TESIS DOCTORAL

Entrenamiento de la marcha en el lesionado medular. Uso de sistemas electromecánicos y estimulación transcraneal no invasiva.

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A mi mujer Vicky, y a nuestros

hijos Claudia, Alex y Marcos

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INDICE

INTRODUCCION

Definición de la lesión medular

La médula espinal forma parte del sistema nervioso central y constituye la vía principal por la que el cerebro recibe información del resto del organismo y envía las órdenes que regulan los movimientos. Su lesión producirá parálisis parcial o total de la movilidad voluntaria, alteraciones o ausencia de sensibilidad por debajo del nivel de la lesión, falta de control de esfínteres, trastornos en la esfera sexual, alteraciones del sistema nervioso vegetativo y el riesgo de graves complicaciones de por vida.

Epidemiología

Las lesiones medulares, en cuanto a etiología, podemos clasificarlas en dos grandes grupos: las de origen traumático y las de causa no traumática. Clásicamente la lesión medular no traumática consituía un tercio del total[1], aunque este porcentaje ha ido aumentando en los últimos años hasta alcanzar aproximadamente el 40%[2], sobre todo por el descenso en las de causa traumática.

Las lesiones medulares traumáticas son las más homogéneas y de las que más información epidemiológica disponemos. Dicha información ha sido recogida ampliamente en los EE.UU. desde el inicio de los años 1970 cuando se iniciaron los programas del “model SCI care system”. Actualmente esta base de datos es conocida como el “National Spinal

Cord Injury Statistical Center (NSCISC)", y de ella se obtienen los datos epidemiológicos más amplios en la lesión medular traumática[3]. De esta manera podemos decir que en los EE.UU. la lesión medular traumática tiene una incidencia aproximada de 40 casos anuales por millón de habitantes, lo que equivale a unos 12.000 casos nuevos por año; con una prevalencia de aproximadamente 270.000 personas. En cuanto a la edad, desde el 2005, la edad media en el momento de la lesión es de 41 años, edad que ha aumentado si la comparamos con los 28,7 años de media que existía en los años 70. El 80,6% de las lesiones medulares ocurre en hombres, y este porcentaje se ha mantenido estable durante años. En cuanto a la etiología, los accidentes de vehículos de motor son la causa más frecuente con un 39,2%, seguido de las caidas con un 28,3%, los actos de violencia (sobre todo por armas de fuego) con un 14,6%, y los deportes con un 8,2%.

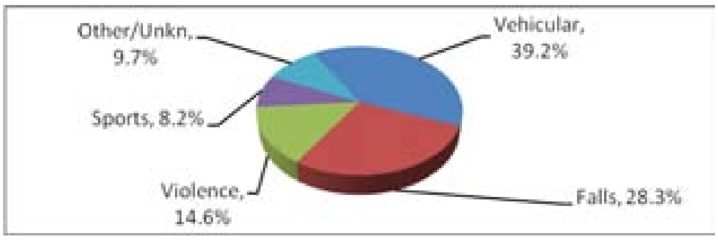

Figura 1: Causas de lesión medular traumática en los EEUU desde el 2005

La incidencia de lesión medular de origen traumático en el resto del mundo y en especial en Europa es inferior, y no excede, en muchos casos, de los 20 nuevos casos por millón de habitantes. Seguramente estas diferencias hay que buscarlas en el alto porcentaje de lesionados medulares por actos violentos que existen en los EE.UU., situación mucho menos frecuente en los países europeos. Globalmente la edad media en el momento de la lesión está aumentando en concordancia con el aumento de la edad de la población en riesgo. Asimismo también se corrobora que las lesiones debidas a las caidas están en aumento[4].

En España la epidemiología de la lesión medular traumatica ha sido recientemente analizada[5], obteniendose una tasa de incidencia de 24,0 casos por millón de habitantes, siendo los accidentes de tráfico la causa mayoritaria con un 36,6%. Globalmente, la tasa de incidencia de lesión medular traumática muestra una tendencia significativa a la reducción de un -1,6% anual, debida principalmente a la reducción de la incidencia de lesión medular por accidentes de tráfico, que muestra una reducción anual de -3,5%.

Las lesiones medulares no traumáticas constituyen un heterogéneo grupo que incluye causas tan diversas como la estenosis del canal medular, los tumores, las causas vasculares (isquemia o hemorragia), las infecciones y la mielitis. De estos grupos la estenosis del canal medular con un porcentaje aproximado del 21% y los tumores con un 10% son las dos causas más frecuentes[2]. La población afectada es generalmente de mayor edad (edad media de 61,2 años) y afecta a hombres y mujeres por igual[2,6].

Clasificación

La lesiones medulares se clasifican por convenio internacional según su nivel neurológico y severidad[7]. La ultima revisión de esta clasificación se realizó en el 2011.

El *nivel neurológico* de lesión se refiere al segmento más caudal de la médula espinal con sensibilidad intacta y con fuerza muscular anti gravitatoria, siempre que sean normales las funciones sensitiva y motora rostrales. Cuando la lesión se localiza a nivel cervical, utilizamos el termino *tetraplejia*, y estaran afectadas las extremidades superiores, tronco, extremidades inferiores y esfinteres. Si la lesión se localiza a nivel dorsal, lumbar o sacro, utilizaremos el termino *paraplejia*, y en este caso las extremidades superiores estaran preservadas, y dependiendo del nivel, se veran afectadas el tronco, extremidades inferiores y esfinteres.

La *severidad* de la lesión medular se clasifica según la escala de deficiencia de la asociación americana de la lesión medular, *ASIA Impairment Scale (AIS)*. El termino ASIA (asociación americana de la lesión medular), ha sido ampliamente utilizado para clasificar la lesión medular, pero recientemente ha sido sustituido por el termino AIS, que incluye en su nomenclatura el anterior. Dado el amplio uso hasta ahora del termino ASIA, en los articulos presentados y a lo largo de esta tesis se utilizará dicho termino para referirnos a la severidad de la lesión medular.

En terminos generales, las lesiones son clasificadas neurológicamente como *completas* o *incompletas* basándose en la definición de preservación sacra. La *Preservación Sacra* se refiere a la presencia de función sensitiva o motora en el segmento sacro más caudal determinado por la exploración. La preservación sensitiva incluye sensibilidad preservada (intacta o dañada) en la unión mucocutánea anal (dermatoma S4-5) en uno o ambos lados para la sensibilidad táctil o dolorosa, o en la presión anal profunda durante el tacto rectal. La preservación motora incluye la presencia de contracción voluntaria del esfínter anal externo detectada durante el tacto rectal. De esta forma utilizamos el termino *lesión completa* cuando hay una ausencia de preservacion sacra, mientras que la lesión será *incompleta* cuando exista preservación sacra (sensitiva y/o motora).

Para valorar la severidad utilizaremos la siguiente nomenclatura:

ASIA A=Completa. No hay función sensitiva o motora preservada en los segmentos sacros S4-S5.

ASIA B=Incompleta sensitiva. La función sensitiva pero no la motora se encuentra preservada por debajo del nivel neurológico e incluye los segmentos sacros S4-S5.

ASIA C=Incompleta motora. La función motora está preservada por debajo del nivel neurológico**, y más de la mitad de los músculos clave por debajo del nivel neurológico de lesión tienen una puntuación motora menor de 3.

ASIA D=Incompleta motora. La función motora está preservada por debajo del nivel neurológico**, y la mitad o más de los músculos clave por debajo del nivel neurológico de lesión tienen una puntuación motora mayor de 3.

ASIA E=Normal. Si las funciones sensitiva y motora exploradas son valoradas como normales en todos los segmentos, y el paciente tenía déficits previos, entonces el grado es E. Alguien sin lesión medular no recibe graduación AIS.

**Para que un individuo reciba un grado C o D, es decir, tener una lesión incompleta motora, debe tener o bien contracción voluntaria del esfínter anal o bien preservación sensitiva sacra (en S4/5 o en el tacto rectal) con preservación de la función motora más de tres niveles por debajo del nivel motor para ese lado del cuerpo. Los estándares en este momento permiten que la presencia de función motora en músculos no-clave a más de 3 niveles por debajo del nivel motor puedan ser usados para determinar el grado motor incompleto (AIS B vs C).

Capacidad de marcha y rehabilitación

Las lesiones medulares presentan, como una de las consecuencias principales, la pérdida completa o parcial de la movilidad voluntaria distal a la lesión que condiciona una dificultad o pérdida de la capacidad de marcha. La recuperación de la capacidad de deambulación constituye uno de los hitos más importantes en el proceso rehabilitador, y uno de los factores con mayor repercusión para la reinserción social y laboral del paciente.

La proporción de lesiones incompletas ha aumentado en los últimos años, probablemente debido a un mayor énfasis en la prevención y los avances en el tratamiento, de manera que actualmente el 62.2% de los lesionados medulares sólo sufren una lesión incompleta[3], y por lo tanto tienen el potencial de alcanzar una marcha independiente o con ayudas técnicas.

La fisiología de la marcha ha sido estudiada en profundidad, si bien todavía no se conocen todos los mecanismos implicados en su regulación. La marcha, en su inicio, es un ejercicio voluntario, que depende de la proyección de órdenes específicas desde el encéfalo hacia la médula espinal, ejerciendo una función de regulación sobre neuronas e interneuronas ubicadas en la médula espinal. Se postula que estas neuronas e interneuronas de la médula espinal se organizan formando un generador de patrones centrales de la marcha (CPG), ubicado en la región lumbar de la médula espinal, basado en la integración de información sensorial y motora[8,9,10]. De este modo, el CPG se vería modulado por: 1) retroalimentación periférica de los receptores musculares, tendinosos y cutáneos, 2) circuitos espinales locales, 3) vías descendentes.

Figura 2: Centro generador de la marcha.

Debemos entender la plasticidad como una propiedad intrínseca del sistema nervioso en condiciones normales y presente también en condiciones patológicas. Los cambios que se producen están guiados por la interacción entre el sujeto y el entorno, así como por el sustrato neurológico que regula esta interacción. Esta reorganización, y el cambio funcional consiguiente, se va a producir con o sin la participación del terapeuta. Por lo tanto, la intervención médica es necesaria para guiar de manera controlada la capacidad intrínseca del sistema y optimizar los resultados funcionales. La reorganización de los mecanismos espinales (entre los que se postulan los generadores de patrones centrales) permite la elaboración más eficaz de respuesta y en consecuencia la posible recuperación de la capacidad de la marcha para el sujeto. La capacidad de reorganización depende de la gravedad de la lesión, y de las aferencias que recibe la médula espinal. Si bien la lesión, hasta el momento, podemos considerarla como un invariable de cada paciente; sí podemos, sin embargo, modular las aferencias sensoriales de forma que permita una reorganización más eficaz[11].

La introducción de modernas técnicas de rehabilitación funcional como el Entrenamiento de la Marcha Asistida con Soporte Parcial del Peso Corporal (EMA-SPPC) tienen su fundamento en los estudios llevados a cabo por Brown al inicio del siglo XX[12]. Brown observó, tras seccionar la médula espinal en gatos, cómo los animales continuaban generando patrones rítmicos de marcha, si recibían un estímulo adecuado, por ejemplo, la estimulación sensorial que recogían sus extremidades puestas sobre un tapiz rodante.

En 1989, el grupo del profesor Barbeau en la Universidad de McGill de Canadá publicó las primeras experiencias sobre el efecto de la eliminación parcial del peso corporal en la rehabilitación de la marcha, entrenada sobre un tapiz rodante, en una población de sujetos con hemiparesia[13]. Un año más tarde, el mismo grupo publicó resultados similares en un grupo de pacientes con lesión medular[14].

A. Wernig también describe la mejoría en la capacidad de marcha de pacientes con una lesion medular tras someterse a terapia intensiva mediante marcha desgravada en cinta sin fin[15]. Asimismo demuestra la eficacia de este tipo de entrenamiento frente a la terapia convencional[16], y la permanencia de estas ganancias a largo plazo[17].

Desde entonces un considerable número de estudios refuerzan la idea que la utilización del EMA-SPPC puede conseguir una notable mejoría funcional de sujetos con lesiones medulares incompletas, acelerando notablemente el proceso de recuperación[18].

Para evitar los inconvenientes del esfuerzo que precisa este tipo de entrenamiento de la marcha en cinta sin fin para los terapeutas, y optimizar el entrenamiento, aumentando el número y duración de las sesiones, se han desarrollado unos sistemas electromecánicos que ofrecen una asistencia controlada y programable en función de las necesidades del sujeto. En la actualidad existen varios tipos disponibles comercialmente. En este trabajo mostraremos los resultados obtenidos con la aplicación de dos de ellos. El sistema diseñado por el grupo del Berlin Klinic, *Gait Trainer GT I®*[19], y el diseñado por el grupo del Uniklinic Balgrist, *Lokomat®*[20].
El *Gait Trainer®* (figura 3) consiste en unas plataformas articuladas donde van sujetados los pies. Estas plataformas son puestas en movimiento por un sistema electromecánico con control de la velocidad y longitud del paso, de tal manera que reproducen un movimiento similar a la marcha fisiológica. El sujeto está suspendido por un arnés, pudiéndose modificar el peso suspendido.

Figura 3: Gait Trainer GT I Reha-Hesse ®.

El *Lokomat®* (figura 4) consiste en un tapiz rodante asociado a un arnés que mantiene al sujeto parcialmente suspendido, y un exoesqueleto desde la cadera hasta los pies, que de una forma mecánica y controlada moviliza las articulaciones de la cadera y rodillas del sujeto. El software del sistema permite en tiempo real la movilización y ajuste optimo de dichas articulaciones, logrando así un patrón de marcha semejante al fisiológico. La movilización de las articulaciones está sincronizada con la velocidad de la cinta rodante. Asimismo el sistema provee al sujeto retroalimentación visual, a tiempo real, que le permite corregir su patrón de marcha y motivación. El sistema permite recoger parametros del paciente como son la rigidez a la movilización de las extremidades inferiores, el balance articular y la fuerza con que desarrolla el sujeto un movimiento voluntario. Por otro lado el equipo incorpora varios dispositivos de seguridad para evitar cualquier incidente.

Figura 4: Lokomat, Hocoma ®

Heese y cols. publicaron el uso de su sistema electromecánico (Gait Trainer GT I) combinado con estimulación eléctrica funcional en un grupo de cuatro pacientes con lesiones medulares incompletas. Tras el entrenamiento, todos los sujetos demostraron una mejora en su capacidad de marcha[21]. Wirz y cols. realizaron un ensayo multicentrico utilizando el Lokomat® en pacientes con una lesion medular incompleta crónica demuestrando mejoras significativas en la velocidad de marcha y resistencia tras el entrenamiento[22]. Desde entonces existen algunos estudios con la utilización de estos sistemas, no obstante los resultados son variables y no concluyentes.

La utilización de sistemas electromecánicos se fundamenta en la movilización pasiva y la movilización asistida de las extremidades en rehabilitación, lo que es una práctica incuestionable. Aún cuando la utilización de sistemas electromecánicos no resultara más eficaz que la asistencia por parte del terapeuta, esta resulta más segura. El riesgo laboral al que se somete el terapeuta en esta terapia es considerablemente alto, por la postura que requiere y la fuerza que tiene que realizar y el número de horas que puede realizar el tratamiento es considerablemente menor.

Por todo ello, planteamos un estudio longitudinal prospectivo en pacientes con una lesión medular utilizando estos dos sistemas (Lokomat® o GaitTrainer GT I®) con una frecuencia y duración del entrenamiento determinadas. La respuesta al entrenamiento la valoramos utilizando escalas clínicas y funcionales ya establecidas que nos permiten objetivar las ganancias obtenidas. De esta manera podemos valorar que condiciones de la muestra (variables secundarias), se relacionan con una respuesta clínica más evidente, medida con distintas pruebas específicas para la evaluación de la marcha (variable principal).

Neurofisiología, modulación del reflejo H

Como otra herramienta de valoración de resultados utilizamos también técnicas neurofisiológicas.

Es conocida la importancia de la modulación de los reflejos para obtener un control motor adecuado. El acto de caminar implica un control preciso de los reflejos de las extremidades inferiores, que depende en parte de la actividad de los centros subcorticales. La lesión medular provoca una pérdida del control de dichos reflejos, por lo tanto la rehabilitación tras la lesión medular va en parte dirigida a la recuperación del control de estos reflejos.

El reflejo aquíleo y su representación electrofisiológica, el reflejo H, son respuestas de circuitos reflejos involucrados en el control de la marcha[23,24]. La amplitud de este reflejo H puede ser modulada en distintas condiciones, como pueden ser: los cambios posturales del cuerpo[25,26], caminar[27], la maniobra de Jendrassik[28], o estímulos auditivos[29]. La estimulación magnética transcraneal (EMT) también ha sido utilizada para estudiar la modulación del reflejo H, tanto en sujetos sanos como en pacientes[30,31]. La EMT induce dos fases de facilitación del reflejo H: una fase temprana, con un pico entre los 10 y los 20 ms, y una fase tardía, con un pico alrededor de los 80 ms; estas dos fases están separadas por un período sin efecto en los intervalos de 40 a 50 ms[30]. La modulación del reflejo H por la EMT también ha sido utilizada para demostrar la preservación de la función de la vía corticoespinal en pacientes con una lesión medular incompleta en los que no se obtenía un potencial evocado motor mediante la EMT de estímulo simple[32].

Por lo tanto planteamos la hipótesis de que si la modulación de los reflejos monosinápticos es uno de los factores requerido para un control adecuado de la marcha, el patrón de modulación del reflejo H por EMT en el lesionado medular, se acercará al patrón de normalidad con la mejora de la capacidad de marcha. Este cambio es esperable que ocurra durante el período de mejora de la marcha y en mayor medida en las fases más tempranas de la lesión. De tal manera estudiaremos el patrón de modulación del reflejo H inducido por EMT en dos grupos de paciente con una lesión medular incompleta motora: aquellos con una lesión medular de menos de 3 meses de evolución, y el otro grupo aquellos cuya lesión medular ocurrió entre los 3 meses y un año. Todos los pacientes participarán en el protocolo de entrenamiento de la marcha con ayuda de sistemas electromecánicos.

Estimulación magnética transcraneal

La EMT, fue introducida por Anthony Barker en 1985[33], de manera que por primera vez, de una forma no invasiva, segura e indolora, se podía activar el cortex motor humano y valorar la integridad de las vías motoras del sistema nervioso central. Desde su introducción, su uso en distintas especialidades como la neurofisiología, neurología, psiquiatría y neurociencia, se ha ido extendiendo ampliamente, sobre todo en investigación, pero con aplicaciones clínicas cada vez más evidentes[34,35,36,37].

La EMT además de como herramienta diagnostica puede ser utilizada de forma terapéutica en su modalidad repetitiva (EMTr). Cuando un tren de pulsos de EMT de la misma intensidad se aplica en un área cerebral concreta a una determinada frecuencia que puede variar entre un estímulo por segundo a 20 o más, esto se conoce como EMTr[37]. La EMTr puede modular la excitabilidad cortical, con un efecto que varía desde la inhibición a la facilitación dependiendo de la frecuencia de estimulación[38,39]. De esta manera, la EMTr de baja frecuencia, en el rango de 1 Hz, puede suprimir la excitabilidad cortical[40]; mientras que la EMTr de alta frecuencia, rango de 20 Hz, puede producir un incremento temporal de la excitabilidad cortical[41,42].

Además de la modulación de la excitabilidad cortical, la EMTr puede inducir cambios en las vías descendentes corticoespinales[43].

