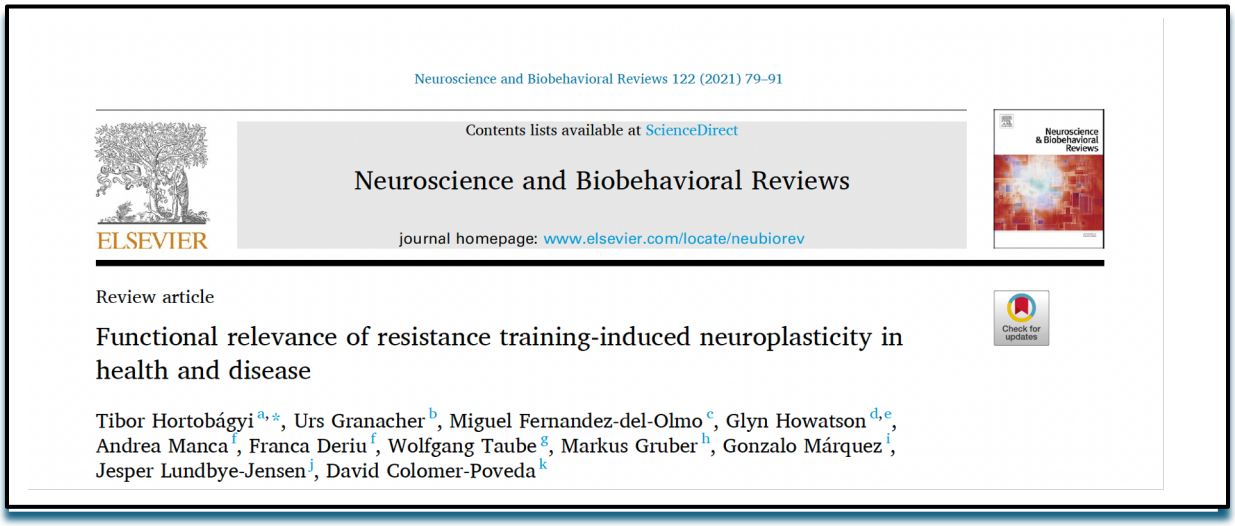

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Review article

Functional relevance of resistance training-induced neuroplasticity in health and disease

Tibor Hortobágyi [a,*], Urs Granacher [b], Miguel Fernandez-del-Olmo [c], Glyn Howatson [d,e], Andrea Manca [f], Franca Deriu [f], Wolfgang Taube [g], Markus Gruber [h], Gonzalo Márquez [i], Jesper Lundbye-Jensen [j], David Colomer-Poveda [k]

Introducción

El entrenamiento de fuerza induce aumentos rápidos y sustanciales en la fuerza muscular voluntaria. Tradicionalmente, estos incrementos iniciales se han atribuido a adaptaciones del sistema nervioso, bajo la idea de que los cambios neurales preceden a la hipertrofia muscular.

Sin embargo, a pesar de que esta explicación se ha convertido en un **dogma ampliamente aceptado**, la evidencia que respalda una relación funcional directa entre la neuroplasticidad inducida por el entrenamiento de fuerza y las mejoras en el rendimiento motor es **menos concluyente de lo que habitualmente se asume**.

El presente artículo corresponde a una revisión que publicamos en *Neuroscience & Biobehavioral Reviews*, una de las revistas de mayor impacto en neurociencia, y representa uno de los análisis más completos y críticos realizados hasta la fecha sobre este tema.

¿Por qué es relevante este artículo?

Esta revisión es especialmente relevante porque:

- Analiza **marcadores neurofisiológicos múltiples**, incluyendo EMG, estimulación nerviosa periférica, TMS, EEG y neuroimagen.
- Evalúa no solo cambios paralelos, sino **la asociación real entre adaptaciones nerviosas y mejoras funcionales**.
- Incluye poblaciones diversas: sujetos sanos, atletas, adultos mayores y pacientes neurológicos.
- Cuestiona interpretaciones históricas que han sido aceptadas sin una evaluación mecanicista rigurosa.

En lugar de asumir que los cambios neurales explican automáticamente las ganancias de fuerza, proponemos que muchos de estos cambios pueden ser **epifenómenos**, no necesariamente mediadores causales del rendimiento.

