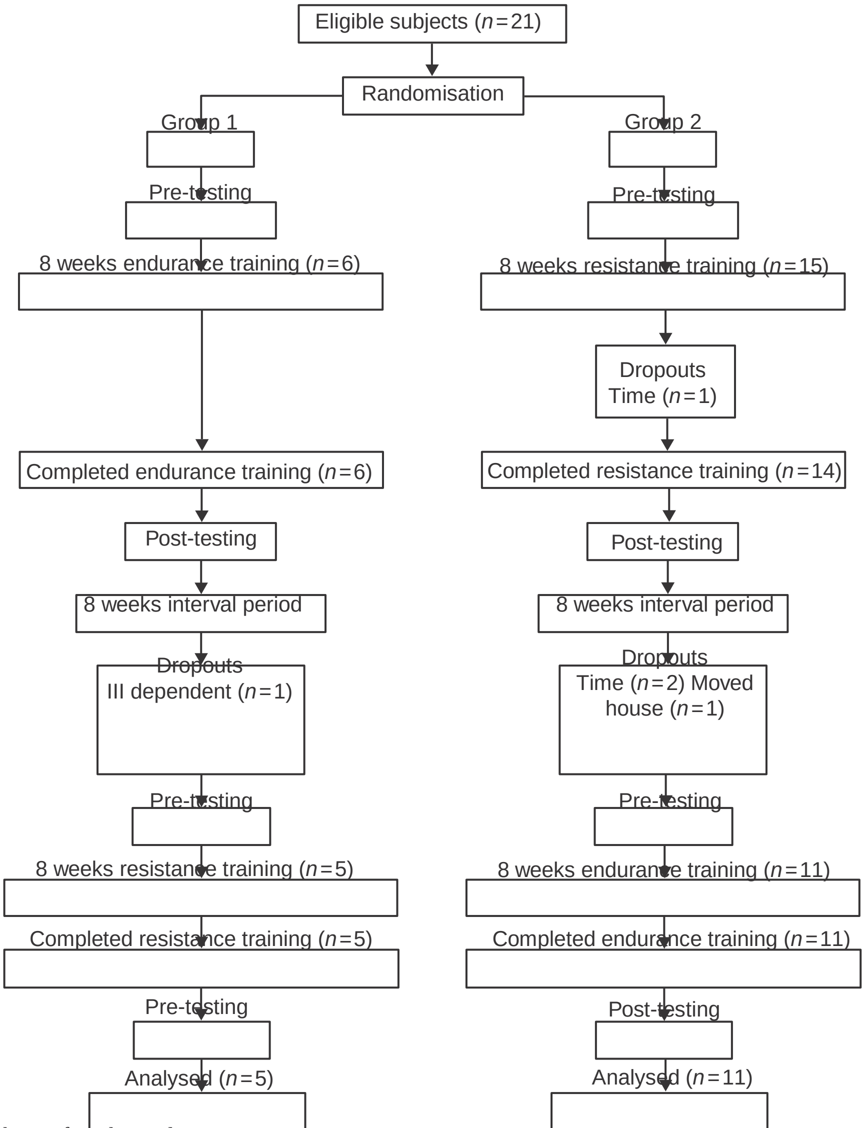

Figure 1 Flowchart of study outline.

at local community health centres and were accepted to participate in the programme. Subjects with multiple sclerosis were included in the study if they could ambulate independently either with or without the use of walking aid. Over the course of the study, five volunteers withdrew from the study for various reasons, including difficulties with time commitments, moving house and ill dependants. Analyses were performed on data collected from 12 female and 4 male subjects aged 47–66 years. Disease severity was assessed by a registered physiotherapist using the Disease Steps Scale.[12] Subject demographic and clinical characteristics are presented in Table 1. Subjects obtained approval for participation in the training programmes from their general practitioner and

Table 1 Subject demographic and clinical characteristics

Age (years SD)	55 7
Gender (male : female)	4 : 12
Disease duration (years SD)	10 10
Disease Steps Score (0–6 scale)	
1	n ¼ 7
2	n ¼ 5
3	n ¼ 4
Disease course	
Relapsing-remitting	n ¼ 10
Secondary progressive	n ¼ 3
Primary progressive	n ¼ 3

Disease Steps Score: 0 ¼ normal; 1 ¼ mild disability, mild symptoms or signs; 2 ¼ moderate disability, visible abnormality of gait; 3 ¼ early cane, intermittent use of a cane; 4 ¼ late cane, cane dependent; 5 ¼ bilateral support; 6 ¼ confined to a wheelchair.

each subject gave their written informed consent to participate in the study.

Measures of physical ability

Several measures of physical ability were used to provide an indication of functional capacity. Grip strength was assessed using a hand-held dynamometer (North Coast Medical hand dynamometer 800-821-9319; North Coast Medical, Morgan Hill, CA, USA). This test was performed in the seated position with the subject's arm held out straight and parallel to the ground at shoulder height. Subjects were instructed to squeeze the hand dynamometer with maximal force. Balance was assessed using the functional reach,[13] and four step square tests,[14] and the timed up and go[15] and six-minute walk tests[16] were used to provide a measure of mobility. The six-minute walk test was administered in accordance to the guidelines outlined by the American Thoracic Society,[16] except that a 25-m, rather than a 30-m track was used in the present study (due to space constraints). In all measures of physical ability, two trials of each task were performed with the best performance used in the data analysis.

Questionnaires

Disease impact was assessed using the Multiple Sclerosis Impact Scale.[17] This scale assesses the individual's view of how their multiple sclerosis has impacted upon their daily functioning during the previous two weeks. The higher the score, the greater the impact of the disease on the patient over the two-week assessment period.

Depression was assessed using the Beck Depression Inventory. This is a 21-item questionnaire, with higher scores indicating more severe depression.[18]

Fatigue impact was assessed using the Modified Fatigue Impact Scale.[19] This questionnaire provides an indication of the impact fatigue has on an individual in three domains: physical, cognitive and psychosocial. Higher scores indicate that fatigue has a greater impact on the individual.