De esta forma podemos utilizar la EMTr para modificar de forma favorable la función del cortex motor. Además de los efectos inmediatos esperados, “on line”, un tren de estimulación puede inducir una modulación de la excitabilidad cortical, que puede perdurar más allá de la duración de la sesión de estimulación. Este enfoque “off line” de modulación de la actividad cortical, local y a lo largo de redes neurales funcionales, puede ser de gran utilidad para el estudio de relaciones cerebro-conducta, pero, además, ofrece la posibilidad de utilizar la EMT de forma terapéutica en enfermedades neurológicas y psiquiátricas[37]. El mecanismo de esta modulación de la excitabilidad cortical más allá de la duración del tren de EMTr todavía no es bien conocido, pero existen evidencias que sostienen su beneficio. La potenciación y depresión sináptica a largo plazo han sido consideradas como posible mecanismo para explicar el efecto de la estimulación de alta y baja frecuencia respectivamente. Estudios en animales sugieren que la modulación de neurotransmisores e inducción génica puede contribuir a los efectos moduladores a largo plazo[44,45]. En pacientes con una lesión medular incompleta se ha observado ausencia o reducción de la regulación descendente natural inhibitoria del córtex motor[46], de manera que una intervención a este nivel cortical podría facilitar una mejor regulación corticoespinal.

Esta modulación cortical a través de la EMTr puede ser utilizada para promover la recuperación de la función motora y de esta manera obtener mayores beneficios de los procesos rehabilitadores. Belci y colaboradores[47], utilizando EMTr de alta frecuencia aplicada en el cortex motor primario sobre el vertex durante cinco sesiones, en cuatro lesionados medulares con una lesión medular cervical crónica, obtienen una mejoría significativa en la escala motora y sensitiva de la escala ASIA, así como en el tiempo para completar el test "peg-board", que valora la funcionalidad de la extremidad superior. Estas mejorías se objetivaron al completar la última sesión y se mantuvieron a las 3 semanas de seguimiento.

De esta forma se plantea la hipótesis que el uso combinado de la rehabilitación de la marcha con EMTr de alta frecuencia en lesionados medulares incompletos, puede promover la recuperación motora de las extremidades inferiores y mejorar la capacidad de marcha del paciente.

PRESENTACION

La grave repercusión que en el sujeto con una lesión medular supone la pérdida parcial o total de su capacidad de marcha, y la aparición de nuevas tecnologías dirigidas a mejorar dicho proceso, motivaron el desarrollo de esta tesis doctoral, que ha sido elaborada como compendio de las siguientes publicaciones:

1. Entrenamiento de la marcha en sujetos con una lesión medular utilizando sistemas electromecánicos: efecto del tipo de sistema y las características del paciente.

Benito-Penalva J, Edwards DJ, Opisso E, Cortes M, Lopez-Blazquez R, Murillo N, Costa U, Tormos JM, Vidal-Samsó J, Valls-Solé J; European Multicenter Study about Human Spinal Cord Injury Study Group, Medina J. **Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics.** Arch Phys Med Rehabil. 2012; 93(3):404-12.

2. Modulación del reflejo H por estimulación magnética transcraneal en sujetos con una lesión medular tras el entrenamiento de la marcha con sistemas electromecánicos.

Benito Penalva J, Opisso E, Medina J, Corrons M, Kumru H, Vidal J, Valls-Solé J. **H reflex modulation by transcraneal magnetic stimulation in spinal cord injury subjects after gait training with electromechanical systems.** Spinal Cord. 2010; 48(5):400-6.

3. Efecto de la estimulación magnética transcraneal de alta frecuencia en las mejoras de la función motora y marcha en pacientes con una lesión medular incompleta.

Kumru H, Benito J, Murillo N, Valls-Solé J, Valles M, Lopez-Blazquez R, Costa U, Tormos JM, Pascual-Leone A, Vidal J. **Effects of high frequency repetitive transcranial magnetic stimulation on motor and gait improvement in incomplete spinal cord injury patients.** Neurorehabilitation and Neural Repair. 2013 Jun; 27(5):421-9.

OBJETIVOS

- Valorar la eficacia terapéutica de los sistemas Lokomat® y GaitTrainer GT I® en la rehabilitación de la marcha de los pacientes con una lesión medular.

- Determinar aquellas características de los pacientes que sugerirían un mayor efecto beneficioso de este tipo de entrenamiento de la marcha.

- Profundizar en los mecanismos neurofisiológicos subyacentes a la mejoría en la capacidad de marcha y evaluar si la modulación del reflejo H por estimulación magnética transcraneal puede tener un valor pronostico.

- Analizar la respuesta clínica de pacientes con una lesión medular utilizando el entrenamiento de la marcha junto a la estimulación magnética transcraneal repetitiva de alta frecuencia.

PUBLICACIONES

1. *Benito-Penalva J, Edwards DJ, Opisso E, Cortes M, Lopez-Blazquez R, Murillo N, Costa U, Tormos JM, Vidal-Samsó J, Valls-Solé J; European Multicenter Study about Human Spinal Cord Injury Study Group, Medina J.* **Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics.** Arch Phys Med Rehabil. 2012; 93(3):404-12.

2. *Benito Penalva J, Opisso E, Medina J, Corrons M, Kumru H, Vidal J, Valls-Solé J.* **H reflex modulation by transcraneal magnetic stimulation in spinal cord injury subjects after gait training with electromechanical systems.** Spinal Cord. 2010; 48(5):400-6.

3. *Kumru H, Benito J, Murillo N, Valls-Sole J, Valles M, Lopez-Blazquez R, Costa U, Tormos JM, Pascual-Leone A, Vidal J.* **Effects of high frequency repetitive transcranial magnetic stimulation on motor and gait improvement in incomplete spinal cord injury patients.** Neurorehabilitation and Neural Repair. 2013 Jun; 27(5):421-9.

PUBLICACION 1

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ORIGINAL ARTICLE

Gait Training in Human Spinal Cord Injury Using Electromechanical Systems: Effect of Device Type and Patient Characteristics

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ABSTRACT. Benito-Penalva J, Edwards DJ, Opisso E, Cortes M, Lopez-Blazquez R, Murillo N, Costa U, Tormos JM, Vidal-Samsó J, Valls-Solé J, European Multicenter Study about Human Spinal Cord Injury Study Group, Medina J. Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics. Arch Phys Med Rehabil 2012;93:404-12.

Objective: To report the clinical improvements in spinal cord injury (SCI) patients associated with intensive gait training using electromechanical systems according to patient characteristics.

Design: Prospective longitudinal study.

Setting: Inpatient SCI rehabilitation center.

Participants: Adults with SCI (n=130).

Intervention: Patients received locomotor training with 2 different electromechanical devices, 5 days per week for 8 weeks.

Main Outcome Measures: Lower-extremity motor score, Walking Index for Spinal Cord Injury, and 10-meter walking test data were collected at the baseline, midpoint, and end of the program. Patients were stratified according to the American Spinal Injury Association (ASIA) category, time since injury, and injury etiology. A subgroup of traumatic ASIA grade C and D patients were compared with data obtained from the European Multicenter Study about Human Spinal Cord Injury (EM-SCI).

Results: One hundred and five patients completed the program. Significant gains in lower-limb motor function and gait were observed for both types of electromechanical device systems, to a similar degree. The greatest rate of improvement was shown in the motor incomplete SCI patients, and for patients <6 months postinjury. The positive response associated with training was not affected by injury etiology, age, sex, or lesion level. The trajectory of improvement was significantly enhanced relative to patients receiving the conventional standard of care without electromechanical systems (EM-SCI).

Conclusions: The use of electromechanical systems for intensive gait training in SCI is associated with a marked improvement in lower-limb motor function and gait across a diverse range of patients and is most evident in motor incomplete patients, and for patients who begin the regimen early in the recovery process.

Key Words: Gait; Rehabilitation; Spinal cord injuries.

AFTER SPINAL CORD INJURY (SCI), the recovery of walking ability is 1 of the most important milestones in the rehabilitation process and 1 of the factors with the greatest impact on social and professional reintegration for the patient.[1] Patients with an incomplete SCI have the potential to regain some ambulatory function; hence, a significant effort in neurorehabilitation is dedicated to gait training. Intensive therapy is known to provide some benefit,[2,3] yet for the characteristics of patients that respond best, the optimal training paradigms and the way to best use emerging technology is presently unclear.[4,5] Based on animal models, a system for locomotor rehabilitation using a treadmill, body weight support, and manual assistance was developed in the late 1980s that was shown to improve walking ability of patients with SCI.[6,7] Importantly, this was more effective than conventional therapy, but did result in persistence of the improvement in the long term.[8] A considerable number of studies have reinforced the idea that the use of body weight–supported treadmill training (BWSTT) can improve the functional status of patients with incomplete SCI[9-13]; however, it may not be superior to overground training.[14]

Robotic BWSTT technologies have become commercially available[15,16] and are being integrated into many neurorehabilitation centers. These devices provide electromechanically assisted locomotion with a constant gait pattern, which is externally paced, and are controlled by the therapist. Robotic BWSTT provides some advantages compared with manual

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List of Abbreviations

ANOVA	analysis of variance
ASIA	American Spinal Injury Association
BWSTT	body weight–supported treadmill training
EM-SCI	European Multicenter Study about Human Spinal Cord Injury
LEMS	Lower Extremity Motor Score
SCI	spinal cord injury
10MWT	10-meter walk test
WISCII	Walking Index for Spinal Cord Injury II

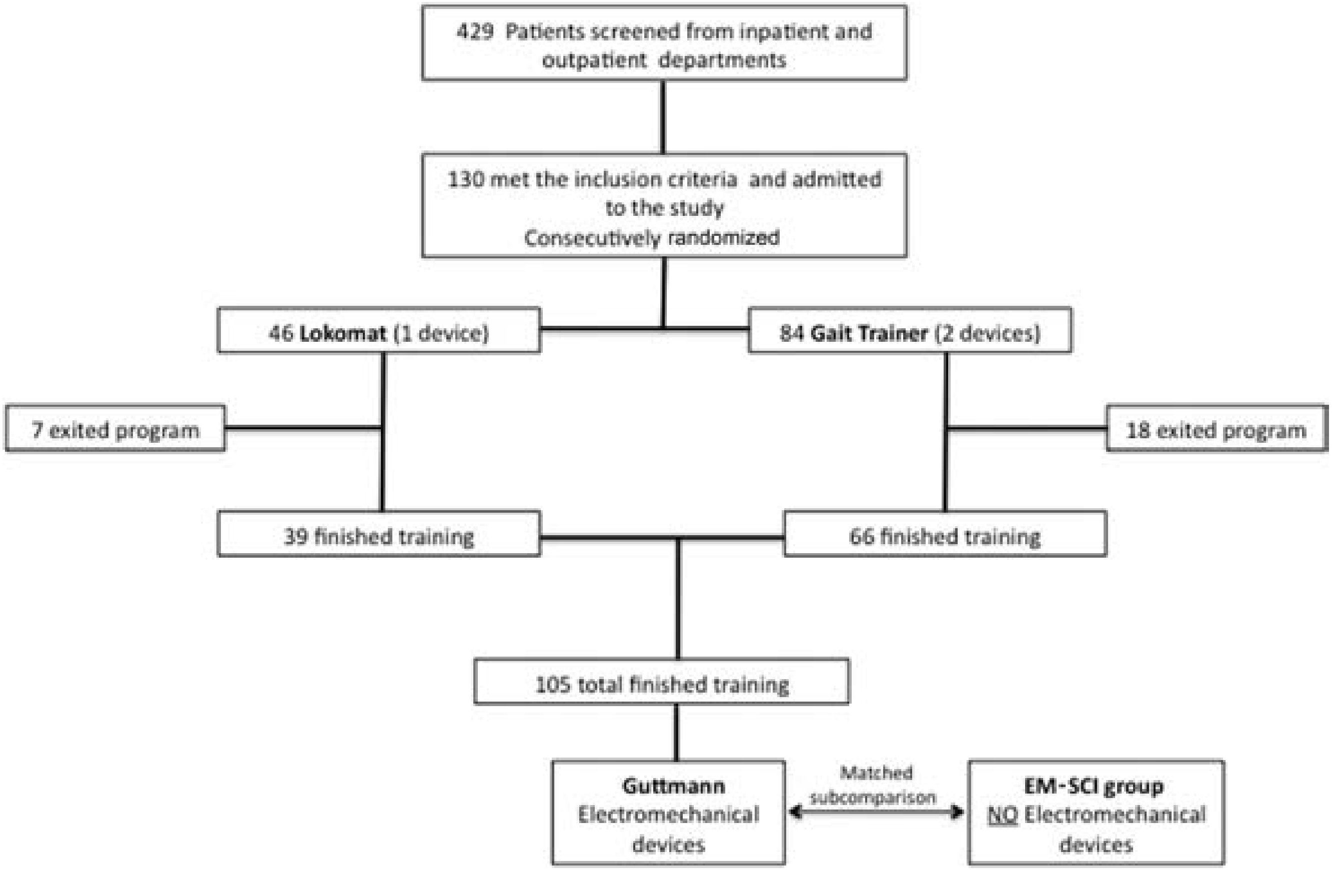

Fig 1. Consolidated Standards of Reporting Trials diagram of SCI patient recruitment and grouping. Eligible patients were consecutively assigned to receive gait training exclusively on 1 of 2 device types: the Gait Trainer (2 devices) or Lokomat (1 device). Of the patients that completed the full 8 weeks of daily training, comparisons were made in functional outcome according to device type, as well as patient characteristics. Patient outcomes were also expressed relative to the conventional standard of care without robotic gait training (EM-SCI database), with patients matched clinically.

BWSTT such as less manpower, longer training sessions, and higher intensity of training.[17]

Reports of improved function using these devices are predominantly in stroke patients,[18-22] and these findings may not necessarily transfer to SCI. Several small studies exist that attest their efficacy in SCI patients,[23,24] but the degree to which they might provide an advantage over other training methods is equivocal.[25] These studies support the safety of electromechanical systems as well as potential functional benefit; however, the evidence remains limited because of the small number of patients and the differences according to training dose and outcome measures. Furthermore, there remains a paucity of data regarding the characteristics of patients who might benefit.

We conducted possibly the first prospective longitudinal study in large patient numbers, to determine the clinical characteristics of patients with SCI that respond better to gait training, receiving the same frequency and duration of training, on 2 different electromechanical devices. The response to training was assessed using accepted clinical impairment and functional scales. We also aimed to determine if nonclinical patient characteristics of age and sex might influence the clinical outcome of the training paradigm. We hypothesized that patients would improve similarly on both types of electromechanical device, because the training dose was the same, but the clinical profile of patients would be an important determinant of outcome.

METHODS

A longitudinal training study was conducted in SCI patients at the Institut Guttmann Neurorehabilitation Hospital, Spain, over a 3-year period. Patients were screened for suitability on admission to the hospital, and randomly assigned (1:2 ratio) to the existing electromechanical devices: 1 Lokomat[a] and 2 Gait Trainer GT I systems[b] (fig 1). Patients trained daily (5d/wk) for 8 weeks using the electromechanical gait training device as a complement to other standard daily therapies. Motor performance change after the training period was compared between the 2 training systems and according to the clinical status at time of study enrollment.

Patient Demographics

Patients were screened for eligibility from the inpatient SCI unit at our hospital, and from the outpatient group, where patients attend daily for rehabilitation. SCI patients were classified according to the American Spinal Injury Association (ASIA) Impairment Scale.[26] We included motor incomplete SCI patients (ASIA grades C and D), and a selected motor complete SCI group (ASIA grades A and B). ASIA grades A and B patients were included when some voluntary movement was present at the segments L2 and L3 (hip flexion and knee extension). All patients were 18 years of age and older and able to tolerate the standing position without orthostasis.

Patients were excluded from the study using the following criteria: cardiorespiratory instability, pressure ulcers that interfered with the mechanical components of the gait devices, severe spasticity (Ashworth Scale ≥3), severe contractures in lower extremities, weight of more than 115kg. Patients gave written informed consent for the study, which was approved by the institutional review board.

Clinical and Functional Assessment

Study outcomes were collected at baseline (week 0), midpoint (week 4), and the end of the gait training program (endpoint, week 8).

Lower Extremity Motor Score. The standardized ASIA clinical exam includes the Lower Extremity Motor Score (LEMS), with 5 key muscles examined in each leg. The grading system for the muscle strength is 0 to 5 (0=absence of muscle contraction, 5=normative active movement with full range of motion against full resistance). The cumulative score for the lower extremities is between 0 and 50.

Walking Index for Spinal Cord Injury II Scale. The Walking Index for Spinal Cord Injury II (WISCI II) scale is an accepted, valid, and reliable clinical quantification of walking ability in SCI patients.[27,28] This scale (0–20) reflects level of walking depending on the use of devices, braces, and physical assistance to cover 10m. A score of 0 indicates that a patient cannot stand and walk, and the highest score of 20 is assigned if a patient can walk 10m without walking aids, braces, or assistance.

10-Meter walk test. The 10-meter walk test (10MWT) is a standardized functional assessment for gait speed.[29,30] This test measures the time (s) to walk 10m, with the most comfortable speed chosen by the patient. Patients were permitted to use braces, walking aids, or assistance.

Gait Training Program

The study participants received locomotor training exclusively on 1 of the systems for 8 weeks, in place of therapist-assisted gait training. If patients improved dramatically such that they reached the maximum score of 20 on the WISCI II scale by week 4 (midpoint assessment), they ceased the training at that time. Single training sessions started with a body-weight unloading of approximately 40%, and a velocity of approximately 1.5km/h, lasting approximately 20min. Sessions progressed to the lowest unloading possible, increasing velocity and duration as tolerated up to 45min. These rules were followed consistently for both training devices.

The patients additionally received the standard of care for therapy (except for over ground gait training) as part of the SCI rehabilitation at our institution in order to achieve the maximal functional status that their lesion allowed.

Expected Recovery With Conventional Therapy and Standard of Care: European Multicenter Study about Human Spinal Cord Injury Group

In order to compare expected recovery course (of Lokomat or Gait Trainer) with conventional therapies, we obtained data from the European Multicenter Study about Human Spinal Cord Injury (EM-SCI) group (with permission; www.emsci.org) that represents carefully documented information on motor recovery in a large number of SCI patients across multiple sites in Europe. Each of the hospitals within the EM-SCI group (including Institute Guttmann) ensures a minimum standard of rehabilitation care, creating some uniformity across sites. We selected data from 7 centers that were using therapist-assisted gait training techniques for traumatic SCI patients, not involving gait training with electromechanical devices.

The inclusion of multiple centers has the advantage of sampling diversity, that would represent current best practice in Europe, without bias for a particular intensity, frequency, or duration of therapy. Because the optimal therapy characteristics remain elusive, socioeconomic factors and clinical decision-making ultimately determine what therapy a given patient receives, when therapy is terminated, and the potential inclusion of outpatient therapy. We matched patients against the EM-SCI database by: (1) etiology–traumatic cause of injury; (2) clinical status as determined by an ASIA grade of C or D; and (3) the LEMS at 3-months postinjury. Following these criteria, a subgroup of 24 patients from Guttmann and 64 patients from the EM-SCI were selected.

Data Analysis

Individual patient data were included for analysis if patients completed the entire 8-week gait training program, or if patients reached the maximum score on the WISCI II scale by midpoint. To study the change between initial and final clinical outcome measurements (LEMS, WISCI, and 10MWT speed), the rate of change or slope of the line between initial and final time points (pre- and posttraining) was calculated [$(\text{Outcome}_{post} - \mathit{Outcome}_{pre})/(\text{time}_{post} - \mathit{time}_{pre})$]. This value represents the change of the clinical outcome with respect to the training time unit, and therefore is the increase of a unit of clinical outcome per month.[31,32]

In order to determine whether patients trained on the Lokomat or Gait Trainer GT I were of comparable demographic and initial clinical status, we used chi-square (categorical data) or unpaired *t* test (continuous data) analysis. To compare the clinical improvement between groups (Lokomat or Gait Trainer GT I), we used an unpaired *t* test on slope for the LEMS, WISCI, and 10MWT.

To analyze for clinical improvement in relation to patient characteristics, we conducted a multifactorial analysis of variance (ANOVA) on pooled data (all patients who completed the program), which simultaneously analyzed for a main effect of variables: age (≤50y, >50y), sex, ASIA grade, time since injury (<6mo, 6–12mo, >12mo), etiology, and their interactions on LEMS, WISCI, and 10MWT slope. Bonferroni post hoc tests were used for specific comparisons. We conducted secondary analyses to determine: (1) change in outcome (LEMS, WISCI, and 10MWT) from pretraining to posttraining raw data using a paired *t* test, and (2) difference in rate of improvement between the EM-SCI (conventional therapy) and Guttmann (electromechanical training) using the Student *t* test. Statistical analyses were performed using SPSS 16.0.[c] The significance level was set at $P<.05$. Group data are presented as mean ± SE unless otherwise stated.