Principales hallazgos

De forma resumida, nuestra revisión muestra que:

- Las mejoras en la fuerza máxima y el rendimiento motor suelen ocurrir **sin una correlación consistente** con los cambios en los marcadores clásicos de neuroplasticidad.
- Muchos estudios informan cambios “en paralelo” (fuerza ↑, marcadores neurales ↑), pero **sin relación estadística o funcional clara** entre ellos.
- La evidencia es especialmente débil cuando se intenta explicar la **transferencia de la fuerza a tareas funcionales** como la marcha, el equilibrio o las actividades de la vida diaria.
- En poblaciones clínicas (ictus, Parkinson, esclerosis múltiple), las mejoras de fuerza **no garantizan mejoras funcionales**, lo que pone en cuestión el papel facilitador de la neuroplasticidad inducida por el entrenamiento de fuerza.

Implicaciones prácticas

Este trabajo invita a replantear:

- El uso indiscriminado del concepto de “adaptaciones nerviosas” como explicación causal.
- La necesidad de **mayor especificidad de tarea** en el diseño del entrenamiento.
- La importancia de combinar el entrenamiento de fuerza con tareas funcionales y de aprendizaje motor.
- El uso de **modelos de mediación causal**, en lugar de interpretaciones basadas solo en cambios paralelos.

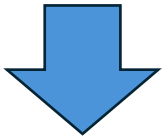
Sobre esta versión

Esta edición incluye:

- Traducción completa al español.
- Comentarios interactivos y aclaraciones conceptuales (**interactúa con los subrayados del documento**).

Su objetivo es facilitar una **lectura crítica**, accesible y aplicada de uno de los artículos más influyentes de los últimos años en este campo.

Que lo disfrutes y no dudes en contactar conmigo para cualquiera aclaración



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Artículo de revisión

Relevancia funcional de la neuroplasticidad inducida por el entrenamiento de fuerza en la salud y la enfermedad

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Haz click sobre el subrayado para obtener más información

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Resonancia Magnética Funcional (fMRI)
Enfermedad de Parkinson (EP)
Esclerosis Múltiple (EM)
Ictus (IC)

ABSTRACT

Las contracciones musculares voluntarias repetitivas, monótonas y esforzadas, realizadas durante unas pocas semanas (es decir, el entrenamiento de fuerza), pueden aumentar sustancialmente la fuerza voluntaria máxima en la tarea practicada y también pueden aumentar el rendimiento motor grueso. Este aumento del rendimiento motor suele ir acompañado de adaptaciónes neuroplásticas en el sistema nervioso central. Si bien los datos históricos han asignado relevancia funcional a dichas adaptaciones inducidas por el entrenamiento de fuerza, esta afirmación aún no se ha examinado sistemática y críticamente en el contexto del rendimiento motor a lo largo de la vida, tanto en la salud como en la enfermedad. Una revisión de la activación muscular, la estimulación cerebral y nerviosa periférica, y los datos de pruebas de imagen revelaron que los aumentos en el rendimiento motor y la neuroplasticidad tienden a estar desacoplados, lo que hace que un vínculo mecanicista entre la neuroplasticidad y el rendimiento motor no sea concluyente. Recomendamos nuevos enfoques, incluyendo modelos analíticos de mediación causal y basados en hipótesis, para corroborar la relevancia funcional de la neuroplasticidad inducida por el entrenamiento de resistencia en las mejoras de la función motora gruesa a lo largo de la vida, tanto en la salud como en la enfermedad.

1. Introducción

Una serie de estudios históricos introdujeron la idea de que las modificaciones estructurales y funcionales en circuitos específicos del cerebro y la médula espinal (es decir, neuroplasticidad) contribuyen al rápido aumento inicial de la fuerza muscular voluntaria máxima (MVC) después de un período de entrenamiento de fuerza (EF) en humanos sanos (Sale y MacDougall, 1981; Sale et al., 1983, 1982). En términos generales, la neuroplasticidad es "*la capacidad del sistema nervioso de responder a estímulos intrínsecos y extrínsecos reorganizando su estructura, función y conexiones*" (p. 1592, (Cramer et al., 2011). La ganancia en la función, es decir, el aumento en la fuerza MVC es una adaptación positiva al EF como resultado de modificaciones en el comando neural y la activación del músculo. Una figura en una revisión adoptada por numerosos libros de texto representa los roles relativos de las adaptaciones neurales y musculares al EF (Fig. 11 en (Sale, 1988). La figura conceptualiza un aumento inicial brusco en las contribuciones del sistema nervioso a las ganancias de fuerza, que se estabilizan después de unas pocas semanas de EF cuando la hipertrofia muscular se convierte en el factor determinante de las ganancias de fuerza.