Quality of life was assessed using the Health Status Questionnaire Short Form-36. This provides scores for eight dimensions which are combined to produce two summary scales: (1) a physical component summary score and (2) a mental component summary score; on all scales higher scores indicate a higher quality of life.[20]

Exercise training

Both the endurance- and resistance-exercise training programmes were eight weeks in duration and consisted of two exercise sessions per week. All training sessions were supervised by two exercise physiologists. Before all training sessions, subjects completed a 5-minute warm-up composed of walking at a self-selected speed. Progression through the exercise training programmes was at the discretion of the exercise physiologists and was based upon the subjects' rating of difficulty for each activity. For both the endurance- and resistance-exercise training programmes, subjects rated the difficulty of each exercise using the Borg Category Ratio Scale[21] immediately after completing each exercise during the training session . This rating was based on the subject's level of exertion. The intensity/difficulty of each activity was adjusted in order to maintain a rating of 3–5 (moderate–hard). The training sessions were concluded with 15–20 minutes of supervised static and dynamic stretching of the major upper and lower body muscle groups. In order to minimize the effect of overheating, oscillating pedestal fans and water spray bottles (on request) were used. All testing and training sessions were performed at Queensland Health facilities (Bundall or Helensvale Community Health Centres).

Endurance-exercise training programme

The endurance-exercise training programme involved a circuit of eight exercise stations composed of six different activities. Subjects exercised for 5 minutes at each station and rested for 2 minutes every 10 minutes (i.e. after the completion of every two activities). The eight exercise stations were: (1) step-ups (step height 10–20 cm), (2) arm cranking (ADPE Duo Bike), (3) upright cycling (Tunturi F35 Competence or York Magnaforce 5000 HRC), (4) arm cranking, (5) recumbent cycling (Vision Fitness R2250 HRT), (6) cross-trainer (Octance Fitness Q35), (7) treadmill walking (Elite DX726 or Pacer 3701), and (8) arm cranking. The exercise-intensity of each activity was increased throughout the programme by adjusting resistance and/or cadence. In addition, exercise time was progressively increased over the eight-week endurance-exercise training programme for those subjects who initially were unable to complete 5 minutes of continuous activity.

Resistance-exercise training programme

The resistance-exercise training programme consisted of three upper body and three lower body exercises as well as one core strength and one stability exercise (Appendix 1). For each exercise, subjects commenced and progressed through a series of exercises dependent upon the individual's initial level of strength and rate of improvement. Subjects performed 2–3 sets, composed of 6–10 repetitions of each exercise per set. Subjects were instructed to have a minimum of 30–60 seconds rest between each exercise set. Progression through the resistance-exercise training programme was facilitated by increasing the resistance of therabands and/or weights used on applicable exercises (Appendix 1) and by progressing through a series of exercises. The progression for each exercise is presented in Appendix 1.

Data analysis

To determine if there were significant differences in baseline measures between training modes and the order the training programmes were completed, a mixed factor ANOVA with baseline values as the within-subject variable and training order as the between-subject variable was conducted using Bonferroni adjustments. Results suggested that there was no carryover effect of the two programmes and that values for the dependent variables prior to commencing endurance- and resistance-exercise training were similar. Therefore, data in this study were analysed as endurance- versus resistance-exercise training irrespective of the order participants completed the training programmes.

Pre- and post-exercise training scores for all outcome measures were assessed using a repeated measures ANOVA with Bonferroni adjustments. Data are presented as the mean standard deviation. For all analysis, statistical significance was accepted at $P50.05$. All tests were two-tailed. Data were analysed using the statistical analysis software package SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

No adverse effects to exercise training were reported during either training programme. Both training programmes were well attended. Of the 16 sessions in the training programme, subjects attended 13.2 1.6 endurance- and 15.8 1.9 resistance-exercise training sessions.

Measures of physical ability

Pre- and post-training results for the measures of physical ability are presented in Table 2. No differences between training modes (endurance-versus resistance-exercise training) were found for any of the measures of physical ability. However, with the exception of grip strength, analysis of the data found that all measures of physical ability significantly improved with eight weeks of exercise training (Table 2).

Questionnaires

Pre- and post-training results on the questionnaires assessing disease impact, fatigue, depression and quality of life are presented in Table 3. No difference in training modes were found on any of the questionnaires utilized in this study. When changes in pre- and post-exercise training scores were examined, significant improvements

Table 2 Performance on functional measures following eight weeks of endurance- or resistance-exercise training

	Endurance training						Resistance training					
	Pre-training		Post-training				Pre-training		Post-training			
Grip strength (kg)	32.4	13.3	33.0	13.0	0.6	2.7	30.3	14.2	31.6	12.8	1.3	7.8
Functional reach test (cm)**	38.6	5.9	40.0	5.3	0.6	9.6	35.8	6.7	41.3	5.2	7.4	13.4
Four step square test (seconds)**	8.8	1.8	8.1	1.9	0.7	0.9	9.5	2.4	8.3	2.1	1.2	1.8
Timed up and go (seconds)**	7.2	1.7	6.7	1.4	0.5	0.7	7.5	2.2	6.8	1.8	0.7	0.8
Six-minute walk test (m)**	484	96	503	100	18.6	40.1	447	111	486	107	38.1	70.0

Values represent mean (SD).
**A within-within repeated measures ANOVA with Bonferroni adjustments revealed a significant main effect for pre/post difference, P50.01.