RESULTS

The electromechanical gait training systems were well tolerated and there were no adverse effects reported. Of the 130 adult SCI patients who commenced the gait training program, 105 patients completed the program, including 4 patients that reached the maximum score on the WISCI II scale by midpoint (71 men, 34 women; mean age, 45y; range, 19–75y; Lokomat=39 patients, and Gait Trainer GT I=66, 33 on each of the GT I devices) (table 1). Twenty-five patients withdrew because of factors unrelated to the training program (early

Table 1: Characteristics of Study Participants

Patient	Total Sample (N=105)	Lokomat (n=39)	Gait Trainer (n=66)
Age (y)	45	45	45
Sex			
Men	71	26	45
Women	34	13	21
ASIA			
Grade A and B	11	5	6
Grade C	44	18	26
Grade D	50	16	34
Level of injury			
Tetraplegic	45	14	31
Paraplegic	60	25	35
Etiology			
Traumatic	53	21	32
Nontraumatic	52	18	34
Time since injury			
<6mo	81	29	52
6–12mo	8	3	5
>12mo	16	7	9

NOTE. No significant differences were found between groups (Lokomat and GT I) for any demographic or clinical variable.

discharge, transfer to other rehabilitation facility or hospital, or medical complications including pneumonia, sepsis, and pressure ulcers). The group of 105 that completed the program was comprised of 44 ASIA grade C patients, 50 ASIA grade D patients, and 11 ASIA grades A and B patients, with 45 tetraplegic and 60 paraplegic. Stratification according to injury etiology gave approximately equal numbers, with 53 traumatic and 52 nontraumatic. Patients were also grouped according to time since injury as: <6 months since injury (81 patients), between 6 and 12 months (8 patients), and more than 12-months postinjury (16 patients). A summary of patient characteristics stratified by electromechanical device is provided in table 1.

Electromechanical System and Clinical Outcome

For the 105 patients that completed the gait training program, all 3 clinical outcomes showed statistically significant improvement after the use of electromechanical systems (LEMS preintervention 22.07±1.08 points, postintervention 30.56±1.15 points, $P<.001$; WISCI preintervention 3.97±.49, postintervention 9.16±.68, $P<.001$; 10MWT preintervention .082±.01m/s, postintervention .26±.03m/s, $P<.001$) (fig 2). The baseline functional level of patients assigned to the Lokomat and Gait Trainer GT I groups was not significantly different for each of the 3 outcomes (LEMS: Lokomat=22.49±1.79, Gait Trainer=21.82±1.37, $P=.767$; WISCI: Lokomat=3.74±.85, Gait Trainer=4.11±.61, $P=.723$; 10MWT: Lokomat=.063±.018, Gait Trainer=.094±.020, $P=.309$). The rate of clinical change across the intensive gait training period was not significantly different between Lokomat or Gait Trainer GT I groups, for any of the 3 outcomes ($P=.162$, $P=.866$, and $P=.940$ for LEMS, WISCI, and 10MWT, respectively) (fig 3). All results according to device type and patient characteristics are displayed in table 2.

Patient Characteristics and Clinical Outcome

The multifactorial ANOVA on LEMS, WISCI, and 10MWT data (slope) revealed significant main effects for ASIA grade (F=5.571, $P=.005$; F=8.269, $P<.001$; F=5.656, $P=.005$, respectively) and time since injury (F=11.008, $P<.001$; F=14.866, $P<.001$; F=6.704, $P=.002$, respectively). There were no other significant main or interaction effects.

ASIA classification and clinical outcome. For the LEMS outcome, the ASIA grade C group had a significantly greater slope (5.37±.83) compared with the ASIA grades A and B group (2.00±.57, $P=.012$). The ASIA grade C group also obtained higher slope if compared with the ASIA grade D group (3.54±.59, $P=.064$); however, the comparison was not significant. The comparison between the ASIA grade D and ASIA grades A and B groups was also not significant ($P=.383$).

For the WISCI outcome, the ASIA grade D group showed the highest slope (3.64±.48) compared with the ASIA grades A and B (1.41±.49, $P=.022$) and ASIA grade C groups (1.39±.39, $P=.002$). The difference in slope between the ASIA grades A and B and ASIA grade C groups was not significant ($P=1.000$).

For the 10MWT outcome, the ASIA grade D group showed the highest slope (.120±.021) compared with the patient groups with ASIA grade C and ASIA grades A and B (.057±0.023, $P=.006$ and .070±.033, $P=.358$, respectively). The difference of slope between ASIA grades A and B and ASIA grade C groups was not significant ($P=1.000$) (fig 4).

Time since injury and clinical outcome. For the LEMS outcome, the early (0–6mo) group slope (5.06±.43) was significantly higher than the more than 12 month group (.88±.34, $P<.001$). In addition, the 6 to 12 month group slope (2.81±.87) was steeper than both the 0 to 6 month group ($P=.235$) and the more than 12 month group ($P=.574$).

For the WISCI, the <6 month group (3.25±.30) showed a significantly higher slope when compared with both the 6 to 12 month group (.69±.35, $P=.010$) and the more than 12 month group (.25±.19, $P<.001$). The difference of slope between the 6 to 12 month and more than 12 months groups was not significant ($P=1.000$).

For the 10MWT, the 0 to 6 month group (.114±.149) also showed a significantly higher slope when compared with both the 6 to 12 month (.005±.003, $P=.037$) and more than 12

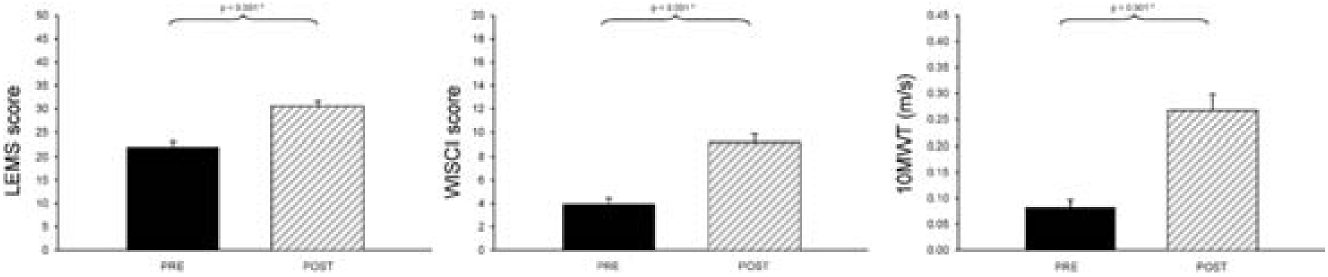

Fig 2. Group mean data showing a significant improvement in function for each of the 3 outcome measures (LEMS, WISCI, and 10MWT) after the 8 weeks of gait training.

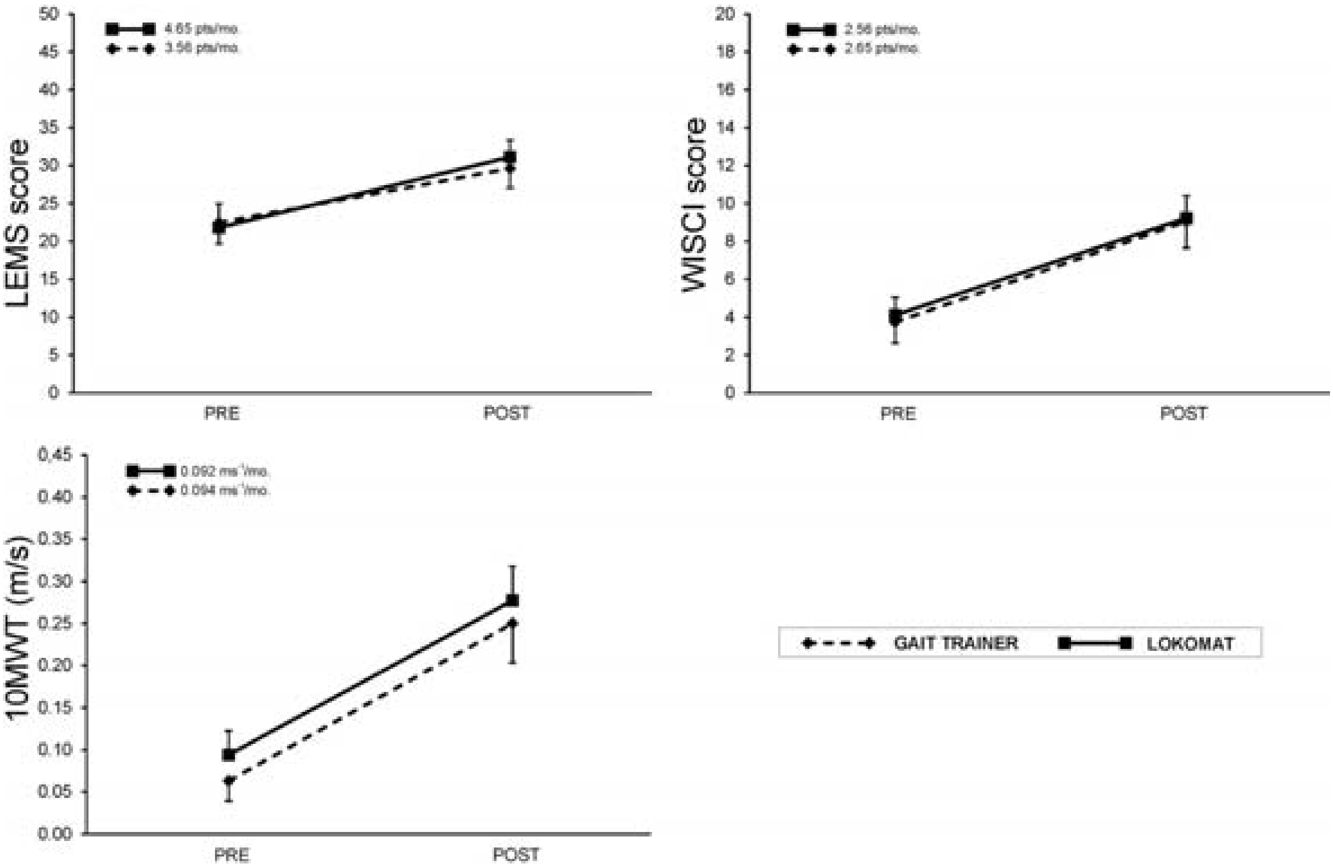

Fig 3. Comparison of electromechanical gait devices for rate of improvement across patients. The improvement trajectory was comparable for the Lokomat and Gait Trainer GT I devices for each of the 3 outcomes. Abbreviation: pts, points.

month groups (.027±.012, $P=.021$). The difference of slope between the 6 to 12 month and more than12 months groups was not significant ($P=1.000$) (fig 5).

Injury etiology, level of injury, age, sex, and clinical outcome. The ANOVA for the 3 outcomes (LEMS, WISCI, and 10MWT) revealed no significant main and interaction effects among etiology, level of injury, age, or sex.

Intensive Training With Electromechanical Systems Versus Conventional Standard of Care

We compared the data from our training protocol using electromechanical device systems with the EM-SCI database showing the expected trajectory with conventional standard of care. For the LEMS, both ASIA grade C and D patients receiving electromechanical device system gait training had a significantly greater rate of change in motor function when compared with matched patients from the EM-SCI group ($P<.001$ and $P<.001$, respectively) (fig 6). A significant improvement relative to the EM-SCI data was also present for ASIA grade D patients in the WISCI and 10MWT ($P=.002$ and $P=.016$, respectively), as well as a similar although nonsignificant trend in ASIA grade C patients (see fig 6).

DISCUSSION

We report significant clinical gains in motor function for SCI patients across an 8-week intensive gait training period using electromechanical systems, without dominance of the electromechanical system used. The trajectory of improvement was significantly enhanced relative to patients receiving conventional standard of care (EM-SCI group). Patient characteristics of time since injury and ASIA grade were important distinguishing factors for the degree of clinical improvement. Patients that started the rehabilitation program early after the injury and patients with motor incomplete lesions showed the greatest rate of improvement. The positive response associated with training was not affected by age, sex, lesion level, or cause of injury. Gait training using electromechanical systems can be safely implemented as a tool for routine gait therapy in neurorehabilitation settings, and is associated with substantially improved gait function in early SCI patients.

Electromechanical System

Because the electromechanical systems reported in the present study have a different design, it was not our intention to control for specifics of how the machine interacts with the patient, but rather to report on how patients respond to the same broad exposure. Both the Lokomat and Gait Trainer GT I use a body weight–support system, but the legs are mobilized in a different manner. The Lokomat uses an orthosis with electrical drives (actuators) in the knee and hip joints and a treadmill, while the Gait Trainer GT I uses 2 motorized footplates to achieve the leg movements. In the present study we found no differences between systems in the outcomes of gait training. When used, as reported in this article, both systems seem to be an adequate and safe tool to enhance the potential for walking in SCI patients.

Table 2: Summary of Patient Results

Patient Categories	n	LEMS Initial	LEMS Final	LEMS Slope	WISCI II Initial	WISCI II Final	WISCI II Slope	10MWT Speed (m/s) Initial	10MWT Speed (m/s) Final	10MWT Speed (m/s) Slope
Electro-mechanical device										
Gait Trainer	66	21.82±1.37	31.12±1.45	4.65±0.48	4.11±0.61	9.23±0.86	2.56±0.33	0.094±0.207	0.277±0.041	0.092±0.016
Lokomat	39	22.49±1.79	29.62±1.91	3.56±0.58	3.74±0.85	9.05±1.13	2.65±0.45	0.063±0.018	0.250±0.047	0.094±0.019
ASIA										
Grade A and B	11	14.55±3.21	18.55±2.94	2.00±0.57	3.64±1.20	6.45±1.76	1.41±0.49	0.067±0.029	0.207±0.089	0.070±0.033
Grade C	44	15.41±1.13	26.18±1.71	5.37±0.83	2.50±0.59	6.20±0.97	1.39±0.39	0.033±0.011	0.143±0.038	0.057±0.023
Grade D	50	29.58±1.26	37.06±1.18	3.54±0.59	5.34±0.81	12.36±0.90	3.64±0.48	0.129±0.027	0.390±0.046	0.120±0.021
Time since injury										
<6mo	81	22.78±1.30	32.89±1.27	5.06±0.43	3.44±0.50	9.94±0.78	3.25±0.30	0.083±0.018	0.311±0.037	0.114±0.149
6–12mo	8	22.25±2.08	27.88±3.26	2.81±0.87	4.00±1.61	5.38±1.88	0.69±0.35	0.041±0.023	0.051±0.025	0.005±0.003
>12mo	16	18.38±2.36	20.13±2.25	0.88±0.34	6.63±1.77	7.13±1.69	0.25±0.19	0.097±0.034	0.151±0.049	0.027±0.012
Etiology										
Traumatic	53	20.30±1.52	27.66±1.62	3.68±0.47	4.09±0.70	8.68±0.91	2.29±0.33	0.071±0.016	0.252±0.023	0.091±0.016
Nontraumatic	52	23.87±1.52	33.52±1.55	4.83±0.58	3.85±0.69	9.65±1.03	2.90±0.41	0.094±0.250	0.282±0.045	0.094±0.019
Level of injury										
Tetraplegic	45	25.87±1.76	34.22±1.59	4.18±0.55	4.40±0.86	9.69±1.13	2.64±0.38	0.107±0.028	0.303±0.049	0.098±0.018
Paraplegic	60	19.22±1.26	27.82±1.54	4.30±0.51	3.65±0.57	8.77±0.85	2.56±0.37	0.063±0.014	0.240±0.039	0.088±0.016
Age										
≤50y	65	22.09±1.41	30.45±1.47	4.17±0.50	5.05±0.65	10.43±0.85	2.69±0.34	0.115±0.022	0.304±0.040	0.095±0.016
>50y	40	22.02±1.72	30.75±1.88	4.36±0.55	2.22±0.66	7.10±1.10	2.43±0.43	0.029±0.013	0.206±0.047	0.089±0.020
Sex										
Men	71	23.11±1.34	31.46±1.43	4.17±0.43	3.79±0.58	9.28±0.83	2.75±0.33	0.089±0.019	0.285±0.037	0.098±0.015
Women	34	19.88±1.81	28.68±1.90	4.39±0.74	4.35±0.93	8.91±1.23	2.28±0.45	0.068±0.022	0.229±0.054	0.081±0.021
Guttmann EM-SCI (ASIA grades C and D)										
Guttmann ASIA grade C	14	12.29±1.77	25.07±2.70	6.39±1.09	1.43±0.59	5.93±1.61	2.25±0.67	0.022±0.013	0.164±0.075	0.071±0.036
EM-SCI ASIA grade C	21	14.69±0.61	21.33±1.36	2.44±0.40	2.83±1.05	7.50±1.15	1.53±0.41	0.046±0.022	0.149±0.034	0.035±0.009
Guttmann grade ASIA D	9	31.56±1.69	40.89±1.38	4.67±1.03	4.89±1.76	13.33±1.62	4.22±0.72	0.071±0.034	0.381±0.089	0.167±0.036
EM-SCI ASIA grade D	43	32.42±0.42	37.05±0.81	1.38±0.25	6.60±0.89	12.15±1.06	1.95±0.28	0.296±0.056	0.504±0.066	0.070±0.016

NOTE. Summary of group data expressed for each patient category and outcome (mean ± SE). Slope refers to the outcome measure rate of change in points-per-month (LEMS, WISCI) or m/s-per-month (10MWT). Time since injury refers to the time at which patients commenced the gait training program, relative to their injury. The EM-SCI group comparison included patients matched by clinical characteristics (motor incomplete, traumatic etiology, approximately 3mo since injury).

ASIA Grade

Modulation of muscle activity during BWSTT in individuals with complete SCI lesions (ASIA grades A and B) has been previously reported in the literature,[33,34] although no evidence for functional ambulatory gains has been found. Because hip flexion and knee extension activity are critical for effective gait,[35] we included ASIA grades A and B patients that had some voluntary motor function at segments L2 and L3. After training, the improvement found in the LEMS was only due to an increase of muscle power in those muscles that already presented some voluntary control. In addition to the LEMS gain, an improvement in the WISCI and 10MWT was found indicating that electromechanical gait training may be useful for these selected ASIA grades A and B patients.

Patients classified as motor incomplete (ASIA grades C/D) are known to have a better prognosis and greater change in

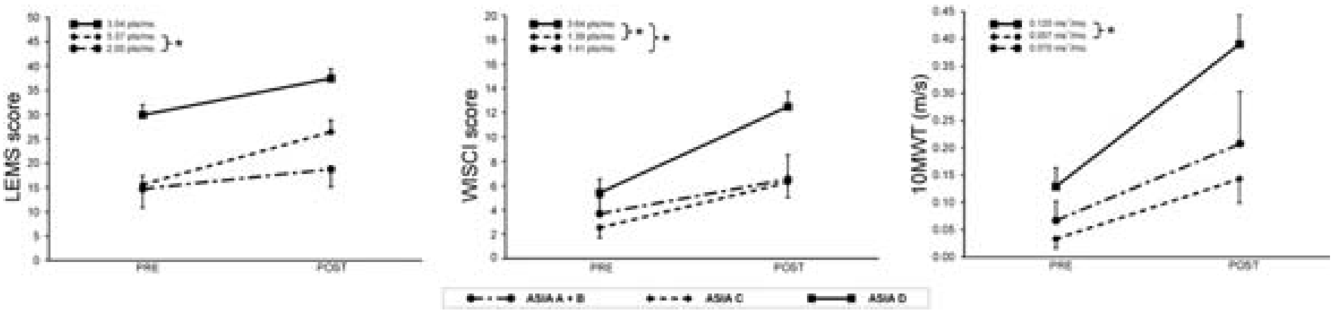

Fig 4. Rate of functional improvement according to ASIA grade from baseline to the endpoint of the training period (slope, group mean data). ASIA grade was a significant main effect for the 3 models: LEMS, WISCI, and 10MWT. Post hoc analysis revealed significant differences between ASIA grades A and B and C groups in LEMS; ASIA grades A and B and D groups, and ASIA grades C and D groups in WISCI; ASIA grades C and D groups in 10MWT. Abbreviation: pts, points.

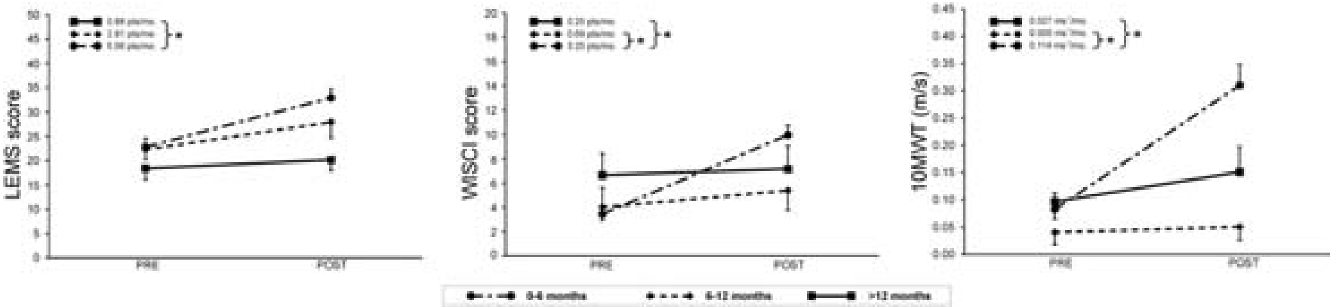

Fig 5. Group mean data for the condition time since injury from the baseline to the endpoint of the training period. Time since injury was a significant main effect for the 3 models: LEMS, WISCI, and 10MWT. *Post hoc analysis revealed significant differences between 0 to 6 months and more than 12 months groups in LEMS; and all groups (<6mo, 6–12mo, and >12mo) in both the WISCI and 10MWT. Abbreviation: pts, points.

motor and functional recovery.[36,37] The findings in the present study using clinical outcomes LEMS, WISCI, and 10MWT, also show greater motor and functional recovery in these patients. Furthermore, the ASIA grade D group showed greater gains in both the WISCI II scale and 10MWT compared with the ASIA grade C group. This may be related to a higher muscle power of the lower extremities that exists in the ASIA grade D group that could enable more effective training.

Time Since Injury

Gait function improved regardless of the time since injury; however, the greatest gains occurred if the training started earlier (<6mo postinjury). These results are consistent with the concept of a therapeutic window for rehabilitation of central nervous system lesions, because the largest gains are observable early after the injury.[38] According to this concept, interventions lose their effectiveness over time, although changes are possible long after initial injury. The practical implication is that gait training with these systems should be conducted early.[5]

Etiology of Injury

The cause of SCI can be broadly categorized as traumatic (eg, car or diving accident) or nontraumatic (eg, infection or tumor). Our findings show that outcomes are similar regardless of injury etiology, and this is consistent with recent literature.[39,40] Therefore, the etiology of the SCI should not interfere in the decision to include SCI patients in the gait training with electromechanical device systems.

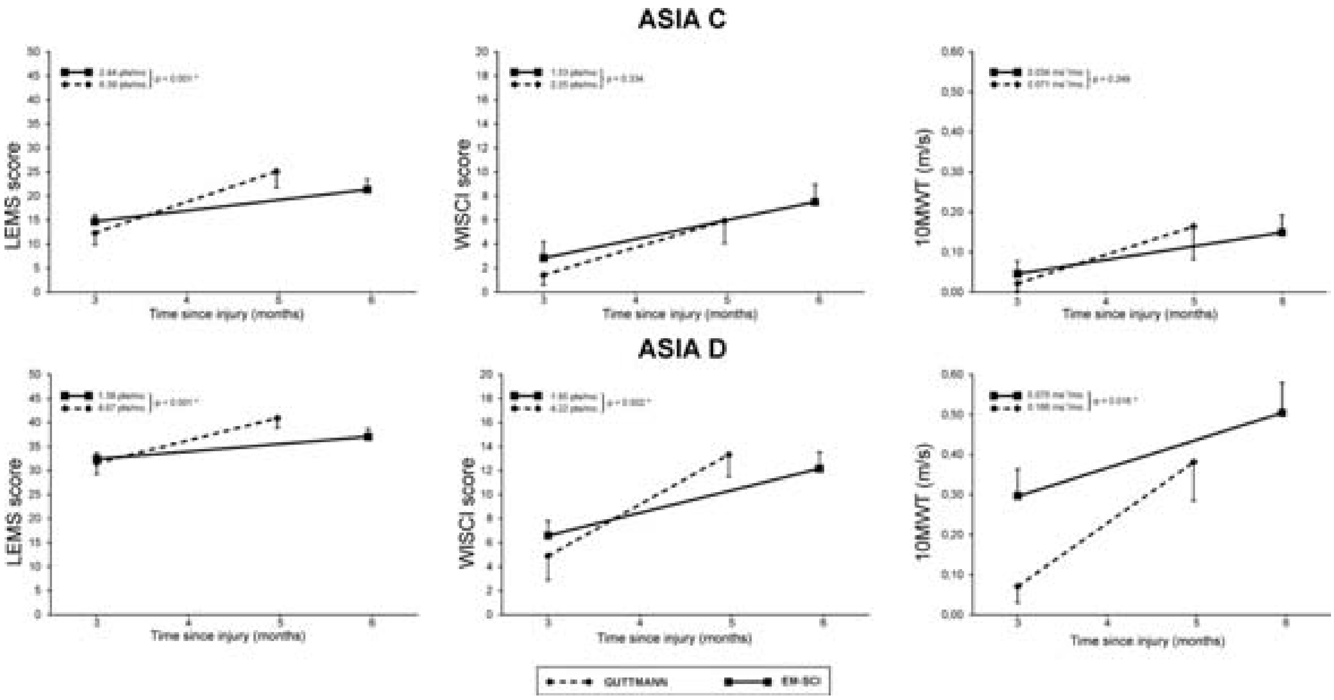

Fig 6. Patients with clinical characteristics matched to the EM-SCI database (nonrobotic training standard of care) are displayed for relative comparison of recovery trajectory (slope). For the LEMS, the trajectory was significantly enhanced in the group (both ASIA grades C and D) using electromechanical systems relative to patients that did not. This pattern was also observed for the WISCI and 10MWT, although was significantly different only for ASIA grade D patients. The use of electromechanical systems for gait training may provide a better rate of improvement than the current standard of care.

Level of Injury

Waters et al[41] studied the degree of recovery in SCI patients, according to whether they were classified as tetraplegic or paraplegic, and complete or incomplete. They reported that 46% of the patients with incomplete tetraplegia recovered strength to ambulate in the community; in contrast, 76% of incomplete paraplegic patients achieved community ambulation status. Our results did not find a better outcome in patients with incomplete paraplegia, supporting that both tetraplegic and paraplegic benefit from gait training.

Comparison With the EM-SCI Group

As with most studies of physical therapy efficacy early after neurologic lesion, changes relating to training are likely to occur on a background of spontaneous recovery. True training-related changes are difficult to discern from potential spontaneous recovery, because patients cannot be ethically denied treatment that is thought to be beneficial. The results of the present study need to be interpreted within this context.[42,43] We expressed our results relative to patients that received the conventional standard of care from specialized SCI rehabilitation centers in Europe (not using electromechanical systems) that are part of the EM-SCI study group. Patients from the EM-SCI group of hospitals did not serve as an experimental control in the present study for conventional gait training, but as a guide to expected outcome without using electromechanical systems. We selected from our patient group and the EM-SCI group, patients with incomplete motor SCI who were matched in clinical and demographic status. ASIA grade D patients using electromechanical devices for gait training showed a greater rate of recovery for the 3 outcome measures, while ASIA grade C patients improved significantly only in the neurologic motor recovery (LEMS). We can interpret within the limitations of this comparison against conventional therapy, that the gait training with electromechanical systems exceed the expected outcomes, making these systems an appealing option, especially for those rehabilitation centers that work with a large group of patients.

Study Limitations

This study did not intend to draw conclusions about the superiority of robotic gait training over conventional gait training. We have included a comparison of conventional therapy without robotics from selected centers of the EM-SCI group as a reference only. The ideal experimental control for this comparison would be a group of patients from our institution that received conventional gait training without using electromechanical devices.

CONCLUSIONS

We have shown data supporting the use of gait training with electromechanical systems for SCI patients in clinical practice, as an alternative to manual gait training as complement to conventional rehabilitation activities. These findings suggest the preferred use in patients with an incomplete motor lesion and that the onset of intervention should not be delayed.

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Suppliers

a. Hocoma AG, Industriestrasse 4, CH-8604 Volketswil, Switzerland.
b. Reha-Stim, Kastanienallee 32, 14050 Berlin, Germany.
c. SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, Il 60606.

PUBLICACION 2

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ORIGINAL ARTICLE

H reflex modulation by transcranial magnetic stimulation in spinal cord injury subjects after gait training with electromechanical systems

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Study design: Prospective longitudinal study.
Objectives: The aim of this study was to examine the effects of transcranial magnetic stimulation (TMS) on the soleus H reflex in patients with spinal cord injury (SCI) before and after locomotion training.
Setting: Neurorehabilitation hospital in Barcelona, Spain.
Methods: H reflex was elicited in 29 incomplete patients with SCI at 20, 50 and 80 ms after single vertex TMS, and compared with 13 healthy subjects. Patients were subdivided in two groups according to time since injury ($<$3 months, 3–12 months), and all received training with electromechanical systems. The H reflex modulation pattern to TMS was reassessed and the results were analyzed as a function of change in the patient clinical score.
Results: Healthy subjects showed a significant H reflex facilitation at 20 ms (186.1%) and at 80 ms (190.6%) compared with the control H reflex. In patients, the H reflex facilitation at 20 ms was significantly reduced before training (142.5%, $P=0.039$) compared with healthy subjects. After training, patients with $<$3 months exhibited an increase in H reflex facilitation at 20 ms (170.7%, $P=0.04$), a greater gait velocity ($P=0.014$) and a positive correlation with the walking index for spinal cord injury (WISCI II) scale ($P=0.050$), compared with those with $>$3 months.
Conclusions: TMS-induced H reflex modulation may help in the assessment of changes in the descending control of leg reflexes. Our results suggest that the changes on reflex modulation in patients with SCI occur within the first 3 months after injury.
Spinal Cord (2010) **48,** 400–406; doi:10.1038/sc.2009.151; published online 24 November 2009

Keywords: spinal cord injury; H reflex; transcranial magnetic stimulation

Introduction

The modulation of reflexes is an important aspect of motor control that implies timely and appropriate traveling of signals and commands in ascending and descending tracts of the spinal cord. Consequently, patients with spinal cord injury (SCI) have difficulties in the control of lower limb movements for performing purposeful acts such as walking.

Incomplete patients with SCI have the potential to regain some form of ambulatory function, predominantly at the early phase after injury.[1] On the basis of previous animal models, Barbeau *et al.*[2] described a system for locomotor rehabilitation using a treadmill, body weight support and manual assistance. This type of training has been considered as an effective method for improving the walking ability of patients with SCI.[3] To provide electromechanically assisted locomotion, new systems have appeared on the market, such as the Lokomat[4] and the Gait Trainer GT I[5] showing improvement in gait of patients with incomplete SCI.[6] However, there is lack of physiological measures correlating with such improvements.

The ankle jerk and its electrophysiological counterpart, the soleus H reflex,[7] are responses of reflex circuits functionally engaged in gait control. The size of the H reflex is modified by changes in body posture,[8] walking[9] and other maneuvers (for review, see Misiaszek[10]). When preceded by a transcranial magnetic stimulation (TMS), the H reflex may show an early inhibition,[11] and two facilitatory phases: an early phase peaking between 10 and 20 ms, and a late phase, peaking at about 80 ms.[11–13]

Such a modulation pattern may reflect the activity in functionally relevant spinal cord circuits and, therefore, it

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may be abnormal in people with SCI. Gait-related phasic modulation of the H reflex does not always show abnormalities in people with chronic SCI.[14] However, we expected that patients with SCI will present with an abnormal pattern of TMS-induced H reflex modulation that could be modified along with improvement in gait capabilities. If such change occurs, it is expected to be more prominent at early than at late phases of the recovery process after SCI. Therefore, we studied the pattern of TMS-induced modulation of the soleus H reflex in two groups of patients with incomplete motor SCI: patients with less than 3 months since injury and patients whose injury occurred between 3 months and 1 year.

Patients and methods

Subjects

We studied 29 patients with motor incomplete SCI (24 men and 5 women, mean age 47 years). Patients were divided in two groups. Group A included 16 patients with less than 3 months after injury (mean 1.84 months, s.e. 0.20). Group B included 13 patients whose injury occurred between 3 months and 1 year (mean 7.93 months, s.e. 2.55). Demographic and clinical data are shown in Table 1. Reference data were gathered from a group of 13 healthy volunteers, 10 men and 3 women, with a mean age of 32 years. Both control subjects and patients gave their informed consent for the study, which was approved by the institutional review board.

Clinical and functional assessment

Main outcome measures, collected at the beginning and end of the study, as follows: (1) lower extremities motor score (LEMS) obtained from the standardized American Spinal Injury Association (ASIA) clinical examination[15]; (2) walking index for spinal cord injury (WISCI II) scale[16] to quantify patient's walking ability; (3) ten-meter walking test (10MWT) for gait velocity assessment.

Table 1 Demographic patient data

	Group A ($\leqslant$*3 months*) n = *16*	*Group B* (> *3 months*) n = *13*
Age (mean years, s.e.)	48 (3)	46 (4.3)
Gender		
Male	14 (87.5%)	11 (84.6%)
Female	2 (12.5%)	2 (15.4%)
Lesion level		
Cervical	10 (62.5%)	7 (53.8%)
Thoracic	6 (37.5%)	6 (46.2%)
ASIA		
C	6 (37.5%)	7 (53.8%)
D	10 (62.5%)	6 (46.2%)
Etiology		
Traumatic	9 (56.3%)	9 (69.2%)
Nontraumatic	7 (43.8%)	4 (30.8%)
Electromechanical system		
Lokomat	6 (37.5%)	6 (46.2%)
Gait trainer	10 (62.5%)	7 (53.8%)

Abbreviations: ASIA, American Spinal Injury Association Impairment scale; C, motor incomplete lesion with >50% muscles distal to the lesion with a strength graded <3; D, motor incomplete lesion with >50% muscles distal to the lesion with a strength graded $\geqslant$3; s.e., standard error.

Gait training program

Patients used the Lokomat or the Gait Trainer GT 1 depending on the availability of the systems. The starting time of the training was determined by the time that patients spent at other hospitals before being transferred to our center. They received training on one of the systems daily, 5 days per week for 8 weeks. The sessions started with 20 min, progressing as tolerated up to 45 min.

H reflex recording and TMS stimulation

Subjects were sitting in the wheelchair, with their right foot resting on a footrest allowing for a stable knee position at an angle of 60°. H reflexes were evoked in the right soleus by electrical stimulation of the posterior tibial nerve. The stimulating electrodes were attached at the popliteal fossa, over the course of the nerve, with the cathode proximal. Stimulus duration was 1 ms. The intensity was adjusted to obtain an H reflex of about 1 mV amplitude with minimal or no concurrent M response. In all subjects, we made sure that this amplitude ranged between 10 and 15% of the M wave obtained with the same recording to supramaximal electrical stimulation. Whenever a small M wave was obtained concurrently with the H reflex, we checked if its size modified along the experiment. If this was the case, we excluded those trials from the analysis and repeated the test. The recording electrode was a bipolar surface electrode with a fixed distance of 2 cm between active and reference, firmly attached to the posterior leg, over the soleus muscle.

For TMS we used a Magstim Super Rapid stimulator (Magstim, Whitland, UK), equipped with a double cone coil, set up to deliver single pulses time-locked to the posterior tibial nerve stimulation. The coil was fixed with an elastic band over the head, in the best position for eliciting a stable motor-evoked potential (MEP) in soleus. In control subjects, we used an intensity of TMS 90% below threshold for the MEP in the soleus. In patients, we first tried to induce an MEP with up to maximum output intensity. Since no MEPs were obtained in any patient, we decided to set up the TMS at a fixed intensity of 10% above the mean threshold for control subjects. The same intensity was applied in both situations (before and after the gait training).

Procedure

All recordings were carried out with a Medelec Synergy electromyograph (Oxford Instruments, Surrey, UK), using a band-pass frequency filter between 20 and 5000 Hz, a gain of 1000 $\mu V\,cm^{-1}$ and a sweep duration of 500 ms. Recordings were digitized and stored for off-line analysis.

We first collected five H reflexes to single posterior tibial nerve stimuli, which were used as the control values. Then we applied the same stimuli preceded by TMS at 20, 50 or 80 ms interstimulus intervals (test trials). These intervals were chosen in view of their relevance for definition of the pattern of TMS modulation of the H reflex.[12,14] We collected five responses at each interval. The intertrial interval was at least 10 s to prevent carryover effects. Interstimuli intervals were randomly mixed. Also, a few control trials were intermingled with the test trials to control for possible baseline shifts in the amplitude of the control H reflex. If that was the case, we made slight adjustments to the stimulus intensity to keep the H reflex control at about 1 mV amplitude along the whole session.

The experiments were performed once in the group of healthy subjects, and before and after the gait training in the patients group (Figure 1). The fact that all patients were included in the gait training program prevented us to examine the effects of such intervention on eventual clinical and neurophysiological changes. However, we considered that a tendency to homogenous outcome would speak in favor of an effect of gait training, whereas differences between the two groups would suggest no relevant effect of gait training.

Data reduction and analysis

At baseline and at all intervals we measured the peak-to-peak amplitude of the H reflex with peak detection software (Matlab, Natick, MA, USA). In both, healthy subjects and people with an SCI, the mean value of the amplitude of the H reflex obtained in control trials was assigned 100%, and the amplitude of the H reflexes obtained from the study at the different intervals was expressed as its percentage value. The results are presented as means along with the standard error of the mean.

In this way, we obtained normalized data for group comparison, avoiding interindividual variability. One-way analysis of variance was used to determine the interval at which the H reflex amplitude was significantly different between control and test trials for each group. We also examined whether the effects of TMS on the H reflex were different in healthy subjects and patients at each interval tested. For this, we used the *t*-test to compare the H reflex amplitude change, expressed in percentage of the mean obtained in control trials, between healthy subjects and patients. Statistical significance was set at $P = 0.05$.

Results

All subjects tolerated well the study and completed the procedure. At baseline, patients had an abnormally reduced LEMS, WISCI and gait velocity. The two SCI groups were homogeneous in all clinical and functional variables before start of training (Table 1). No differences were present in the size of the supramaximal M wave or the size of the H reflex in control trials between healthy subjects and patients of the two groups.