Table 3 Fatigue, depression and quality of life scores following eight weeks of endurance- or resistance-exercise training

	Endurance training						Resistance training					
	Pre-training		Post-training				Pre-training		Post-training			
MSIS Physical Score*	43.5	12.4	39.1	12.9	4.1	9.6	43.8	15.3	39.3	13.1	6.3	12.2
MSIS Psychological Score	19.6	8.0	16.9	6.1	2.7	6.5	20.0	9.3	17.1	7.2	1.9	8.2
Beck Depression Inventory	9.7	11.6	10.3	11.6	0.6	3.9	9.8	9.0	8.7	7.7	2.3	5.4
MFIS Physical Scale*	19.6	7.6	16.9	5.5	2.7	5.3	18.3	7.5	16.6	7.1	1.6	3.3
MFIS Psychosocial Scale**	3.1	1.5	2.4	1.5	0.8	1.4	3.6	1.8	2.4	1.8	1.6	11.6
MFIS Cognitive Scale	15.8	10.2	13.5	10.0	2.3	6.0	14.4	10.0	12.3	9.5	3.3	7.8
SF-36 physical component summary score	37.8	6.7	37.7	7.7	0.2	6.8	36.1	9.1	39.8	7.3	3.7	7.0
SF-36 mental component summary score	48.1	13.3	50.4	12.8	2.3	10.6	53.2	11.2	51.3	12.9	1.9	9.7

Values represent mean (SD).
MSIS, Multiple Sclerosis Impact Scale; MFIS, Modified Fatigue Impact Scale; SF-36, Health Status Questionnaire Short Form 36.
*A within-within repeated measures ANOVA with Bonferroni adjustments revealed a significant main effect for pre/post difference, P50.05.
**A within-within repeated measures ANOVA with Bonferroni adjustments revealed a significant main effect for pre/post difference, P50.01.

on the physical scale of the Multiple Sclerosis Impact Scale, and the physical and psychosocial scales of Modified Fatigue Impact Scale were observed. We found no significant changes in the psychological scale of the Multiple Sclerosis Impact Scale, cognitive scale of the Modified Fatigue Impact Scale, Becks Depression Inventory, or the Health Status Questionnaire Short Form-36.

Discussion

The aim of this study was to compare changes in grip strength, balance, mobility, fatigue impact, depression and quality of life following eight weeks of endurance- and resistance-exercise training in people with multiple sclerosis. When the two modes of exercise training were compared, neither the resistance- or endurance-exercise training elicited greater improvements in any of the outcome measures used in this study.

Measures of physical ability

When pre- and post- training scores were examined improvements in balance and mobility were observed following both the endurance- and resistance-exercise training programmes.

The finding that resistance-exercise training was associated with improved balance is in contrast to the findings of a previous study. De Bolt et al.[22] reported no improvements in balance after a home-based resistance-training programme in people with multiple sclerosis. The supervised exercise setting used in the present study, when compared to the home-based training described in the study by De Bolt et al.,[22] may explain the discrepancies in balance adaptations observed following resistance-exercise training. Similarly, a recent meta-analysis on walking mobility in people with multiple sclerosis found that walking mobility improved with exercise training when conducted in a supervised environment, but not when the training was home-based.[23]

In the current study, like the resistance-exercise training programme we observed that performance on the functional reach and four step square tests improved following endurance- exercise training. These results are supported by two previous case studies that have reported improvements in balance in people with multiple sclerosis following regular treadmill walking.[24,25]

The type of endurance-exercise training performed may be of importance in determining balance outcomes. A study conducted in older adults with balance deficits investigated different types of endurance-exercise training and found that balance improved when the activities performed 'stressed' the subject's balance.[26] That is, those activities during which the individual was required to maintain their centre of mass over their base of support in response to either an internal or external perturbation. These authors reported that cycling did not improve balance, whereas walking and aerobic-exercise classes did.[26] In the present study, our endurance-exercise training programme was composed of six different activities. It is possible that the activities that stressed balance (treadmill, cross-trainer and step-ups) contributed to the improvement in balance observed. However this is an area that requires further investigation.

In agreement with previous investigations, this study reported improvements in mobility following both endurance- and resistance-exercise training.[23] The mechanisms through which endurance- and resistance-exercise lead to improvements in mobility have not yet been determined. A previous three-week balance training programme reported improvements in both the Berg Balance Scale and Dynamic Gait Index Score and suggests that balance training improved both balance and mobility in people with multiple sclerosis.[27] In addition, a relationship between postural sway and brisk walk time in people with multiple sclerosis has been reported.[28] It is possible that the improvements in mobility observed in the present study are secondary to improvements in balance. However other factors, such as improved gait kinematics (gait pattern) and cardiorespiratory fitness, cannot be ruled out.

Resistance-exercise training has previously been shown to improve gait kinematics in people with multiple sclerosis.[29] This may enable patients to walk quicker and further without tiring. Similarly, endurance-exercise training may improve efficiency through gait kinematics, although this relationship has not yet been examined in multiple sclerosis. Alternatively, endurance-exercise training may improve exercise tolerance in people with multiple sclerosis by improving cardiorespiratory fitness.[7,30] Improved cardiorespiratory fitness may enable the patient to ambulate quicker (or exercise at a higher intensity), as well as improve walking endurance. However, as we did not analyse gait kinematics or directly measure cardiorespiratory fitness in this study we are unable to examine or comment on these relationships.

Of the measures of physical ability examined in this study, the only measure in which we did not observe an improvement with exercise training was grip strength. It is possible that grip strength was not influenced in the current study, as neither programme focused on activities which involved the forearm extensor and flexor muscles.

Questionnaires

In the current study we found that fatigue impact in the physical and psychosocial domains decreased following exercise training. Surprisingly, we found that neither endurance- or resistance-exercise training was associated with improvements in depression or quality of life.

Fatigue in multiple sclerosis is defined as 'A subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual or desired activities'.[31]

Previous studies have produced conflicting results on the impact of exercise training on fatigue. An overall score 438 on the Modified Fatigue Impact Scale (score when three subscales are combined) has been suggested as a cut-off score for determining fatigued and non-fatigued patients.[32] Based on this cut-off, 8 of 16 subjects before endurance-exercise training, and 6 of 16 subjects before resistance-exercise training were classified as experiencing significant fatigue in the present study. This decreased to 4 of 16 subjects following both endurance- and resistance-exercise training.