H reflex modulation by TMS in patients before training compared with healthy subjects

In healthy subjects, TMS induced a significant H reflex facilitation at 20 ms (early phase, $186.1 \pm 17.8\%$) and at

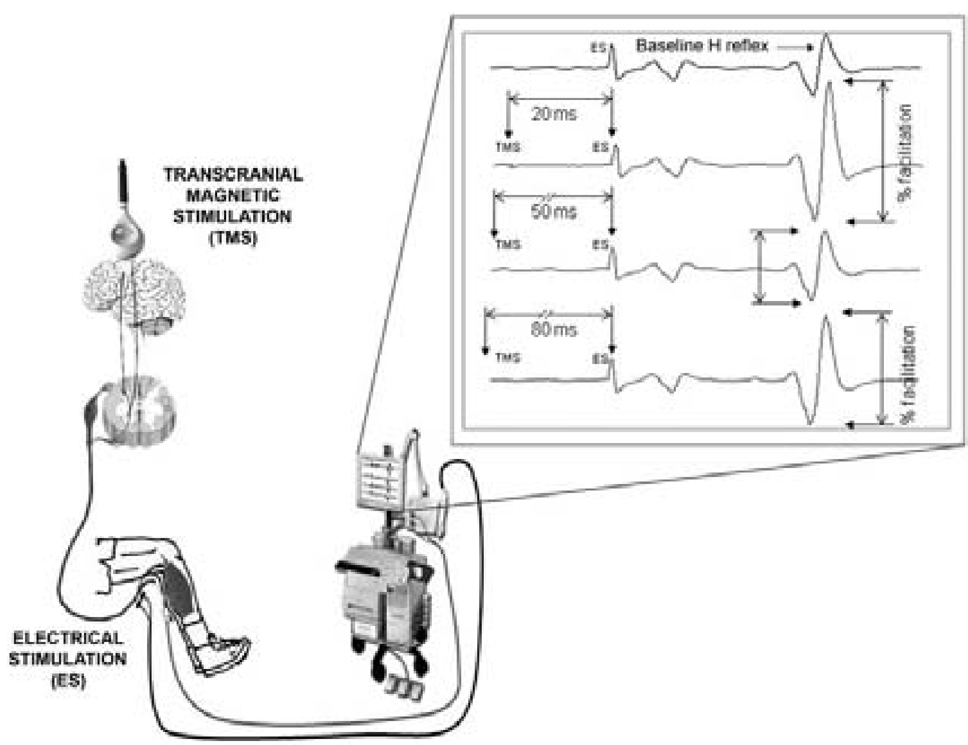

Figure 1 Experimental procedure. Baseline H reflex was obtained applying the electrical stimulation (ES) to the posterior tibial nerve. To induce a modulation of the H reflex, we used cortical transcranial magnetic stimulation (TMS). We studied the modulation of the H reflex when the ES was applied at 20, 50 and 80 ms after the TMS.

80 ms (late phase, 190.6 ± 15.1%), but not at 50 ms (135.9 ± 14.5%).

In patients with SCI, the H reflex was significantly larger when modulated by TMS at the three intervals than at baseline without TMS ($P<0.05$). However, such facilitation did not follow the pattern found in healthy subjects because of significantly reduced facilitation at the interval of 20 ms in the SCI group (142.5 ± 7.8%, $P=0.039$) with respect to healthy subjects. There was a reduced facilitation also at the interval of 80 ms (160.3 ± 10.8%) that was not significantly different from control subjects. Examples of the recordings are given in Figure 2 and the results of all subjects are represented in Figure 3.

Changes in the H reflex modulation by TMS in the two groups of SCI subjects before and after gait training

After training, there was a significantly greater facilitation of the H reflex at the early phase ($P=0.04$) on subjects of group A (170.7 ± 10.2%), compared with those of group B (125.3 ± 5.6%) (Figure 4). No significant modifications were observed in the effects of TMS at intervals of 50 and 80 ms.

Clinical and functional parameters (LEMS, WISCI II and 10MWT)

In general, all parameters improved after the gait training period (Figure 5). We found significant differences in the outcomes studied before and after training: LEMS ($P=0.003$, group A; $P=0.001$, group B), WISCI ($P=0.001$, group A; $P=0.008$, group B) and velocity ($P=0.002$, group A; $P=0.016$, group B). The percentage change in gait velocity after training was significantly greater in group A than in group B ($P=0.014$).

Correlation between clinical improvement and H reflex modulation by TMS

Because the early phase (20 ms) of H reflex modulation was the one showing a larger increase after gait training, we analyzed whether this change was correlated with improvement in clinical outcomes in the two groups of patients separately. There was a statistically significant positive correlation between the improvement in WISCI and early H reflex facilitation in patients of group A ($P=0.050$), whereas no other significant correlations were found (Figure 6).

Six patients had no change in the functional outcomes after the training but showed a slight increase in the H reflex facilitation (40.39 ± 14.4%).

ASIA, SCI etiology, electromechanical system and H reflex modulation by TMS

As to the type of incomplete motor SCI (ASIA C vs D), etiology of the SCI and type of electromechanical system used, we found no differences at any of the intervals studied before and after the gait training.

Discussion

Our results have furnished three relevant conclusions: (1) patients with incomplete motor SCI have an abnormal TMS-induced modulation of the soleus H reflex; (2) the H reflex facilitation at the interval of 20 ms increased in all patients, but the percentage increase was significantly larger in

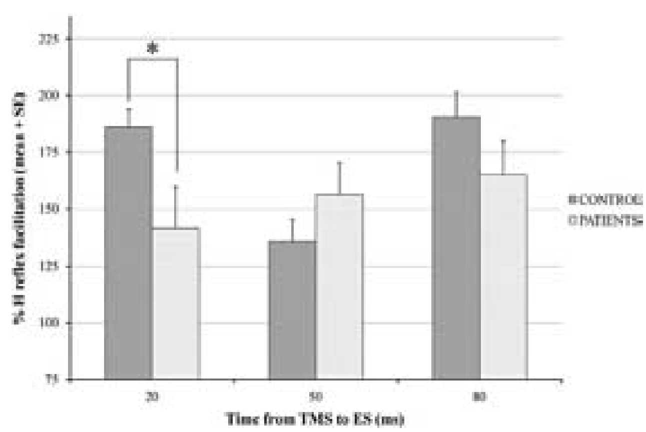

Figure 3 H reflex modulation by transcranial magnetic stimulation (TMS) before training in all groups of subjects. Both the control subjects and the patients exhibited significant facilitation of the H reflex with respect to baseline (100%) at all intervals tested except for the interval of 50 ms in control subjects. Facilitation at the interval of 20 ms was significantly reduced in the spinal cord injury group with respect to control subjects (asterisk).

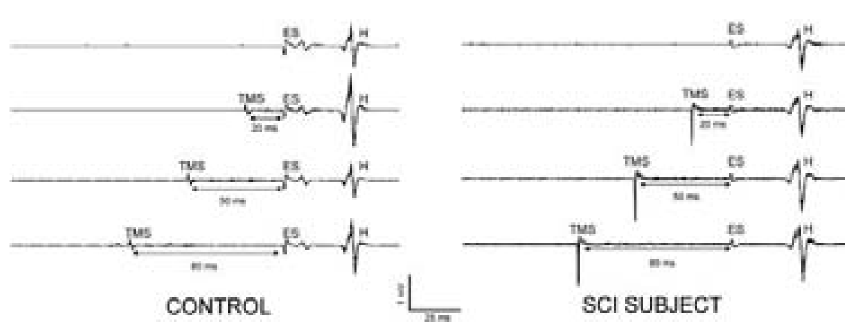

Figure 2 Example of H reflex modulation by transcranial magnetic stimulation (TMS). Once the H reflex was obtained, the combined TMS/electrical stimulation (ES) was applied at different intervals between each other obtaining a modulation of the H reflex. This modulation was different in controls compared with spinal cord injury (SCI) subjects, observing a greater H reflex facilitation in the control group at the early and late phases. Single sweeps are shown superimposed.

patients within 3 months than in patients with longer time after injury; (3) there was a good correlation between the increase of H reflex facilitation and the improvement in functional aspects after 8 weeks of training in the group with less than 3 months after injury.

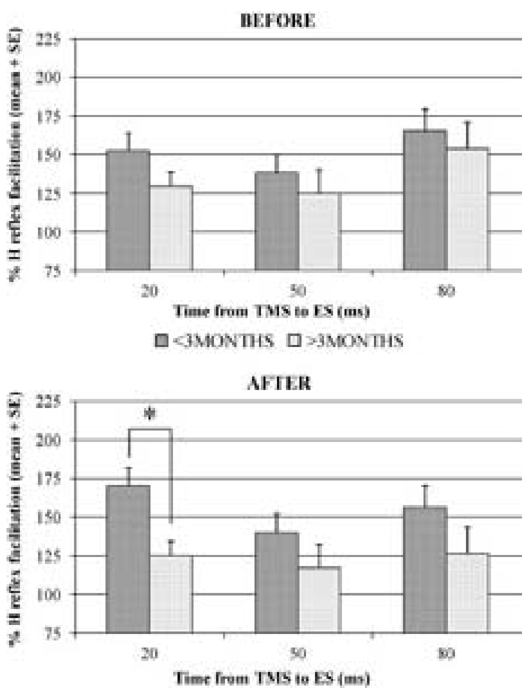

Figure 4 H reflex modulation by transcranial magnetic stimulation in spinal cord injury subjects before and after training. Before training, the H reflex facilitation was not different between groups A (less than 3 months after injury) and B (more than 3 months after injury). After training, H reflex facilitation at 20 ms was significantly greater in group A than in group B (asterisk). No other differences were found between groups A and B before or after training.

In healthy subjects, the H reflex amplitude modulation by TMS shows an early phase, peaking at 10–30 ms, and a late phase, peaking at 60–130 ms.[12–14] According to Valls-Solé and co-workers,[13] the first phase may result from the generation of an excitatory postsynaptic potential (EPSP) in the α-motoneuron, whereas the mechanisms responsible for the second phase are not clear. In a study of patients with SCI, Wolfe *et al.*[17] reported the absence of modulation in patients with complete motor lesions, and a partial facilitation present on incomplete motor lesions (ASIA C and D). The results in our patients at baseline are comparable with those reported in incomplete motor lesions by Wolfe *et al.*[17] and suggest an effective TMS-induced motoneuronal EPSP. Furthermore, the pattern of TMS-induced H reflex modulation changed more in patients with shorter time after injury. Interestingly, the change occurred mainly in the early phase (20 ms). We assume that this increase in facilitation is due to the arrival of a more effective and probably larger EPSP to the spinal cord motoneurons innervating leg muscles with progression of recovery.

A few patients with no improvement in the functional outcome measures exhibited a slight increase in the H reflex facilitation in the follow-up examination. A possible explanation for this observation is that gait training would induce a subclinical change in H reflex modulation. Because all our patients were engaged in some form of gait training, we cannot know the role of gait training in the changes described. We do not know, either, if another form of rehabilitation or even no rehabilitation at all would have led to the same effect or not. However, the fact that no significant changes of the H reflex modulation were seen in the follow-up examination in patients that had the SCI more than 3 months before the study, suggests that time after injury might be the most important variable to take into account for plasticity changes in the spinal cord that lead to better modulation of the H reflex.

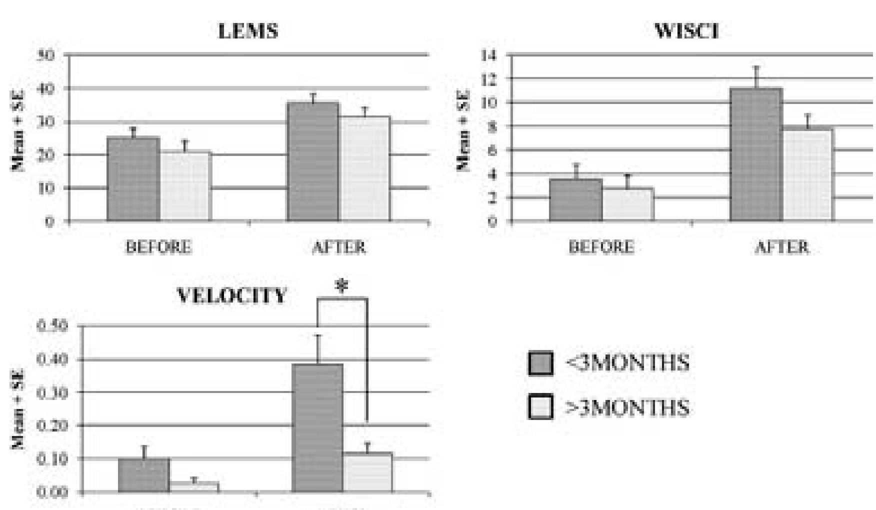

Figure 5 Lower extremities motor score (LEMS), walking index for spinal cord injury (WISCI) and gait velocity changes after training. Mean and standard error of the mean for the LEMS, WISCI and velocity in patients before and after gait training for group A (less than 3 months after injury) and group B (more than 3 months after injury). A significant increase in LEMS, WISCI and velocity was found after training for both groups of subjects ($P<0.05$) but the percentage increase in velocity was significantly greater in group A than in group B ($P=0.014$).

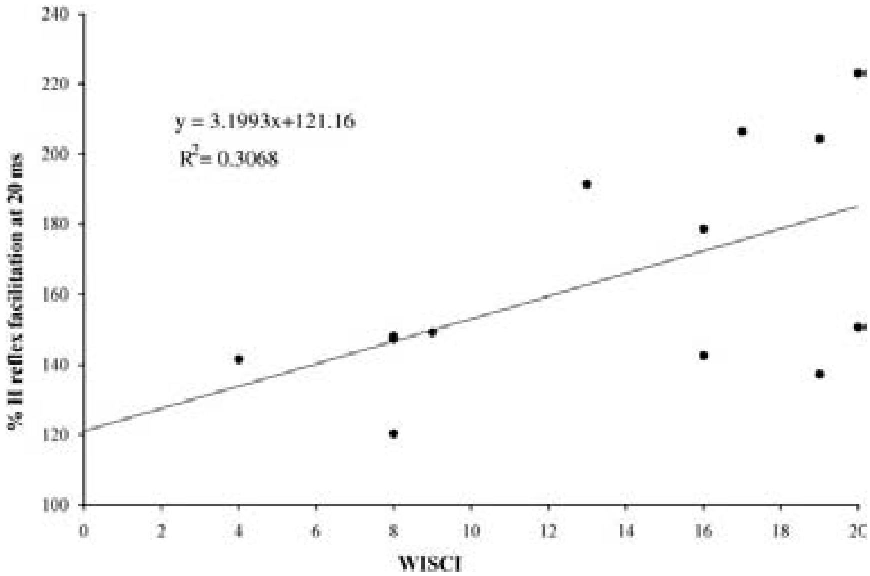

Figure 6 Correlation between walking index for spinal cord injury (WISCI) and H reflex facilitation by transcranial magnetic stimulation at the interval of 20 ms after training in subjects with less than 3 months after injury. The improvement in WISCI scale after the training was related to a greater percentage of H reflex facilitation ($P = 0.050$).

In terms of neural tracts involved in this process, the fast corticospinal tract seems to mediate the early phase of facilitation, as previously described by Wolfe *et al.*[17] The origin of the late facilitation is less clear, with different hypothesis: corticobulbospinal projections,[18] peripheral afferent inputs[19] or a summation of corticospinal, brainstem and peripheral influences.[20]

Patients that were included in the study within 3 months after the SCI had different outcomes defined by clinical improvement. Patients with better clinical outcome had a larger facilitation of the H reflex, with a statistically significant positive correlation with the WISCI scale score. This is an important aspect adding evidence from the neurophysiological point of view to the importance of the early training after SCI.

The H reflex modulation by TMS may be an interesting clinical neurophysiological tool to provide quantified measures to the supraspinal control of lower limb reflexes in patients with SCI. Its correlation with improvement in gait abilities during the first 3 months after injury suggests that it may have clinical applicability.

Conflict of interest

The authors declare no conflict of interest.

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PUBLICACION 3

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Effects of High-Frequency Repetitive Transcranial Magnetic Stimulation on Motor and Gait Improvement in Incomplete Spinal Cord Injury Patients

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Abstract

Objective. Incomplete spinal cord injury (SCI) patients have the potential to regain some ambulatory function, and optimal reorganization of remaining circuits can contribute to this recovery. We hypothesized that repetitive transcranial magnetic stimulation (rTMS) may promote active recovery of motor function during gait rehabilitation. *Methods*. A total of 17 incomplete SCI patients were randomized to receive active rTMS or sham stimulation coupled with rehabilitation therapy; 3 patients who began in the sham group crossed over to the active rTMS group after a washout period of more than 3 weeks. Active rTMS consisted of 15 daily sessions over the leg motor area (at 20 Hz). We compared lower-extremity motor score (LEMS), 10-m walking test for walking speed, timed up and go, Walking Index for SCI Scale, Modified Ashworth Scale, and Spinal Cord Injury Spasticity Evaluation Tool at baseline, after the last session, and 2 weeks later in the active rTMS and sham stimulation groups. *Results*. A significant improvement was observed after the last rTMS session in the active group for LEMS, walking speed, and spasticity. Improvement in walking speed was maintained during the follow-up period. Sham stimulation did not induce any improvement in LEMS, gait assessment, and spasticity after the last session and neither during follow-up. *Conclusion*. In incomplete SCI, 15 daily sessions of high-frequency rTMS can improve motor score, walking speed, and spasticity in the lower limbs. The study provides evidence for the therapeutic potential of rTMS in the lower extremities in SCI rehabilitation.

Keywords

incomplete SCI, functional improvement, transcranial magnetic stimulation, rehabilitation

Introduction

The spinal networks involved in locomotion require input from supraspinal structures for adequate control of gait in humans.[1] Only those with motor-incomplete spinal cord injury (SCI) demonstrate improvement in their ability to walk overground following gait training, suggesting that supraspinal centers play a critically important role in the recovery of overground locomotor function.[2-4] Walking function is highly related to motor-evoked potential (MEP) recovery in the tibialis anterior muscle (TA) in SCI patients.[5] Thomas and Gorassini[6] reported that the degree of locomotor recovery after intensive locomotor training correlated positively with the percentage increase of MEP in the TA or vastus lateralis muscle. With functional magnetic resonance imaging, Winchester et al[2] found an increase in activity of the leg motor area after improving gait in persons with SCI.

Spasticity is classically defined as a motor disorder[7] that contributes to impairment of voluntary movements in SCI.[8] Improvement in spasticity might induce some improvement in motor strength in the lower extremity.[9]

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive and painless procedure to modulate cortical

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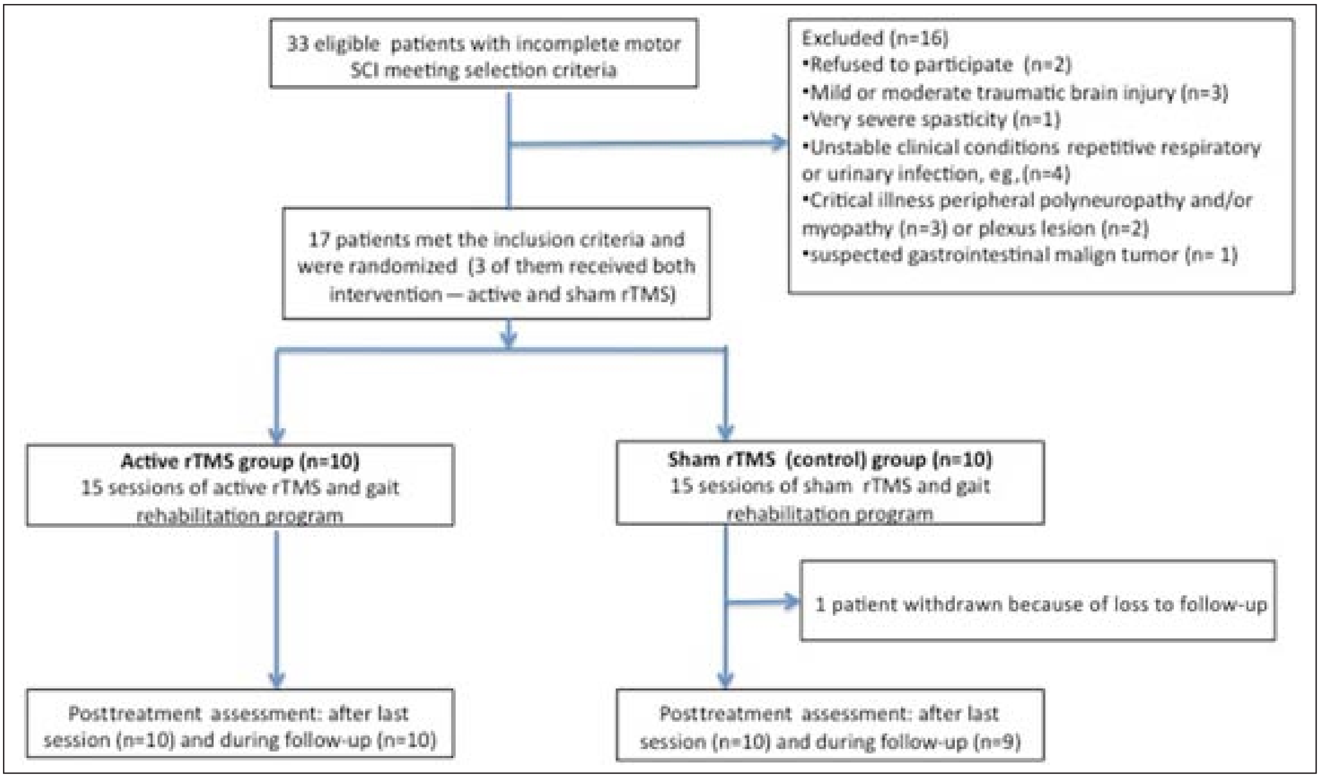

Figure 1. Flow diagram of patient categorizations. Abbreviations: SCI, spinal cord injury; rTMS, repetitive transcranial magnetic stimulation.

excitability of motor areas and induce changes over the descending corticospinal output.[10-12] This modulation may be useful to promote active recovery of motor function and to obtain functional benefit from gait rehabilitation. Through the use of repetitive high-frequency rTMS, improvement has been reported in motor and sensory functions measured by the American Spinal Cord Injury Association (ASIA) Impairment Scale (AIS) and time to complete a peg-board task in 4 chronic incomplete cervical SCI patients.[10]

Here we hypothesized that high-frequency rTMS coupled with gait training can improve motor recovery in the lower extremities and locomotion in incomplete SCI patients to a greater degree than sham stimulation.

Methods

The study was a randomized, double-blind, sham-controlled trial. We recruited 17 patients with SCI (see details in the following) to be randomly distributed in 2 study groups: an active rTMS group and a sham group. Three patients who began in the sham group were crossed over to the active rTMS group after a washout period of more than 3 weeks. Therefore, 10 individuals were studied in each group. All patients underwent 15 consecutive daily sessions (3 weeks) of active or sham rTMS. Patients and investigators were blinded to the treatment arm except for HK, who applied rTMS.

Patients

Inclusion criteria were the following: (1) incomplete SCI AIS-D,[13] with possible gait capacity; (2) cervical or thoracic SCI; (3) time lapse since SCI between 3 and 12 months; (4) no changes in medical treatment at least 1 week before and during the study; (5) no limitation of passive range of movement in joints; and (6) written informed consent for the study, which was approved by the institutional review board of Institut Guttmann. All patients were naive to rTMS and unaware of the purpose of the study.

A total of 33 individuals were identified as potential participants for this study, and 17 gave informed consent and participated in the study (Figure 1). All patients received standard care for SCI rehabilitation at our institution. The program comprises 5 hours of therapy 5 days per week, including training in activities of daily living, occupational therapy for the upper extremities for patients with cervical SCI, fitness training, sports, hydrotherapy, and gait training.

Patients received daily gait training therapy (5 d/wk) during the 3 weeks of rTMS session and for 2 more weeks during follow-up. Each training session lasted 1 hour and consisted of overground gait training assisted by a therapist using orthesis and technical aids as needed, in accordance with the functional level of each patient. The session of overground gait training was performed immediately (within less than 30 minutes) after active or sham rTMS sessions for all patients.

Clinical and Functional Assessment

Primary outcome measurements included the following: (1) lower-extremity motor score (LEMS), obtained from the standardized AIS clinical exam[14]; (2) 10-m walking test (=time in seconds to walk 10 m) for walking speed[15] (patients were asked to walk at their fastest but most comfortable speed); (3) timed up and go (TUG) test[16]; and (4) Walking Index for SCI Scale (WISCI-II; to quantify walking ability).[17]

Secondary outcome measures included the following: (1) Modified Ashworth Scale (MAS) evaluated at both knees for spasticity assessment[18] and (2) the Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET).[19]

rTMS Protocol

Patients received 15 rTMS sessions, 5 d/wk for 3 weeks, in the morning between 9:00 and noon. We used a MagStim Super Rapid magnetic stimulator (MagStim Company, Whitland, Wales, UK) equipped with a commercially available double-cone coil (each wing measuring 110 mm in diameter), which was held over the vertex. All active and sham rTMS sessions were conducted at rest, with the patient lying supine.

For active (real) rTMS, we applied 2-s long bursts at 20 Hz (40 pulses/burst) with intertrain intervals of 28 s, for a total of 1800 pulses over 20 minutes. These rTMS parameters were selected for this study because when we used it in patients with incomplete SCI for spasticity, some of our patients reported better gait function (data not reported in the article).[20] Also, according to previous publications, the magnitude and duration of the after-rTMS effects seem to depend on the total number of stimuli, with longer periods of rTMS inducing a more consistent and persistent change in corticospinal excitability.[11,21,22]

Electromyographic recordings (EMGs) were obtained with pairs of Ag-AgCl surface EMG electrodes placed over the first dorsal interosseous, abductor pollicis brevis, and biceps brachii muscles. We also recorded motor threshold at rest (RMT) in TA on both sides. The intensity of repetitive TMS was set at 90% RMT of the upper-extremity muscles.

For motor threshold determination, the double-cone coil was held lateral to the vertex over the optimal scalp position overlying the contralateral hemisphere to the less-affected side from SCI, from which single-pulse TMS evoked responses of maximum amplitude in muscles in the upper extremity. The EMG signal was amplified (×50) with filters set as 10 to 2000 Hz. RMT was defined as the lowest intensity that elicited MEPs of >50 µV peak-to-peak amplitude in at least 5 of 10 consecutive stimulations.

For sham stimulation, the double-cone coil was held over the vertex but was disconnected from the main stimulator unit. Instead, a second coil (8-shaped) was connected with the MagStim stimulator and discharged under the patient's pillow. Thus, no current was induced in the brain, and although the patients did not experience a tapping sensation on the scalp, they were exposed to a similar clicking noise. When explicitly asked at the end of the trial, 8 of the 10 patients in the sham stimulation group thought that they had received active stimulation; 2 patients were not sure whether it was active or sham stimulation.

Experimental Design

The experimental protocol included the following steps:

1. Clinical and functional assessment at baseline
2. After the first rTMS session, spasticity reevaluation by MAS
3. Daily rTMS sessions for 14 additional days
4. Clinical and functional assessment after completion of the 15th rTMS session
5. Follow-up of functional outcomes (gait) 2 weeks after the last session of rTMS and spasticity reevaluation by SCI-SET.

Data Analysis

MAS was calculated for both knees and the results averaged. Data are presented as mean ± standard deviation. Change scores were calculated by subtracting baseline data from the last session of rTMS data and from follow-up period data.

Because the distribution of the data was not normal according to the Kolmogorov-Smirnov test, the Friedman test was used for multiple repeated-measures comparisons and the Wilcoxon *t* for post hoc comparisons. The Mann Whitney *U* test and χ^2 test were used to compare data between different groups of patients. The significance level was set as $P < .01$, with Bonferroni correction for multiple comparisons.

Spearman ρ was used to study correlations between the absolute value of MAS or of SCI-SET and LEMS or gait function and between the change scores in LEMS, SCI-SET, and gait functions. The significance level was set as $P < .05$.

Results

Demographic and clinical characteristics of the patients included in the study are summarized in Table 1. Both groups were homogeneous for age, gender, time lapse since injury, etiology, AIS scale, and LEMS for active and sham

Table 1. Clinical and Demographic Characteristics of Patients.

rTMS	Sex	Age, y	Neurological Lesion Level	AIS	Time Since SCI, mo	Etiology	Pharmacological Treatment
Active	M	29	T12	D	8	Trauma	Baclofen, gabapentin
Active[a]	M	19	T1	D	6	Tumor	Baclofen, fluoxetina
Active	M	47	C6	D	8	Trauma	Baclofen
Active	M	21	C5	D	9	Trauma	Baclofen
Active	F	51	T7	D	12	Tumor	Clonazepam
Active	M	60	T7	D	3	Infection	Baclofen
Active[a]	M	19	T5	D	12	Myelitis	Baclofen, fluoxetina
Active[a]	M	24	C6	D	5	Trauma	Baclofen
Active	F	40	C4	D	8	Trauma	Baclofen, venlafaxina, tizanidina
Active	M	21	T2	D	12	Trauma	Baclofen
Sham[a]	M	18	T1	D	4	Tumor	Baclofen, fluoxetina
Sham	M	50	C4	D	5	Trauma	Gabapentin, clonazepam, venlafaxina
Sham[a]	M	18	T5	D	9	Myelitis	Baclofen, fluoxetina
Sham	M	56	C6	D	10	Trauma	Baclofen
Sham	M	34	T7	D	11	Infection	Baclofen
Sham	M	37	T3	D	12	Trauma	Sirdalud, baclofen
Sham[a]	M	24	C6	D	3	Trauma	Baclofen
Sham	F	41	T2	D	5	Infection	Diazepam, gabapentin, mirtazapina
Sham	M	54	T3	D	3	Infection	Lorazepam
Sham	F	33	C5	D	6	Tumor	—

Abbreviations: rTMS, repetitive transcranial magnetic stimulation; M, male; F, female; C, cervical; T, thoracic; AIS, American Spinal Cord Injury Association (ASIA) Impairment Scale.
[a]Three patients who received sham stimulation first and then received active stimulation after at least a 3-week washout period.

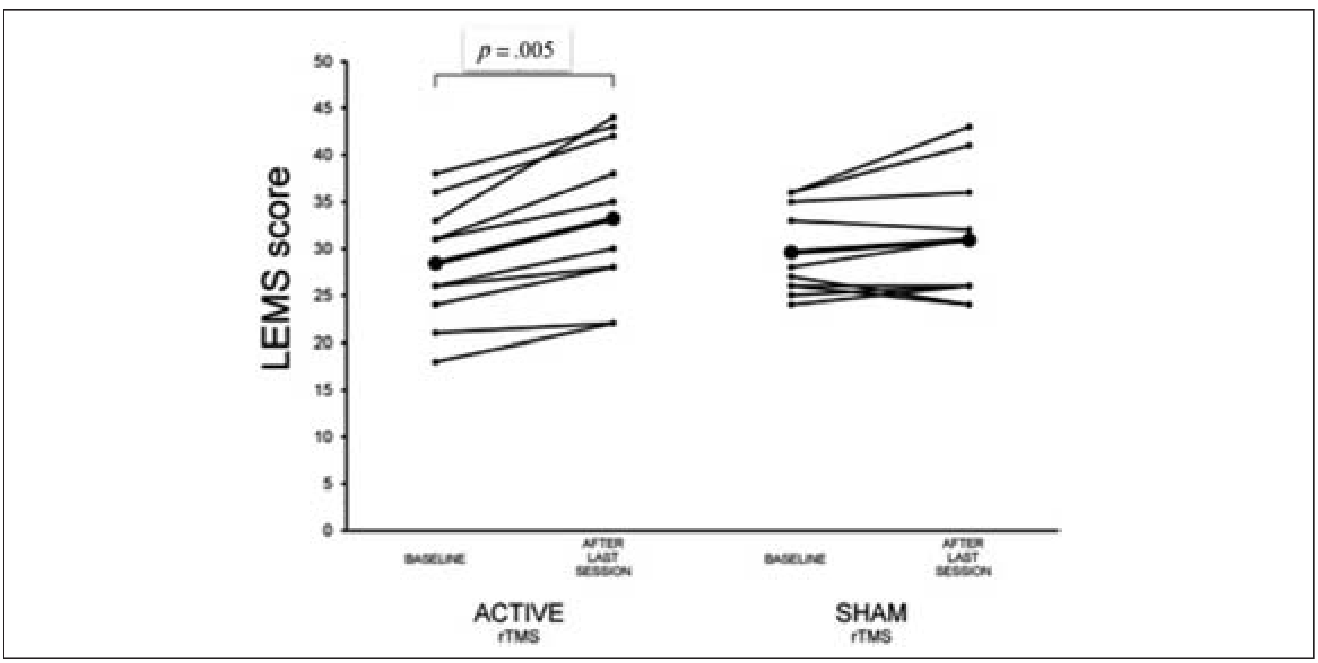

Figure 2. Total motor score in the lower extremities at baseline and after the last rTMS session for each studied patients (small black circle) and the average of the each group (big black circle). Abbreviations: LEMS, lower-extremity motor score; rTMS, repetitive transcranial magnetic stimulation.

Table 2. Change Scores for Spasticity and Functional and Clinical Assessment After First and Last Session of rTMS and During the 2-Week Follow-up Period in Active and Sham rTMS.[a]

	First Session			Last Session			Follow-up		
	Active	Sham	*P*	Active	Sham	*P*	Active	Sham	*P*
LEMS	—	—		4.80 (2.78)	1.30 (3.09)	.006	NA	NA	
Walking speed	—	—		0.16 (0.20)	0.08 (0.21)	.20	0.25 (0.24)	0.14 (0.24)	.14
TUG	—	—		−26.0 (20.17)	−16.0 (19.01)	.40	−35.1 (26.76)	−17.2 (26.82)	.43
WISCI-II	—	—		1.6 (2.41)	2.0 (2.56)	.93	1.5 (2.32)	3.0 (2.47)	.54
MAS	−0.68(0.35)	0.18 (0.2)	<.0001	−0.70 (0.55)	0.28 (0.66)	.001	NA	NA	
SCI-SET	—	—		0.36 (0.32)	0.04 (0.42)	.02	0.44 (0.57)	0.13 (0.35)	.04

Abbreviations: rTMS, repetitive transcranial magnetic stimulation; LEMS, lower-extremity motor score; TUG, timed up and go; WISCI-II, walking index for SCI; SCI, spinal cord injury; MAS, Modified Ashworth Scale; SCI-SET, spasticity evaluation tool; NA, not available.
[a]Change scores were expressed as mean (standard deviation) for each group. *P* value: comparison is between active versus sham rTMS groups.

groups (Table 1 and Figure 2). The mean age of patients in the active rTMS group was 32.9 ± 15.4 years and 36.5 ± 13.9 years in the sham rTMS group. The mean time lapse since injury was 8.3 ± 3.1 months in the active rTMS group and 6.8 ± 3.4 months in the sham rTMS group.

At baseline, MEPs could be obtained in the TA in only 5 patients, 3 assigned to the active rTMS group (with an RMT of 60%, 48%, and 80%) and 2 assigned to the sham rTMS group (with an RMT of 48% and 86%). In all other patients, we were unable to elicit MEPs in the TA even at 100% TMS intensity. The motor threshold in the TA did not change after 15 days of rTMS sessions in both groups. The mean rTMS intensity used for active rTMS was 39.8% ± 5.8% of maximum stimulator output.

Adverse Effects

All patients tolerated the study without complications, and no adverse effects were reported, with the exception of 6 patients who complained of a slight twitching of facial muscles during the first session of active stimulation.

Between-Group Comparisons

Absolute mean values at baseline for LEMS, walking speed, TUG, and WISCI-II were similar in both sham and active rTMS groups (Mann-Whitney *U* test, $P > .2$ for all comparisons). At baseline, patients included in the sham group had a significantly lower MAS score than those included in the active rTMS group (Mann-Whitney *U*, $P = .04$). There were no between-group differences in SCI-SET (Mann-Whitney *U*, $P = .39$). There were no differences between the active and sham rTMS groups at the end of the last session of rTMS and during follow-up in LEMS and gait scales, MAS, and SCI-SET (Mann-Whitney *U* test, $P > .1$ for each comparison).

Change scores revealed significant improvement in LEMS and in spasticity measured by MAS after 3 weeks of active rTMS in comparison to sham rTMS (Table 2). Improvement in gait parameters was larger in the active rTMS group than in the sham group, but the change scores reached no significant level, neither after the last session of rTMS nor during the follow-up period (Table 2).

Within-Group Comparisons

Primary outcome measurements. Total lower-extremity muscle strength (ie, LEMS) improved significantly (Table 3, Figure 2) after the last session in the active rTMS group (Wilcoxon *t*, $P = .005$) but not in the sham group (Wilcoxon *t*, $P = .25$).In the 3 patients who received both stimulations, LEMS improved 18.6% with active rTMS and 3% with sham rTMS.

In patients who received active rTMS, walking speed showed significant improvement after the last session, and the effect was maintained during follow-up ($P < .01$ for all comparisons; Table 3, Figure 3). No significant changes were observed in the TUG and WISCI-II (Table 3, Figure 3).

Secondary outcome measurements. There was significant reduction of spasticity according to MAS after the first and last sessions in the active rTMS group (Wilcoxon *t*, $P = .0001$ for both comparisons; Table 3) but not in the sham rTMS group. SCI-SET did not change significantly after the last session or during the follow-up period in both groups (Table 3).

Correlation Analysis

The change scores of LEMS were significantly correlated with the change scores of walking speed in the active rTMS group ($\rho = 0.708$; $P = .02$) but not in the sham rTMS group ($P = .06$). There was no correlation between absolute value of gait scales and MAS and SCI-SET. The change scores of gait scales were not correlated with the change scores of SCI-SET at any time of evaluation in both groups (Spearman ρ, $P > .1$ for each comparison).

Table 3. Primary and Secondary Outcome Measurements.[a]

	rTMS	Baseline	First Session	Last Session	Follow-up
Primary outcome measures					
LEMS	Active	28.4 (6.8)	NA	33.2 (8.8)[b]	NA
	Sham	29.6 (4.8)	NA	30.9 (7.0)	
Walking speed	Active	0.24 (0.32)	NA	0.40 (0.44)[b]	0.48 (0.53)[b]
	Sham	0.26 (0.20)	NA	0.34 (0.26)	0.39 (0.31)
TUG	Active	84.6 (76.19	NA	62.1 (57.9)	54.11 (46.0)
	Sham	74.0(55.84)	NA	49.0 (40.1)	43.4 (41.1)
WISCI-II	Active	9.50 (5.7)	NA	11.1 (4.4)	11.0 (4.4)
	Sham	10.6 (5.2)	NA	12.1 (4.6)	13.1 (4.3)
Secondary outcome measures					
MAS	Active	2.30 (0.8)	1.62 (0.77)[b]	1.60 (0.9)[b]	NA
	Sham	1.30 (0.7)	1.58 (0.76)	1.78 (0.7)	NA
SCI-SET	Active	−067 (0.4)	NA	−0.31 (0.5)	−0.23 (0.5)
	Sham	−0.47 (0.9)	NA	−0.43 (0.8)	−0.34 (0.7)

Abbreviations: LEMS, lower-extremity motor score; TUG, timed up and go; WISCI-II, walking index for SCI; SCI, spinal cord injury; MAS, Modified Ashworth Scale; SCI-SET, spasticity evaluation tool; rTMS, repetitive transcranial magnetic stimulation; NA, not available.

[a]The data show mean (standard deviation, Wilcoxon test) of LEMS, walking speed, TUG test, WISCI-II, MAS, and SCI-SET at baseline, after first and last sessions of rTMS, and during follow-up.

[b]$P < .01$ in comparison to baseline.