Fatigue pathology in multiple sclerosis is complex. It may result from the disease pathology itself, caused by secondary factors including medication use, sleep disturbance or depression, or may be the consequence of physical deconditioning caused by physical inactivity.[33] It is likely that underlying fatigue pathology is largely responsible for the variability in results observed in different exercise intervention studies. As exercise modality was not found to elicit different effects on fatigue impact in the present study, we believe that both endurance- and resistance-exercise training may be useful strategies in the management of fatigue in people with multiple sclerosis. Most importantly, this study suggests that exercise training does not exacerbate fatigue in people with multiple sclerosis.

Previous cross-sectional studies have suggested a relationship between physical activity levels and a reduced incidence of depression in people with multiple sclerosis.[34] In this study we found no changes in depression following exercise training. However, our ability to investigate depression was limited because of the small number of subjects in this study who suffered from depression. Based on previous establish criteria (Beck Depression Inventory score 13),[35,36] only 3 of the 16 subjects in this study experience depression prior to both the endurance- and resistance-exercise training programmes. Therefore we are unable to make any interpretation on the different effect of the two training programmes on depression.

In the current study we observed no changes in quality of life following either endurance- or resistance-exercise training. A score of 50 10 on both the physical and mental component summary scores represents normative quality of life scores in the general population.[37] Although scores for the subjects in the current study indicated a reduced quality of life in the physical domain, the mental component summary score was similar to that of the general population. Therefore, we would not expect to see large changes in the mental component summary score, restricting our ability to examine the impact of exercise training on this outcome measure.

Previous studies investigating the impact of exercise training on quality of life in people with multiple sclerosis have reported conflicting results. Some studies have reported improvements in quality of life with exercise training[30,38] while other studies have not.[39–41] Overall, as indicated by a recent meta-analysis,[11] the literature does seem to suggest that exercise training is associated with a small improvement in quality of life in people with multiple sclerosis.

This study has several limitations that must be considered when interpreting the results of this study. This study is composed of a small group of patients with mild–moderate multiple sclerosis and results will not necessarily translate to patients with more severe disability. The sample size in this study is small, increasing the chance of making a type II error. Further investigation with a larger sample of patients is required. Although standardized criteria were used in all pre- and post-testing, two of the four assessors were not blinded to the order in which the subjects had completed the training programmes. Our process of randomization (coin toss) led to a larger number of subjects completing the resistance-exercise training programme first. Also, as no non-exercising cohort was investigated, we are unable to assess if exercise training is better than no exercise training. Finally, this study is subject to the limitations of a cross-over design. This study is based on the assumption that an eight-week period provided a sufficient period of time for a 'washout' period to occur. Although statistical analysis of the data supported this, we cannot rule out that a type II error occurred (concluding that there was no carryover effect between the two programmes when there was).

The results of the present study suggest that both endurance- and resistance-exercise training appear to provide similar benefits to people with multiple sclerosis. However further investigation with a larger sample size is required to confirm the findings of this study.

Clinical messages

Both endurance- and resistance-exercise training is well tolerated by people with multiple sclerosis.
Endurance- and resistance-exercise training provides similar effects for people with multiple sclerosis.
Exercise training does not exacerbate fatigue in multiple sclerosis.

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Competing interests

We have no competing interests to declare.

Contributors

NS: study design, conducting study, data analysis, writing and editing manuscript. CM: study design, data analysis, editing manuscript. GT: study design, conducting study, collation of data. SB: study design, editing manuscript.

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Appendix 1 – Progression of exercises during resistance exercise training

Upper body exercises

Exercise 1	Exercise 2	Exercise 3
Chest press with theraband*	Seated row with theraband*	Shoulder abduction with theraband*
Chest press with dumbbell*	Upright row with dumbbell*	Shoulder abduction with dumbbell*
Wall push-up		
Push-up on parallel bar		
Knee push-up on ground		
Full push-up		

(Progression of exercises ↓)

Lower body exercises

Exercise 1	Exercise 2	Exercise 3
Sit-to-stand	Static lunge with support (inside parallel bars)	Hip abduction
Standing half squats with support (standing inside parallel bars)	Static lunge without support	Hip abduction with ankle weights*
g ball squats (using Swiss ball)	Dynamic lunge with return	Lateral step-ups (increasing from small to medium to large step height)
Full ball squats	Dynamic lunge with return off step (increasing from small to medium to large step height)	Lateral step-ups with ankle weights*
Full ball squats with hand weights*	Dynamic lunge off step with ankle weights*	

(Progression of exercises ↓)

Core and lower limb stability exercises

Core exercise	Stability exercise
Prone support (on hands and knees) with single leg extension	Tandem stance
Prone support with arm and leg extension of contralateral limbs	Tandem stance on foam mat
Laying supine on floor, knees bent with hip lift	Heel-to-toe walk along foam beam
Laying supine on floor, feet elevated on swiss ball with hip lift	Single leg stance
Front support on elbows and knees	Single leg stance on foam
Front support on elbows and toes	Standing on wobble board

(Progression of exercises ↓)

Participant's progression through the above series of exercises was dependent upon the individual's rate of improvement during the programme.
*Indicates that the theraband or dumbbell/ankle weight used in these exercises was increased prior to progression to the next exercise. Four theraband resistances were used (red, green, blue, black), dumbbell weights of 1 kg, 2 kg, 3 kg and 4 kg, and ankle weights weighing 1 kg, 1.5 kg, 2 kg, 2.5 kg and 5 kg were used. This rate of progression was monitored and directed by an exercise physiologist.

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Fall risk and incidence reduction in high risk individuals with multiple sclerosis: A pilot randomized control trial

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Abstract

Objective: To determine the feasibility of three fall prevention programs delivered over 12 weeks among individuals with multiple sclerosis: (A) a home-based exercise program targeting physiological risk factors; (B) an educational program targeting behavioral risk factors; and (C) a combined exercise-and-education program targeting both factors.

Design: Randomized controlled trial.