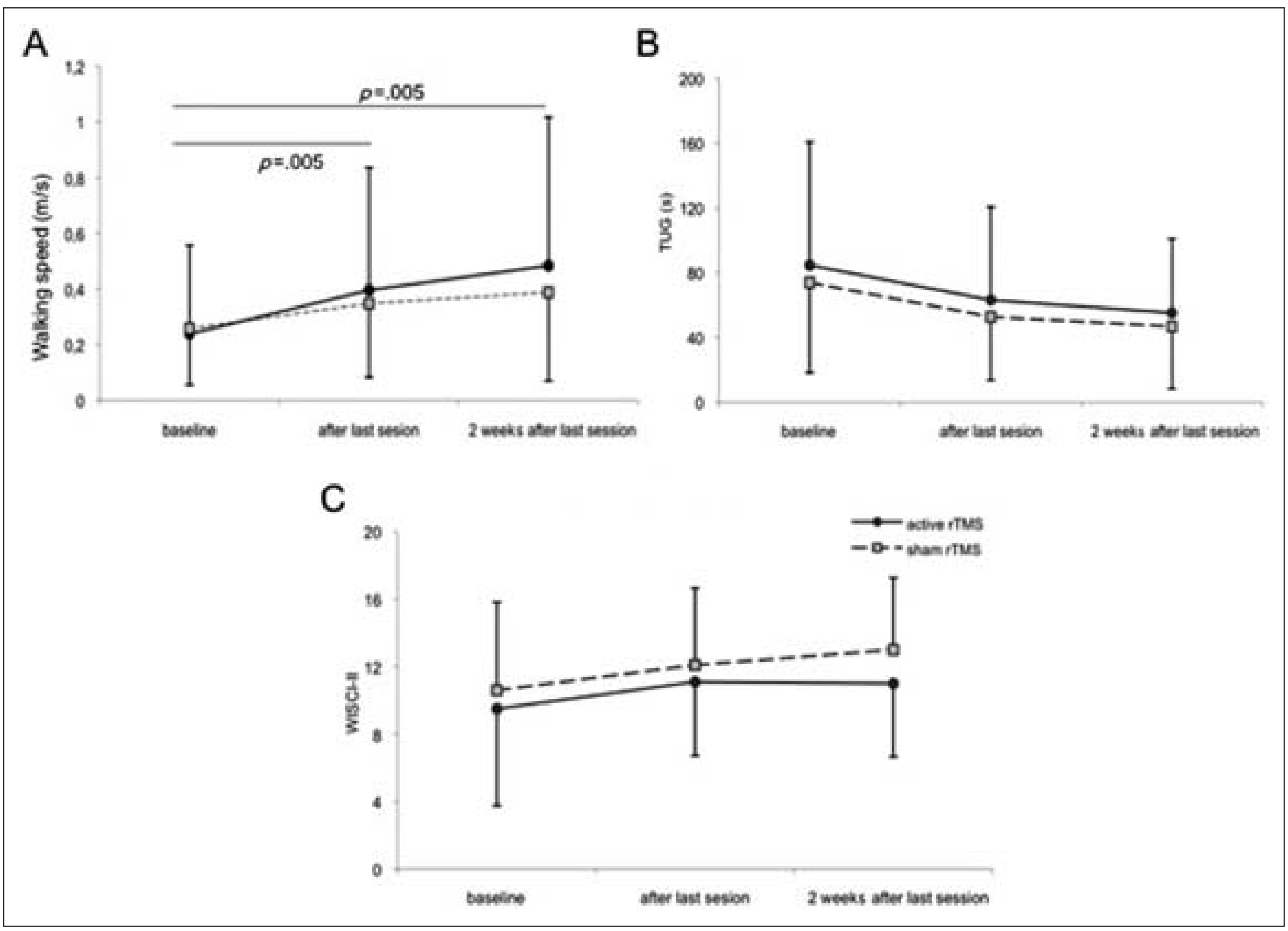

Figure 3. Gait scales at baseline, after the last rTMS session and during follow-up period (2 weeks after the last session). Abbreviations: TUG, timed up and go; WISCI-II, walking index for SCI; SCI, spinal cord injury; rTMS, repetitive transcranial magnetic stimulation.

Discussion

The main findings of our study are a significant improvement in LEMS, walking speed, and spasticity after high-frequency rTMS in motor-incomplete SCI patients. The main effects of 15 daily sessions of stimulation on LEMS and walking speed were found in the active rTMS group after the treatment, and it lasted for at least 2 weeks during the follow-up period. In contrast, patients receiving sham stimulation did not show any improvement in clinical and functional assessment after treatment or during follow-up.

Our results demonstrate that high-frequency rTMS combined with rehabilitation therapy can be more effective in the management of motor impairment and spasticity in lower limbs following incomplete SCI than rehabilitation therapy coupled with placebo. In the literature, Belci et al[10] reported improvement in general motor score (upper and lower extremities) and in upper-extremity function in 4 patients with incomplete chronic cervical SCI after applying high-frequency rTMS over the vertex for 5 days. High-frequency rTMS at subthreshold intensity can lead to an increase in regional glucose metabolism immediately after the end of the stimulation, suggesting the possibility of an rTMS-induced increase in overall neuronal activity in the stimulated motor area (M1).[23] The magnitude and duration of the after effects seem to depend on the intensity and the total number of stimuli, with longer periods of rTMS inducing a more consistent and persistent change in corticospinal excitability.[11,21,22] The facilitation of corticospinal excitability induced by high-frequency rTMS could be long lasting.[20,24,25] According to the other study, rTMS also could reduce corticospinal inhibition, which consequently could induce motor improvement in SCI.[10] It is possible that motor score improvement and amelioration of spasticity with rTMS in SCI can be induced through enhancement of descending corticospinal projections and/or reduction in corticospinal inhibition.[20] Enhancement of descending corticospinal projections may induce amelioration of spasticity through some effect on propriospinal interneurons, as has been hypothesized before.[20,24] Further studies are needed to understand the effect of rTMS on the improvement of spasticity.

Our results showed also that there was improvement in walking speed in the active rTMS group, which was correlated with the improvement in LEMS. Supraspinal centers are activated during locomotion, especially to provide equilibrium and visuomotor control and to coordinate leg responses.[26] In patients with SCI, MEP amplitudes in the TA seem to allow for prediction of recovery of function mediated by the corticospinal tracts.[5,6] Furthermore, walking function is highly related to MEP recovery in the TA in these patients.[5] It is striking that the length of time since injury onset in SCI may have affected the efficacy of synaptic plasticity within the spinal cord, within supraspinal centers, or between those centers.[26,27] It is possible that some improvement in gait function can be induced through the facilitation of corticospinal excitability,[20,24,25] with reduction in corticospinal inhibition[10] and with motor score improvement in the lower limbs. In this study, LEMS with active rTMS improved 4.8 out of 50 in 3 weeks, which was correlated with walking speed. This did not occur with sham rTMS, in which LEMS improvement was 1.3 out of 50. Prior studies had shown that the higher the LEMS, the more likely a patient was to recover the ability to walk without physical assistance.[28,29] Greater motor control for walking in terms of walking speed and strength was found as the LEMS approached and exceeded 40 of a possible 50 points.[30] In this study, the mean time since SCI was 4.5 weeks, and reevaluation was done in 12 weeks.[30] However, in our patients, the mean time since SCI was 6.8 months, and reevaluation was done in 3 weeks.

Timing of stimulation during performance of a psychological task is crucial to producing a TMS-related effect.[31,32] Production of facilitatory effects appears to be time dependent. In studies reporting facilitation, TMS is often applied immediately before a block of trials[31] or, within each trial, immediately before a response is to be made.[32] In our patients, rTMS was applied less than 30 minutes before onset of training therapy.

Improvement in LEMS and some gait parameters with rTMS was maintained during the follow-up period. Previous studies have demonstrated that cumulative plastic changes can be produced by rTMS in healthy participants[33] as well as in those with SCI,[20] multiple sclerosis,[24] and stroke.[25] Another mechanism might be that repeated episodes of long-term potentiation (LTP) lead to remodeling with an increase in active synapses.[34,35] LTP is a long-lasting enhancement in signal transmission between 2 neurons that results from stimulating them synchronously.[36] One of several phenomena underlying synaptic plasticity is the ability of chemical synapses to change in strength. LTP is widely considered to be one of the major cellular mechanisms that underlie learning and memory.[36]

The limitations of our study are as follows: (1) the stimulation intensity applied during active rTMS was relatively low for leg muscles (90% RMT in the lowest muscle threshold of the upper extremity because of absent MEP in the lower extremity in most patients or very high RMT in the 3 other patients); (2) the time lapse since SCI was less than 12 months, which limits the possibility of spontaneous or training-induced recovery to that time; however, according to the literature, greater gains in gait function in SCI occur when training is begun earlier (<6 months postinjury),[37] and in this study, only 2 patients from the active rTMS had less than 6 months of evolution, in contrast to 5 patients from the sham group; (3) our patients had variable causes of SCI, and it is unknown whether or not the natural progression of improvement in the first 6 months differs based on SCI etiology; (4) another possible weakness of our study is that improvement in gait parameters may occur when the participant becomes familiar with a given test; to rule out learning the test, inclusion of multiple baseline tests would have been preferable; and (5) MAS used for spasticity evaluation has poor reliability in SCI.[15]

In conclusion, our results indicate that rTMS combined with gait training is beneficial for motor recovery in the lower limbs, walking speed, and reduction of spasticity in SCI patients. Based on the small effect size for the LEMS and walking speed, a larger trial may need approximately 75 to 100 subjects in each arm to determine efficacy with a moderate effect size for the experimental intervention. At a more conceptual level, our findings show potential advantages of combining rehabilitation strategies with noninvasive brain stimulation techniques to optimize outcome. These beneficial effects were achieved with minimal side effects and with good tolerability. Challenges that remain include exploring the optimal dose and timing of stimulation, developing better strategies for rehabilitation therapy, determining the most responsive characteristics of SCI patients, and examining how to extend the duration of motor and functional improvement to the long term in a larger sample population after SCI.

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RESUMEN DE LOS RESULTADOS

Artículo 1:

Benito-Penalva J, Edwards DJ, Opisso E, Cortes M, Lopez-Blazquez R, Murillo N, Costa U, Tormos JM, Vidal-Samsó J, Valls-Solé J; European Multicenter Study about Human Spinal Cord Injury Study Group, Medina J. **Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics.** Arch Phys Med Rehabil. 2012; 93(3):404-12.

De los 130 sujetos que iniciaron el entrenamiento con los sistemas electromecánicos 105 completaron el programa. En la valoración global utilizando los datos de todos los pacientes, en las 3 variables clínicas estudiadas [balance muscular de las extremidades inferiores (BMEI), escala de valoración de la marcha (WISCI II) y el test de los 10 metros (T10M)] se observó una mejoría estadísticamente significativa tras el período de entrenamiento.

En relación al tipo de sistema electromecánico utilizado (Lokomat vs Gait Trainer), no se observó ninguna diferencia tras el entrenamiento en ninguna de las variables clínicas estudiadas.

En cuanto a las características de los sujetos en relación al grado de cambio o “pendiente” entre los resultados finales y basales obtenidos en las 3 variables clínicas encontramos los siguientes resultados:

- Según la clasificación ASIA: Para el BMEI, los ASIA C tiene una ganancia significativamente mayor que los A-B; también mayor ganancia aunque no estadísticamente significativa que los ASIA D. Para el WISCI II, los ASIA D presentan ganancias significativas en relación a los A-B y C. Para el T10M los ASIA D tiene una ganancia significativamente mayor que los C; también mayor ganancia aunque no estadísticamente significativa que los ASIA A-B.

- Según el tiempo desde la lesión: Para el BMEI, el grupo con lesiones más tempranas (0-6 meses) tiene una ganancia significativamente mayor que los más tardíos (>12 meses). Para el WISCI II y el T10M el grupo de 0-6 meses presenta una mayor ganancia significativa en relación a los de 6-12 meses y >12 meses.

- En cuanto a las variables etiología de la lesión (traumática vs no traumática), nivel de lesión (tetraplejia vs paraplejia), edad (≤50 vs >50) y sexo, no se observó que ninguna de ellas pudiera influir en los resultados de las 3 variables clínicas estudiadas.

En la comparación de los sujetos que recibieron entrenamiento de la marcha con sistemas electromecánicos con los que recibieron entrenamiento convencional (estos últimos obtenidos de la base de datos europea EM-SCI) observamos:

- Para el BMEI, los sujetos ASIA C y D que recibieron entrenamiento de la marcha con sistemas electromecánicos presentaron un grado de cambio del balance muscular significativamente mayor que un grupo comparable que recibió entrenamiento convencional.

- Para el WISCI II y el T10M, los sujetos ASIA D entrenados con sistemas electromecánicos obtuvieron una mejora significativamente mayor que los del entrenamiento convencional. En los ASIA C también se observó esta mejoría pero no estadísticamente significativa.

Artículo 2:

Benito Penalva J, Opisso E, Medina J, Corrons M, Kumru H, Vidal J, Valls-Solé J. **H reflex modulation by transcraneal magnetic stimulation in spinal cord injury subjects after gait training with electromechanical systems.** Spinal Cord. 2010; 48(5):400-6.

Los resultados hacen referencia a 29 sujetos con una lesión medular motora incompleta (ASIA C y D) divididos en 2 grupos: El grupo A incluye 16 sujetos con <3 meses desde la lesión; el grupo B incluye 13 sujetos con una lesión entre 3 meses y un año.

- Modulación del reflejo H por EMT en los sujetos antes de iniciar el entrenamiento con los sistemas electromecánicos comparado con sujetos sanos: Los sujetos sanos tienen un patrón determinado de modulación del reflejo H por EMT, con una facilitación significativa en la fase temprana (20 ms) y tardía (80 ms). Los lesionados medulares presentan una modulación del reflejo H con una facilitación en las 3 fases pero perdiendo el patrón encontrado en los sujetos sanos, y con una diferencia significativa en la facilitación del reflejo H en la fase de los 20 ms comparado con el grupo control.

- Cambios en la modulación del reflejo H por EMT en los 2 grupos de paciente antes y después del entrenamiento de la marcha: Tras el entrenamiento se observa una mayor facilitación del reflejo H en la fase temprana en los sujetos del grupo A en comparación con el B.

- Variables clínicas (BMEI, WISCI II y T10M): De manera global todos los parámetros mejoran de manera significativa tras el entrenamiento. Además se observa que el porcentaje de cambio en el T10M tras el entrenamiento es significativamente mayor en el grupo de sujetos de <3meses desde la lesión (grupo A).

- Comparación entre las ganancias clínicas y la modulación del reflejo H por EMT: Existe una correlación positiva entre la mejoría en la escala WISCI II y la facilitación del reflejo H en la fase temprana en los sujetos del grupo A.

- En relación a las variables tipo de lesión motora incompleta (ASIA C vs ASIA D), etiología de la lesión (traumática vs no traumática) y tipo de sistema electromecánico (Lokomat vs Gait Trainer), no se observa que ninguna de ellas pueda influir en la modulación del reflejo H por EMT en los intervalos estudiados.

Artículo 3:

Kumru H, Benito J, Murillo N, Valls-Sole J, Valles M, Lopez-Blazquez R, Costa U, Tormos JM, Pascual-Leone A, Vidal J. **Effects of high frequency repetitive transcranial magnetic stimulation on motor and gait improvement in incomplete spinal cord injury patients.** Neurorehabilitation and Neural Repair. 2013 Jun; 27(5):421-9.

Los resultados hacen referencia a un total de 17 sujetos con una lesión medular incompleta motora (ASIA D), que participan en el programa de rehabilitación de la marcha. Previo al entrenamiento de la marcha los sujetos reciben EMTr activa (grupo activo, n=10) o EMTr placebo (grupo placebo, n=10).

Ambos grupos son homogéneos para edad, sexo, tiempo desde la lesión, etiología de la lesión, escala ASIA y BMEI.

Las variables analizadas son escalas clínicas [BMEI, T10M, Timed up and go (TUG), WISCI II] y escalas de valoración de la espasticidad [Escala de Ashworth modificada (MAS) y la escala de valoración de la espasticidad en el lesionado medular (SCI-SET)].

- Comparación entre grupos: Se observa una mejoría significativa en el BMEI y en la espasticidad medida por MAS después de 3 semanas en el grupo de EMTr activa en comparación al grupo placebo. La mejoría en los parámetros de marcha fue mayor en el grupo activo pero sin alcanzar parámetros de significancia estadística.

- Comparación “intra” grupos: El BMEI mejoró de manera significativa tras el entrenamiento de la marcha en el grupo que recibió EMTr activa, no así en el grupo placebo. Asimismo, en el grupo que recibió EMTr activa, la velocidad (T10M) mejoró significativamente después de la última sesión, y esta ganancia se mantuvo durante el seguimiento a las 2 semanas. No se apreciaron cambios significativos en el TUG y WISCI II. Se observó una reducción significativa de la espasticidad medida por MAS en el grupo de EMTr activa, no observada en el grupo placebo. La escala SCI-SET no cambio de manera significativa en ninguno de los dos grupos.

- Análisis de correlación: La mejora en la puntuación del BMEI se correlaciona de manera significativa con la mejora en la velocidad de la marcha (T10M) en el grupo activo, no así en el grupo placebo. No existe una correlación entre los valores absolutos de las escalas de marcha y espasticidad. Las mejoras en la puntuación de las escalas de marcha no se correlacionan con el cambio de puntuación del SCI-SET en todos los tiempos de valoración en ambos grupos.

DISCUSION

Una de las funciones que más repercusión tiene en los pacientes que han sufrido una lesión medular y las secuelas que ello conlleva, es la pérdida parcial o total de su capacidad de marcha. Por ello, en los programas de rehabilitación dirigidos al paciente con una lesión medular se hace especial hincapié en la rehabilitación de la marcha. De esta manera, la utilización de diferentes técnicas, protocolos, uso de nuevas tecnologías y demás variables dependerá del centro encargado de conducir la rehabilitación del paciente, que dependiendo de su experiencia, conocimiento y medios utilizará los métodos más adecuados en cada momento para intentar conseguir los mejores resultados y de esta forma influir de forma significativa en la calidad de vida de estos sujetos.

Al añadir una nueva técnica en nuestra práctica clínica habitual, lo hacemos con el objetivo de mejorar nuestros resultados o si no es posible mejorarlos, obtenerlos de manera más eficiente. De la misma forma, dependiendo del tipo de centro rehabilitador, volumen de pacientes atendidos y personal disponible, el uso de nuevas tecnologías y/o métodos rehabilitadores también puede influir de manera positiva en un mejor aprovechamiento de los recursos disponibles.

De esta forma, con el objetivo principal de mejorar la calidad de vida de nuestros pacientes, buscamos nuevas herramientas rehabilitadoras que permitan recuperar o mejorar esa capacidad de marcha que nuestra población de lesionados medulares tiene alterada en mayor o menor medida.

Entre estas nuevas herramientas rehabilitadoras, la aparición de sistemas electromecánicos dirigidos al entrenamiento de la marcha, como son el Lokomat® y el Gait Trainer GT I®, supone un aliciente en cuanto a poder disponer de nuevas técnicas que nos permitan alcanzar una mejora en la capacidad de marcha de nuestros pacientes. Pero para poder definir su papel adecuado en el campo de la rehabilitación, debemos realizar estudios objetivos que nos permitan concretar sus indicaciones de la manera más correcta. Para ello realizamos un estudio en pacientes con una lesión medular utilizando estos dos sistemas (Lokomat® o Gait Trainer GT I®) con una frecuencia y duración del entrenamiento determinadas. La respuesta al entrenamiento la valoramos utilizando escalas clínicas y funcionales ya establecidas que nos permiten objetivar las ganancias obtenidas. Como otra herramienta de valoración de resultados utilizamos también técnicas neurofisiológicas, en concreto examinamos la modulación del reflejo H por estimulación magnética transcraneal (EMT) y su evolución tras el entrenamiento de la marcha. Esta EMT además de como herramienta diagnostica puede ser utilizada de forma terapéutica en su modalidad repetitiva (EMTr). De esta forma nos planteamos el uso combinado de la rehabilitación de la marcha con EMTr de alta frecuencia y su influencia en los resultados funcionales del paciente.

Durante los años 90, los estudios del grupo de Barbeau[13,14] en Canadá y Wernig[15,16,17] en Alemania, refuerzan la idea de que el entrenamiento de la marcha de los pacientes con una lesión medular utilizando sistemas de cinta sin fin con suspensión parcial del peso corporal, suponen una ventaja frente al entrenamiento convencional empleado hasta entonces. Con esta premisa, aparecen los sistemas electromecánicos como el Lokomat® y el Gait Trainer GT I® y los estudios iniciales[21,22] con sus prometedores resultados. Sin embargo en el año 2006 el grupo de Dobkin[48] presenta los resultados de un estudio aleatorizado del entrenamiento de la marcha utilizando la cinta sin fin con la suspensión parcial del peso corporal, frente al entrenamiento "convencional" en el que el paciente entrena la marcha erguido con ayuda de los terapeutas. En este estudio no encuentran diferencias en cuanto a los resultados finales de la capacidad de marcha obtenidos en ambos grupos de tratamiento, poniendo en duda la supuesta eficacia del uso de la cinta sin fin con la suspensión parcial del peso corporal. Lo que parece que queda claro es la importancia del entrenamiento de forma que el paciente esté erguido con su peso corporal sobre las extremidades inferiores, y el hecho de asistir este proceso utilizando medios manuales (terapeutas) o mecánicos (cinta sin fin y arnés para suspensión del peso corporal) no sea el factor determinante en el resultado final del proceso. No cabe duda que se plantea el dilema del volumen de personal utilizado para uno u otro medio de entrenamiento y los costes del personal frente al de los medios mecánicos utilizados. De todas formas este estudio no hace una referencia directa a los sistemas electromecánicos, aunque estos se basan en la supuesta efectividad de la cinta sin fin y la suspensión parcial del peso corporal, que sí son objeto del estudio.

En una revisión sistemática de la literatura sobre el uso del entrenamiento de la marcha con suspensión parcial del peso corporal en sujetos con una lesión medular incompleta, realizada por Wessels y colaboradores[49], publicada en el 2010, de un total de 17 estudios realizados, encuentran 2 en los que se aprecia una mejoría en el apartado de locomoción de la escala de medida de independencia funcional FIM en el grupo de entrenamiento convencional, pero acaban concluyendo en la necesidad de más estudios para clarificar la efectividad de un sistema frente a otro.

En otra revisión de la literatura, pero esta vez realizada con el uso de sistemas electromecánicos para la rehabilitación de la marcha en el lesionado medular, realizada por Swinnen[50] y colaboradores en el 2010, encuentran 5 estudios utilizando el Lokomat® y uno con el Lokohelp®, en los que aparecen alguna mejora en el balance muscular y velocidad de marcha, pero dado el tamaño de las muestras y la heterogeneidad de los entrenamientos utilizados concluyen que no hay evidencia suficiente para poder decir que mejoran la capacidad de marcha en mayor medida que otros medios de entrenamiento, y que son necesarios más estudios para clarificar su mayor eficacia.

De esta manera, durante los últimos 20 años se han desarrollado estos modelos de entrenamiento de la marcha, por un lado la suspensión parcial de peso corporal y cinta sin fin, y posteriormente los sistemas electromecánicos que simulan la marcha. Durante este tiempo se han realizado diversos estudios que intentan confirmar su mayor eficacia frente a las terapias convencionales. A pesar del esfuerzo en los estudios realizados, no se ha podido llegar a un consenso en cuanto a un beneficio claro de estos sistemas y unos criterios claros de aplicación. Dobkin y Duncan[51] reflexionan sobre estos aspectos en su artículo del 2012. Dada la falta de evidencia científica en el uso de este tipo de sistemas para el entrenamiento de la marcha, justifican su uso sólo en ensayos de investigación, recomendando que la práctica clínica habitual continúe con las terapias convencionales.

Lo que no queda claro es lo que se entiende hoy en día por "terapia convencional" del entrenamiento de la marcha. Se entiende que no se utilizan sistemas para desgravar el peso del paciente, ni otros sistemas que movilicen las extremidades del sujeto, es decir, los terapeutas se encargan de realizar este trabajo. Pero no hay un criterio en el que se especifique el número de terapeutas que deben intervenir durante el entrenamiento, ni la duración de cada entrenamiento, ni la frecuencia del mismo, ni la extensión en el tiempo de este proceso. Además la variabilidad de esta terapia convencional es enorme entre los distintos centros de neuroreabilitación. Por lo tanto, la idea de descartar estas nuevas tecnologías que intentan que el proceso de mejora de la capacidad de marcha de los sujetos con una lesión medular sea lo más eficiente posible, no debe tomarse sin tener en cuenta los aspectos de organización que cada centro conlleva, y en el que el número de pacientes atendidos, y la disponibilidad de recursos juegan un papel fundamental.

Sin embargo, después de la reflexión de Dobkin, Alcobendas[52] y colaboradores publican a finales del 2012 un estudio aleatorizado comparando el uso del Lokomat® con la terapia convencional en un grupo de 80 sujetos con una lesión medular incompleta. En este caso encuentran que el grupo de sujetos entrenados con el Lokomat® alcanzan un balance muscular de las extremidades inferiores mayor que en el grupo control, así como un menor uso de ortesis y ayudas técnicas, reflejado en la escala de WISCI II. Sin embargo en la velocidad de marcha no encuentran diferencias entre ambos grupos. De manera que en este caso, en algunos aspectos importantes de la marcha, se obtiene una mayor ventaja con el uso de los sistemas electromecánicos frente al tratamiento conservador.

El trabajo de esta tesis es una aportación más en la discusión sobre las ventajas de los sistemas electromecánicos de entrenamiento de la marcha en el lesionado medular. Presentamos una serie de artículos acerca de nuestro proceso investigador en esta materia durante estos últimos años. Como novedades importantes además de aportar más información acerca del Lokomat®, presentamos resultados de otro sistema electromecánico poco utilizado en el lesionado medular, como es el Gait Trainer GT I®; asimismo incluimos las valoraciones neurofisiológicas como un parámetro objetivo del análisis de resultados, en concreto examinamos la modulación del reflejo H por EMT; y finalmente añadimos el uso de la EMTr de alta frecuencia combinado con la rehabilitación de la marcha como una técnica novedosa para influir de manera positiva en una mayor calidad de marcha en el lesionado medular.

En nuestro primer artículo, en el que valoramos el uso de los sistemas electromecánicos Lokomat® y Gait Trainer GT I®, aportamos una serie de resultados que contribuyen a una mejor selección de pacientes que pueden beneficiarse de estos sistemas. En primer lugar observamos que ambos sistemas son adecuados para el entrenamiento de la marcha en el lesionado medular, sin objetivar en las ganancias obtenidas un predominio de un sistema sobre el otro. En cuanto al tipo de lesión medular, es conocido que las lesiones medulares incompletas motoras (ASIA C y D) tienen un mejor pronóstico[53,54], y es en este grupo de pacientes en el que las ganancias obtenidas son de mayor relevancia, y por lo tanto los que más se benefician de este tipo de entrenamiento. Sin embargo también observamos que en un grupo concreto de lesiones medulares motoras completas (ASIA A y B), había una mejoría, aunque en menor medida. Este grupo se caracterizaba por tener al inicio algo de movilidad voluntaria en los segmentos L2 y L3 (flexión de cadera y extensión de rodilla, respectivamente), movilidad necesaria para una marcha efectiva[55], y la mejora observada en cuanto a balance muscular, se centraba en esos segmentos con movilidad inicial. Por lo tanto, sujetos con estas características determinadas, a pesar de considerarse lesiones motoras completas por definición, también pueden beneficiarse de este tipo de entrenamiento.

El tiempo desde la lesión es uno de los factores más influyentes en cuanto a la recuperación del lesionado medular. Es conocido que las mayores ganancias se obtienen en las fases iniciales tras la lesión[56], y es en este grupo, en concreto en los primeros 6 meses desde la lesión, cuando encontramos los mayores beneficios del uso de este tipo de entrenamiento. Esta ventana terapéutica debe ser aprovechada y dedicar los mayores esfuerzos en cuanto a rehabilitación durante este periodo.

Otro aspecto interesante es la causa de la lesión. Esta puede ser categorizada en dos grandes grupos, traumática y no traumática. Los resultados funcionales en ambos grupos han sido estudiados y se observa que ambos alcanzan resultados similares[57,58]. Nosotros también encontramos que ambos grupos se benefician de igual manera con este tipo de entrenamiento, por lo tanto la etiología no debe ser considerada criterio de exclusión alguno. Asimismo, analizando otros factores como la edad y el sexo, tampoco encontramos diferencias.

En cuanto al nivel de la lesión, Walters y colaboradores[59] observaron que los pacientes con una paraplejia incompleta alcanzaban una capacidad de marcha en la comunidad en un porcentaje mayor que los tetrapléjicos incompletos (76% vs 46%). Sin embargo en nuestro estudio encontramos que ambos grupos obtienen unos beneficios similares, por lo que ambos grupos son buenos candidatos para este tipo de entrenamiento.

Desde hace años el grupo *European Multicenter Study about Human Spinal Cord Injury*[60] (EM-SCI), viene recogiendo datos acerca de la evolución de los lesionados medulares traumáticos durante el primer año tras la lesión. En estos centros europeos de rehabilitación del lesionado medular, se obtienen datos acerca de la exploración neurológica según el ASIA, pruebas funcionales y de neurofisiología. Muchas de estas pruebas son las mismas que hemos recogido nosotros durante nuestro estudio, por lo que nos pareció interesante comparar un grupo homogéneo de lesiones traumáticas de nuestro estudio con este grupo pseudo-control del EM-SCI, que supone ser la evolución natural de un lesionado medular en Europa tras realizar su proceso rehabilitador en alguno de los centros de rehabilitación del grupo EM-SCI. Al hacer la comparación solicitamos datos de los centros que no disponían de sistemas electromecánicos. Con las limitaciones que esta comparación conlleva, observamos que los sujetos que participaron en el entrenamiento de la marcha con sistemas electromecánicos en nuestro centro obtuvieron unos resultados mejores que los sujetos del grupo EM-SCI. En concreto, los sujetos ASIA D mostraron un mayor grado de recuperación en los 3 aspectos analizados, balance muscular de extremidades inferiores, escala de marcha WISCI II y velocidad de marcha. Asimismo los sujetos ASIA C mostraron una mayor ganancia en el balance muscular de las extremidades inferiores. Por lo tanto, y recordando las limitaciones de esta comparación, los resultados obtenidos con el entrenamiento de la marcha con sistemas electromecánicos superan las expectativas de recuperación en relación a los resultados esperados con el entrenamiento convencional según los datos del EM-SCI.

De esta manera podemos concluir que los sistemas electromecánicos son una herramienta segura y que puede contribuir de manera positiva al proceso rehabilitador del entrenamiento de la marcha del lesionado medular. Serán aquellos sujetos con una lesión medular incompleta motora y un inicio del entrenamiento temprano, los que más se benefician de su uso.

Como otra forma de interpretación de resultados, tenemos las técnicas neurofisiológicas, y en concreto el reflejo H y su modulación por la estimulación magnética transcraneal. En sujetos sanos, la amplitud del reflejo H tras la EMT, muestra una fase temprana entre los 10-30 ms, y una fase tardía entre los 60-130 ms[61,62,63]. Según Valls-Solé y colaboradores[62], esta fase inicial podría ser el resultado de la generación de un potencial postsinaptico excitatorio a nivel de la α-motoneruona, mientras que el mecanismo de la segunda fase no está claro hoy en día. Wolfe y colaboradores[64] muestran una facilitación parcial del reflejo H en sujetos con una lesión motora incompleta. Dicho hallazgo es comparable a nuestros resultados, en los que durante la valoración inicial, antes de comenzar el entrenamiento con sistemas electromecánicos, los sujetos muestran una facilitación parcial del reflejo H por EMT. La facilitación del reflejo H por EMT incrementa tras el entrenamiento de la marcha en aquellos sujetos con lesiones más recientes, en concreto en el grupo de sujetos con menos de 3 meses desde la lesión. Esto sugiere que el tiempo desde la lesión es una de las variables más importantes a tener en cuenta en cuanto a la plasticidad neuronal que acontece en la medula espinal, lo que lleva a una mejor modulación del reflejo H.

En este grupo de sujetos que iniciaron el entrenamiento de la marcha antes de los 3 meses, aparte de obtener una mayor facilitación del reflejo H por EMT, obtuvieron una mejoría en las 3 variables clínicas estudiadas (balance muscular de extremidades inferiores, escala de marcha WISCI II y velocidad de marcha), siendo de forma claramente significativa las ganancias en cuanto a velocidad de marcha en comparación con el grupo de más de 3 meses de evolución.

Aquellos sujetos del grupo de menos de 3 meses desde la lesión que tuvieron mejores resultados clínicos, obtuvieron también una mayor facilitación del reflejo H, existiendo una clara correlación entre la facilitación del reflejo H por EMT y la escala de marcha WISCI II en este grupo de menos de 3 meses de evolución. De nuevo nos encontramos con el concepto de “ventana terapéutica” que refuerza la idea, en este caso desde el punto de vista neurofisiológico, de la importancia del inicio temprano del proceso rehabilitador.

En cuanto a las vías neuronales involucradas en este proceso, la vía rápida corticoespinal parece mediar esta fase temprana de facilitación, lo cual ha sido previamente descrito por Wolfe[64]. La facilitación tardía no tiene una explicación tan clara, existiendo distintas hipótesis, en las que intervienen proyecciones corticobulboespinales[65], aferencias periféricas[66] o una suma de influencias corticoespinales, del tronco cerebral y periféricas[67].

De esta manera con la modulación del reflejo H por EMT encontramos una herramienta neurofisiológica, que de una forma cuantitativa aporta medidas del control supraespinal sobre los reflejos de las extremidades inferiores en el lesionado medular.

Como hemos comentado anteriormente, la estimulación magnética transcraneal podemos utilizarla en su forma repetitiva (EMTr) como herramienta terapéutica. En nuestro estudio utilizamos la EMTr de alta frecuencia junto a la rehabilitación de la marcha como una forma de potenciar los resultados funcionales del paciente. De esta forma conseguimos que el grupo de sujetos que reciben esta intervención alcancen una mejoría significativa en el balance muscular de las extremidades inferiores, la velocidad de marcha y la espasticidad, en comparación con el grupo placebo. Belci y colaboradores[47] también encontraron una mejoría en el balance muscular global y en la función de las extremidades superiores en un grupo reducido de 4 sujetos con una tetraplejia incompleta tras aplicar la EMTr de alta frecuencia sobre el vertex durante 5 días. Como mecanismo implicado en la mejora de la función motora, se ha visto que existe un aumento del metabolismo de la glucosa a nivel local inmediatamente después de la estimulación, lo que sugiere que la EMTr puede inducir un aumento en la actividad neuronal en el área motora estimulada[68]. Asimismo, la magnitud y duración de los efectos parecen depender de la intensidad y el número total de estímulos aplicados, de forma que cuanto mayor es el periodo de EMTr, más consistente y persistente son los cambios en la excitabilidad corticoespinal[69,41,70]. El concepto de que la facilitación de la excitabilidad corticoespinal inducida por la EMTr de alta frecuencia pueda perdurar en el tiempo, ha sido introducido por varios autores[43,71,72]. Belci y colaboradores[47] en su estudio con EMTr en lesionados medulares propone que la EMTr podría reducir la inhibición corticoespinal, lo que podría inducir una mejora motora en el lesionado medular. Asimismo, Kumru y colaboradores[43] plantean el concepto de que la mejora motora y la disminución de la espasticidad con la EMTr en el lesionado medular puedan deberse al aumento de las proyecciones corticoespinales descendentes y/o a la reducción en la inhibición corticoespinal. Este concepto de que el aumento de las proyecciones corticoespinales puede inducir una mejora en la espasticidad también ha sido propuesto por Centone y colaboradores[71].

El tiempo en el que la EMT es aplicada en relación a la tarea de entrenamiento es crucial en el efecto esperado en relación a la estimulación[73,74], de forma que la EMT es aplicada habitualmente inmediatamente antes de la tarea. En nuestro estudio la EMTr se utilizó antes de iniciar el entrenamiento de la marcha, siempre con menos de 30 minutos de intervalo con el fin de obtener el mayor beneficio con el entrenamiento de la marcha.

Otro factor importante cuando aplicamos una técnica como la EMTr de alta frecuencia, es la duración de sus efectos en el tiempo tras la estimulación. Nuestro estudio realiza un seguimiento a las 2 semanas tras la estimulación, y en ese momento las ganancias obtenidas se mantienen en el tiempo. Esta duración de los efectos de la EMTr ha sido previamente descrita tanto en sujetos sanos[75], como en lesionados medulares[43], esclerosis multiple[71] e infarto cerebral[72]. Un posible mecanismo implicado en la permanencia a largo plazo de los efectos obtenidos tras la estimulación es el concepto de "potenciación a largo plazo"[76], de manera que la transmisión de señales entre dos neuronas se ve aumentada y es de mayor duración en el tiempo cuando son estimuladas de forma sincronizada. Cuando estos episodios de "potenciación a largo plazo" se realizan de forma repetida, se llega a una remodelación con un aumento de las sinapsis activas[77,78].

De esta forma podemos concluir que la EMTr de alta frecuencia es una de las técnicas de estimulación cerebral no invasiva que combinada con la rehabilitación de la marcha, muestra un gran potencial como herramienta rehabilitadora para optimizar los resultados esperados. Es interesante seguir desarrollando este técnica para poder determinar la dosis y duración más adecuada de la estimulación y como perpetuar los efectos obtenidos a más largo plazo.

CONCLUSIONES

1. Hemos presentado resultados que avalan el uso de los sistemas electromecánicos para el entrenamiento de la marcha en el lesionado medular en la práctica clínica, y que estos sistemas pueden utilizarse como alternativa o como complemento al entrenamiento convencional de la rehabilitación de la marcha.

2. Los resultados apoyan el uso preferente de estos sistemas en pacientes con una lesión motora incompleta y que los mayores beneficios se encuentran cuando se inicia el entrenamiento en las fases tempranas, dentro de los 6 primeros meses tras la lesión.

3. Los pacientes con una LM incompleta motora tienen alteraciones en el control de los reflejos espinales segmentarios, cuyo correlato neurofisiológico se encuentra en una disminución de la facilitación del reflejo H inducida por EMT (en la fase de 20 ms.).

4. La facilitación temprana (20 ms) del reflejo H por EMT aumenta en mayor medida tras la rehabilitación en aquellos pacientes que empezaron su entrenamiento con < 3 meses desde su lesión.

5. Existe una correlación positiva entre el incremento de facilitación del reflejo H por EMT y la mejora en la funcionalidad (WISCI II) tras el entrenamiento en aquellos pacientes con < 3 meses de evolución.

6. La modulación del reflejo H por EMT puede ser otra herramienta para la valoración de los lesionados medulares aportando medidas cuantitativas del control del cortex motor sobre los reflejos de las extremidades inferiores.

7. La EMTr asociada al entrenamiento de la marcha en sujetos con una lesión medular incompleta mejora el balance muscular de las EEII, la espasticidad y la velocidad de marcha. Las ganancias funcionales se mantienen por lo menos 2 semanas tras el tratamiento.

8. Se postula que el mecanismo a través del cual la EMTr produce las mejoras descritas en los sujetos con una lesión medular incompleta es a través de la facilitación de las proyecciones corticoespinales

9. Podemos considerar la EMTr como una herramienta prometedora en los programas de rehabilitación de la lesión medular.

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ABREVIACIONES

AIS: *American Spinal Injury Association Impairment Scale.* Escala de deficiencia de la asociación americana de la lesión medular.

ASIA: *American Spinal Injury Association.* Asociación americana de la lesión medular.

BMEI: Balance muscular de extremidades inferiores.

CPG: *Central Pattern Generator*. Generador de patrones centrales.

EMA-SPPC: Entrenamiento de la marcha asistida con soporte parcial del peso corporal.

EM-SCI: *European Multicenter Study about Spinal Cord Injury*. Estudio multicéntrico europeo acerca de la lesión medular.

EMT: Estimulación magnética transcraneal.

EMTr: Estimulación magnética transcraneal repetitiva.

MAS: *Modified Ashworth Scale*. Escala de Ashworth modificada.

SCI-SET: *Spinal Cord Injury Spasticity Evaluation Tool*. Escala de valoración de la espasticidad en el lesionado medular.

T10M: Test de los 10 metros.

TUG: *Time up and go*.

WISCI: *Walking index for spinal cord injury*. Escala de valoración de la marcha en el lesionado medular.