Setting: Home-based training with assessments at research laboratory.

Participants: A total of 103 individuals inquired about the investigation. After screening, 37 individuals with multiple sclerosis who had fallen in the last year and ranged in age from 45–75 years volunteered for the investigation. A total of 34 participants completed postassessment following the 12-week intervention.

Intervention: Participants were randomly assigned into one of four conditions: (1) wait-list control (n = 9); (2) home-based exercise (n = 11); (3) education (n = 9); or (4) a combined exercise and education (n = 8) group.

Measures: Before and after the 12-week interventions, participants underwent a fall risk assessment as determined by the physiological profile assessment and provided information on their fall prevention behaviors as indexed by the Falls Prevention Strategy Survey. Participants completed falls diaries during the three-months postintervention.

Results: A total of 34 participants completed postintervention testing. Procedures and processes were found to be feasible. Overall, fall risk scores were lower in the exercise groups (1.15 SD 1.31) compared with the non-exercise groups (2.04 SD 1.04) following the intervention ($p < 0.01$). There was no group difference in fall prevention behaviors ($p > 0.05$).

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Conclusions: Further examination of home-based exercise/education programs for reducing falls in individuals with multiple sclerosis is warranted. A total of 108 participants would be needed in a larger randomized controlled trial.

ClinicalTrials.org #NCT01956227

Keywords

Multiple sclerosis, balance, gait, mobility, accidental falls, fall risk factors, education

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Introduction

Over 50% of the multiple sclerosis community report falling over a six-month period[1–5] and those who do fall often require medical attention for injuries.[6,7] Additionally, individuals with multiple sclerosis who have suffered a fall report worse physical and psychological health status (i.e. health-related quality of life) compared with non-fallers with multiple sclerosis.[8] The adverse impact of falls in multiple sclerosis has led to research examining predictors,[9–11] consequences,[7,12,13] and prevention strategies.[14,15] However, there have been relatively few interventions aimed at reducing fall incidence in this population.[8,16] The few interventions that have been evaluated focused on intrinsic or extrinsic factors in isolation. For instance, an investigation indicated that a 10-week physiotherapy (group and individual) intervention resulted in a decrease in fall incidence.[8] Another investigation indicated that fall risk behaviors can be reduced with an educational intervention.[17]

Given that falls typically result from diverse and interacting risk factors,[18] interventions that address both intrinsic/physiological and extrinsic/behavioral risk factors, might have the greatest promise to reduce fall incidence in adults with multiple sclerosis.[19] The purpose of this pilot investigation was to examine the feasibility of three distinct 12-week fall prevention rehabilitation interventions on physiological and behavioral fall risk and fall incidence in high risk adults with multiple sclerosis: (A) a home-based exercise program targeting physiological risk factors; (B) an educational program targeting behavioral risk factors; and (C) a combined exercise and education program targeting both physiological and behavioral risk factors.

Methods

All procedures were approved by the University of Illinois at Urbana-Champaign institutional review board. All participants provided written informed consent prior to taking part in the investigation. The study was a two (home-based exercise) by two (education) factorial randomized control trial with assessments occurring prior to and following the 12-week intervention (ClinicalTrials.org #NCT01956227).

Participants were recruited through the North American Research Committee on Multiple Sclerosis patient registry during the spring of 2013 (April–June). To be included in this study, participants were required to have a neurologist-confirmed diagnosis of multiple sclerosis; be ambulatory with or without aid; demonstrated comprehension of English; self-reported a fall in the last 12 months; be between 45–75 years of age; lived within a 175 mile radius of the testing site; and have been relapse free for 30 days prior to participation. These inclusion criteria resulted in a sample at high risk of falls.[11]

Participants were assessed at baseline and immediately following the 12-week intervention. Baseline assessments occurred in late spring/early summer while postintervention assessment occurred in autumn of 2013. Upon initial arrival to the laboratory for baseline assessments, participants provided informed consent and completed demographic questionnaires concerning their health history, self-reported disability,20 and frequency in which they engaged in fall prevention behavior. Participants then underwent fall risk assessment.

After baseline assessment, participants were randomized into groups (exercise, education, exercise plus education, and control) using a simple randomization method with a 1:1:1:1 allocation ratio (independent of baseline assessment) by computer-generated random numbers. Group allocation for each participant was concealed in opaque envelopes. The outcome assessors were blinded to group allocation.

Primary outcome measures of this investigation were fall risk score, as determined by the short form of the Physiological Profile Assessment,[18] and frequency in which participants engaged in fall prevention behavior, as determined by the Falls Prevention Strategies Survey (FPSS).[21] The physiological profile assessment is a standardized test battery that assesses vision, lower limb proprioception, strength, postural sway, and cognitive function. The outcome of each test was combined to generate an overall fall risk score ranging from –2 to +4.[18] Using this scale, higher scores are indicative of a person being at greater risk of falling. The physiological profile assessment is predictive of falls in persons with multiple sclerosis.[22]

The frequency of engagement of fall prevention strategies was indexed with the Falls Prevention Strategy Survey.[21] This survey is an 11-item self-report instrument addressing protective behaviors related to fall risk in individuals with multiple sclerosis. Behaviors include, but are not limited to, adjusting home environment to reduce fall risk, and use of assistive devices. Response options reflect the frequency participants engaged in behavior (i.e. never, sometimes, regularly). Higher values on the Falls Prevention Strategy Survey indicate greater frequency of engagement of fall protective behaviors.

Secondary measures included self-reported falls prior to, during, and following the intervention. During baseline assessment, participants self-reported falls in the three months prior to the intervention. A fall was defined as an event where the participant unintentionally came to rest on the ground or a lower level.[1] During the intervention period, participants were contacted via telephone every two weeks to access the incidence of falls and whether they sought medical attention for a fall-related injury. Following the intervention, participants self-reported falls and falls-related injury with a monthly falls diary. Falls diaries were mailed back to the research laboratory in prepaid envelopes. Upon receipt, the diaries were reviewed by a research assistant for clarity. Clarifying phone calls were made by a research assistant if necessary. During the three-month postintervention period, participants were contacted via telephone every two weeks to encourage use of the fall diaries and to inquire about any fall-related injury.

Feasibility outcomes include recruitment, adherence and retention rates, and ability to collect primary and secondary outcomes.[23] Recruitment rate was calculated as the percentage of potential participants that contacted the research laboratory and were enrolled in the investigation. Adherence rate was calculated as the percentage of total number of exercise sessions completed by the participants in the exercise and exercise+education group. Retention rate was calculated as the percentage of enrolled participants that completed postassessment. Ability to collect outcome assessments was operationalized as the percentage of total possible number of assessments that were completed at baseline and follow-up assessments.

Intervention groups

Participants in the intervention groups attended a total of four sessions spread over the first two months of the 12-week intervention period. Participants in the intervention groups had the same number of visits of the same duration. In the initial visit participants were provided with infor- mation specific to their group allocation. Following the initial visit, participants completed the final three sessions returning for training in the first month (Weeks 2 and 4) and once again in the sec- ond month (Week 8).

Home-based exercise group. The home-based exercise protocol focused on improving balance, and lower limb/core muscle strength – all measures previously described as potential determinants of falling in persons with multiple sclerosis.[5,11,24] The exercise protocol has been described in detail previously.[25] In brief, participants were taught a standardized series of exercises that focuses on balance, lower limb muscle strength, core muscle strength, and stretching. Participants were instructed to perform the exercises three times a week in their home as outlined in a manual that was provided. The exercises were progressive in nature over the three-month period, with several levels of difficulty. Consistent with previous work,[25] compliance of at-home exercise was assessed with diaries that participants completed.

Education group. The education group visited the laboratory at baseline, and Weeks 2, 4, and 8. The sessions were led by trained interventionists who delivered information to small groups ranging in size from two to four people and lasted about an hour. The education program drew upon psycho-educational group theory,[26] as well as several specific practices from the self-management literature, including group brainstorming, problem-solving, and action planning.[27] The program also applied the core principles of self-efficacy enhancement, in particular, peer modeling, vicarious learning, social persuasion, and guided mastery.[28]

Home-based exercise and education group. During the first visit, participants were taught the standardized series of exercises. The exercise trainings were the same as the exercise only group, however, the instruction focused on main concepts and less time was afforded to mastery of exercise technique. Like the four-session educational program, the content of the education sessions delivered were based upon self-management practices, self-efficacy theory, and psycho-educational group theory, however, key concepts were discussed in less depth. Both exercise and education programs were led by a trained specialist. The organization of the combined group was chosen to ensure that there was the equivalent contact time across all intervention groups.

Control group. We used a wait-list control as recommended for developmental trials.[29] Participants in the control group completed the study measures before and after the intervention and subsequently received the intervention after the study completion. They were instructed to continue their normal activities during the intervention period.

Statistical analysis

The data analysis was performed in SPSS v20 (IBM, Chicago, IL) and only participants who completed the intervention were included, consistent with a completers analysis for a Phase-I trial. Normality was assessed with the Shapiro–Wilk test and corrected when appropriate (i.e. log transformed). Postintervention between group differences were analyzed with a two (education vs. no education) by two (exercise vs. no exercise) univariate analysis of covariance with baseline values as the covariate for variables. Effect sizes associated with F statistics are expressed as eta-squared (η^2). To examine the distribution of fallers as a function of condition, an independent samples McNemar test was conducted. All analyses used two-sided tests, and p values equal or less than 0.05 were considered statistically significant.

Results

Participant flow is outlined in Figure 1. A total of 716 individuals with multiple sclerosis who met the inclusion criteria were sent recruitment materials via the North American Research Committee on Multiple Sclerosis Patient Registry. A total of 103 individuals responded to the recruitment letter and contacted the research laboratory. After screening, a total of 37 individuals enrolled in the investigation. The recruitment rate of 36% indicates that recruitment procedures need to be re-evaluated for future investigations. Although there were numerous reasons potential volunteers did not enroll, unwillingness to travel to the research laboratory was the most common.

Following enrollment, three individuals withdrew. One withdrew due to concerns about traveling; another had their phone disconnected and was unable to be contacted; and one participant withdrew because of scheduled spinal surgery. Data from these participants were excluded from analyses (see Figure 1). There was no statistical difference between participants (age, disability status, multiple sclerosis duration, or subtype) who withdrew and those that completed the intervention. A total of 34 participants completed the postintervention assessment (n = 8 control; n = 10

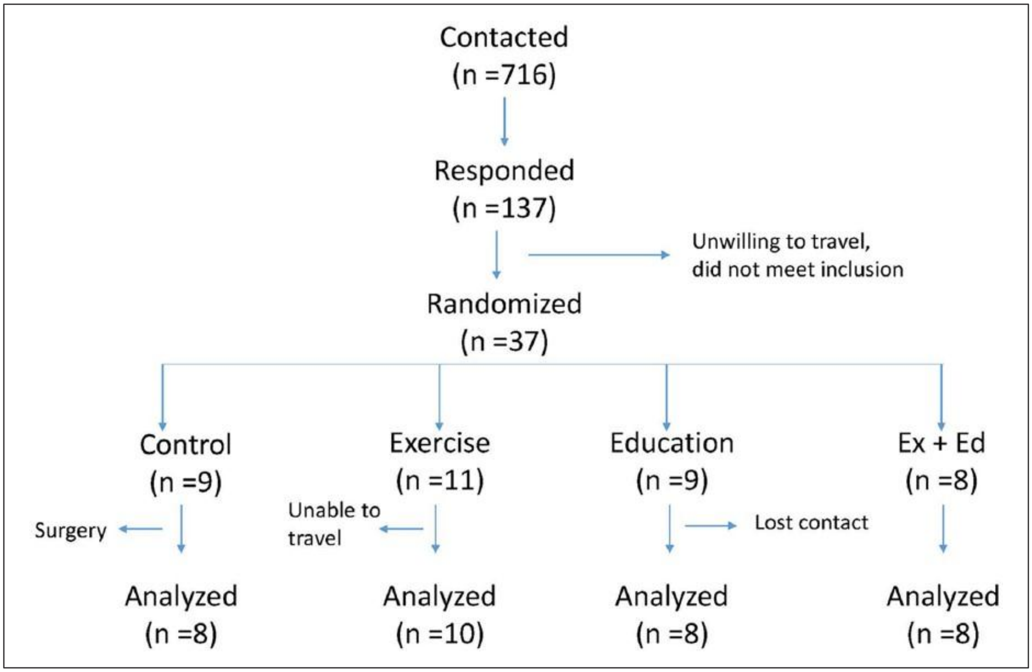

Figure 1. Participant flow.

exercise; $n = 8$ education; $n = 8$ exercise+education). The retention rate of 92% suggests that our retention efforts were appropriate.

The average age of participants was 62.3 years (SD 8.7). A total of 12 males and 22 females participated in the investigation. Among participants, multiple sclerosis duration ranged from 5 to 40 years with an average of 16.3 years (SD 8.4). A total of 17 participants had relapse-remitting (RR), 10 had secondary progressive, five had primary progressive, and two participants did not report multiple sclerosis type. Self-reported disability ($EDSS_{SR}$) as indexed by the self-report expanded disability status scale ranged from 1.0 to 7.0 with a median of 6.0. At baseline testing, 10 individuals utilized bilateral support, 13 utilized unilateral support, and 11 did not require an assistive device during ambulation.

Sample characteristics as a function of group are reported in Table 1. There were no group differences in age, multiple sclerosis duration, gender composition, or assistive device use ($p > 0.05$). The control and exercise-only group had a greater proportion of participants with relapse remitting than the other groups, which were more evenly distributed between relapse remitting and progressive subtypes.

On average, the exercise and exercise+education groups completed 82.6% of the prescribed exercise sessions. In addition, 61% ($n = 11$) of persons in these groups reported including other forms of exercise, such as low impact walking and biking in their weekly routine. Individuals in the education and control groups did not report starting any new exercise/rehabilitation activities during the intervention. Our relatively high adherence rate suggests that our methods to encourage compliance is feasible.

Among all participants, baseline fall risk, as indexed by the physiological profile assessment, ranged from –0.60 to 3.95 with an average of 1.53. Statistical analysis revealed a main effect of exercise ($F(1,30) = 9.9$; $p < 0.01$; $\eta^2 = 0.29$). Individuals in the exercise and exercise+education groups had lower physiological profile assessment scores following the intervention than the education and control groups when controlling for baseline values. There was neither a main effect of education

Table 1. Sample characteristics as a function of group.

	Control (*n* = 8)	Exercise (*n* = 10)	Education (*n* = 8)	Exercise+Education (*n* = 8)
Age (years (mean (SD))	63.3 (11.2)	62.3 (7.5)	61.0 (7.5)	59.3 (6.5)
Gender (male/female)	2/6	2/8	3/5	2/6
MS subtype (RR/SP/PP)*	7/1/0	7/1/2	3/3/2	3/4/1
MS duration (years)	19.0 (9.3)	15.0 (5.6)	14.6 (10.9)	20.0 (7.4)
Assistive device (none/unilateral/bilateral support)	3/2/3	4/4/2	3/2/3	2/3/3
$EDSS_{SR}$ (median(IQR))	6.0 (2.0)	5.5 (1.5)	6.0 (3.0)	6.0 (2.0)

*Significant effect of group; $p < 0.05$.
IQR: interquartile range; MS: multiple sclerosis; PP: primary progressive; RR: relapse remitting; SD: standard deviation; SP: secondary progressive; EDSS: Expanded Disability Status Score self report.

Table 2. Fall risk, Fall Prevention Strategy Score and Proportion of Fallers as a function of group and time.

Group	Physiological profile assessment		Fall Prevention Strategy Score		Proportion of Fallers (Number of fallers)	
	Pre	Post	Pre	Post	Pre	Post
Control	0.95 (1.1)	1.6 (1.0)	13.5 (3.6)	14.7 (2.9)	60% (*n* = 5)	80% (*n* = 6)
Exercise	2.1 (0.7)	1.4 (1.2)	11.2 (3.3)	11.6 (3.8)	50% (*n* = 5)	33% (*n* = 3)
Education	1.5 (0.7)	2.0 (1.1)	11.2 (4.1)	13.9 (4.6)	25% (*n* = 2)	60% (*n* = 5)
Exercise+Education	1.5 (1.3)	1.1 (1.6)	11.4 (5.2)	12.3 (5.2)	60% (*n* = 5)	38% (*n* = 3)

nor an interaction of exercise and education on fall risk ($p > 0.05$) (see Table 2).

The mean scores of the Fall Prevention Strategy Survey are reported in Table 2. Statistical analysis revealed that none of the interventions resulted in a significant change in reported use of fall prevention strategies ($p > 0.05$).

At baseline, there was no difference in proportion of fallers across groups ($p = 0.25$). However, following the intervention a trend for group effect ($p = 0.13$) with a seemingly smaller proportion of fallers in the exercise and exercise+education groups was noted (see Table 2). Subsequent analysis revealed that, following the intervention, the exercise and exercise+education groups had a smaller proportion of fallers than the education and control.

Adverse events

None of the participants in the exercise, education, or exercise+education groups reported injuries directly associated with the interventions (e.g. carrying out exercises). During the intervention, six participants reported seven injuries related to falls. These injuries included contusions, mild concussion, knee injury, and broken ribs. The injurious falls were distributed evenly throughout the groups with one injury occurring in the control group, two in the education group, one in the exercise group, and three in the exercise+education group. Following the intervention, two participants (one each from the exercise and exercise+education groups) reported injuries related to falls. These injuries included contusions, a broken foot, and concussion.

Discussion

The principal finding of this pilot randomized controlled trial was that home-based exercise in isolation and in combination with an educational program is a feasible approach to reduce physiological fall risk and may have the potential to reduce fall incidence in older adults with multiple sclerosis. Additionally, there were no adverse events related to the three interventions reported. Lessons learned from this pilot investigation can maximize the success of larger fall prevention interventions.

Consistent with previous research, a 12-week, home-based exercise program focusing on balance and lower limb strength was found to reduce physiological fall risk in individuals with multiple sclerosis.[25] Indeed, within the current sample, physiological fall risk was reduced on average by ~20% in both the exercise and exercise combined with education groups. This observation supports the growing evidence of the beneficial effect of exercise as a fall risk prevention strategy,[8,16] and further highlights the benefits of home-based exercise as a feasible fall prevention strategy in this neurological population.

The novel contribution of the current investigation was that the home-based exercise program targeting balance and lower limb strength not only led to a reduction in fall risk,[25] but also appears as a feasible approach to reduce the proportion of fallers in a high risk sample. It is important to highlight that no change in proportion of fallers following the intervention was observed for the education and control groups. Given that this was a feasibility study, and not powered to detect changes in proportion of fallers, caution should be used when interpreting these results. Previous fall prevention interventions in multiple sclerosis samples have reported a reduction in fallers have primarily utilized either clinic-based[16] or community-based[8] exercise. The current results, in combination with previous findings, collectively indicate that exercises targeting balance and lower limb strength may have the potential to reduce fall incidence in multiple sclerosis. The observations also highlight that feasibility of collecting prospective fall data in older adults with multiple sclerosis with calendars returned via post on a monthly basis.

In contrast to the growing body of research examining exercise-based fall prevention programs, there has only been a single investigation examining the feasibility of education as fall prevention strategy in individuals with multiple sclerosis. Specifically, a pilot investigation of a fall risk management program found that 12 hours of group educational sessions lead to gains in knowledge concerning falls and use of prevention strategies.[17] Indeed, the current educational program was based in part on this fall risk management program.

Although, the education program used in this investigation had no detectable effect on the frequency of engagement in fall prevention strategy or proportion of fallers, it was found to be feasible. There are several potential reasons for the null results concerning the education program. Although participants did self-report making specific changes to their behavior to reduce fall risk in the group settings, it is possible that these changes were not captured with the Fall Prevention Strategy Survey. For instance, one participant reported installing a chair lift to minimize the risk of falling on the stairs, but this large environmental change had little impact on this participant's overall Fall Prevention Strategy Survey score. This observation highlights the importance of collecting open-ended quantitative information regarding participants change in behavior/environment. Additionally, there were significant differences between the original intervention[17] and the educational intervention delivered in this study, which may explain the null results. For instance, the current program was shorter in duration (two to four hours vs. 12 hours). Additionally, education sessions were spread out over two months to mimic the home-based exercise program, as opposed to once a week for five weeks followed by a one month break and then a final session, as per the original program. It is possible that the distribution of sessions in the current investigation made it difficult for participants to use and integrate the knowledge. We suggest that future investigations utilize education sessions closer in time to potentially maximize the chance for knowledge integration and incorporate open-ended questions to insure that investigators capture changes relevant to the individuals.

Within the current investigation, *during* the intervention period, 7 out of 74 falls (9.5%) were injurious and *following* the intervention 2 out of 86 falls (2.6%) were injurious. The incidence of injurious falls was similar to previous investigations.[6,30] Although there appears to be a reduction in the number and percentage of injurious falls following the three interventions, the small number of injurious falls precludes any definitive conclusions. However, it does highlight that future interventions should include injurious falls as an outcome measure.

Despite the promising observations, this study did have weakness. We note that the majority of these weaknesses are common in feasibility studies.[23] The small sample size limits the generalizability of the results and reduces the observed power. Based on the observations of this current investigation, a sample of 108 with 27 participants per group would be needed to observe a significant reduction in proportion of fallers. It should be noted that caution should be used when estimating sample sizes based on feasibility studies such as the current investigation.[31] The current investigation excluded individuals younger than 45 years of age. This criterion was based on the notion that advanced age is a risk factor for falls in the general public[32] and has been suggested to be related to falls in cross-sectional studies of persons with multiple sclerosis.[1,10] Recently, prospective investigations have reported that younger age is a risk factor for falls in persons with multiple sclerosis.[33] It remains to be seen if home-based exercise in isolation or in combination with education will reduce fall risk and/or incidence in younger adults with multiple sclerosis.

It is important to note that falls prior to the intervention were based on retrospective recall, whereas falls during and following the intervention were collected prospectively. This creates difficulty in comparing fall prevalence and incidence as a function of the intervention. However, it is important to note that previous reports have found a significant association between retrospective recall of falls and prospective recording of falls in multiple sclerosis.[5]

The completion of this pilot randomized control trial has provided valuable information concerning falls prevention trials in older adults with multiple sclerosis. Specifically, future inves- tigations need to include prospective falls prior to and following the intervention. Minimizing the travel/transportation burden on participants will likely improve recruitment rates. The importance of collecting data on injurious falls within a fall prevention intervention was also noted. Lastly, the possibility of altering the timing of the education sessions to maximize the chance for knowledge integration was highlighted.

Conclusions

The findings add to the knowledge concerning the feasibility of exercise and fall prevention education on falls among people with multiple sclerosis. Future studies involving larger sample sizes, longer follow-up period, more frequent education sessions consistent with adult learning theories, and practices investigating the relative benefits of exercise in isolation and combined with education are warranted.

Clinical message

- Fall risk can be minimized with targeted home-based exercise in persons with multiple sclerosis.
- Fall behavior education is feasible in persons with multiple sclerosis.
- Combining fall behavior education with home-based exercise reduces fall risk in persons with multiple sclerosis.

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Conflict of interest

The authors declare that there is no conflict of interest.

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