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Tabla 1
Definición de términos clave y marcadores de plasticidad.

Key term (abbreviation)	Definition
Corticospinal excitability, CSE	Probabilidad y magnitud de las respuestas a la estimulación magnética transcraneal de las estructuras excitables del tracto corticoespinal, desde la corteza motora primaria hasta el músculo.
Gross motor performance	Actividades funcionales multiarticulares como caminar, saltar y lanzar.
Hoffman reflex, H-reflex	Respuesta a la estimulación eléctrica nerviosa periférica débil: estimación de la excitabilidad de las motoneuronas espinales e inhibición presináptica aferente Ia.
Maximal compound muscle action potential, Mmax	Respuesta a la estimulación eléctrica nerviosa periférica de máxima intensidad, que representa la suma de los potenciales de acción dispersos de las unidades motoras bajo la zona de un electrodo de recodificación en la superficie de la piel.
Maximal voluntary contraction force, MVC force	Fuerza generada durante una contracción muscular de esfuerzo máximo en una sola articulación contra una resistencia, con o sin retroalimentación continua.
Motor unit discharge rate	Frecuencia con la que las unidades motoras descargan potenciales de acción durante una contracción muscular.
Motor unit recruitment	Número de unidades motoras activas durante una contracción muscular.
Movement related cortical potentials, MRCP	Potenciales superficiales negativos detectados en el cuero cabelludo durante movimientos voluntarios que reflejan actividad cortical.
Neuroplasticity / Neural adaptations	Modificaciones estructurales y funcionales en circuitos cerebrales y espinales específicos.
Resting-state connectivity	Asociaciones entre las fluctuaciones en la señal hemodinámica de las regiones cerebrales.
Short-interval intracortical inhibition	Respuesta a la estimulación magnética transcraneal de pulsos pareados, que refleja la eficacia de la inhibición intracortical mediada por neuronas intracorticales GABA-α inhibitorias de bajo umbral.
Silent Period	Respuesta a la estimulación magnética transcraneal de pulso único, que refleja la eficacia de la inhibición mediada por neuronas intracorticales GABA-β.
Surface electromyograph-ic activity, sEMG	Suma de los potenciales de acción descargados por las unidades motoras reclutadas bajo el territorio de los electrodos EMG durante una contracción muscular.
Volitional wave, V-wave	Respuesta a un nervio periférico de intensidad supramáxima durante una contracción voluntaria máxima, que refleja la salida de la motoneurona espinal eferente al músculo.
Voluntary activation, VA	Respuesta calculada a la estimulación nerviosa periférica de intensidad máxima, con una duración de milisegundos, en reposo y durante la contracción muscular voluntaria máxima, que refleja la capacidad del músculo esquelético para activarse mediante una orden voluntaria.

La revisión afirma que "…*los aumentos en la fuerza máxima y la tasa de desarrollo de la fuerza están asociados con una mayor activación de los músculos motores primarios*" (p. s135, (Sale, 1988). Sale revisó posteriormente este esquema y postuló que las adaptaciones musculares inducidas por el entrenamiento de fuerza (hipertrofia) ocurren ya después de una sesión de entrenamiento de fuerza en sujetos no entrenados, como lo demuestra el daño a las fibras musculares y una estimulación posterior de la síntesis de proteínas (Fig. 11, p. 305) (Sale, 2003).

Desde la publicación de estos artículos seminales hace más de 30 años, casi 20 revisiones han destacado varias adaptaciones estructurales y funcionales a nivel espinal y supraespinal con un papel en las ganancias de fuerza durante las primeras 2 a 12 semanas de EF (Tabla 1, Figura 1) (Aagaard, 2003, 2018; Aagaard et al., 2010; Carroll et al., 2001, 2011; Cormie et al., 2011a, b; Duchateau et al., 2006; Enoka, 1988; Folland y Williams, 2007; Gabriel et al., 2006; Hedayatpour y Falla, 2015; Hor-tob'agyi y Maffiuletti, 2011; Kidgell et al., 2017; Kidgell y Pearce, 2011; Kraemer et al., 1988; Markovic y Mikulic, 2010; Mason et al., 2019; Oranchuk et al., 2019; Siddique et al., 2019). Se suponía que estas adaptaciones aumentan la fuerza de la CVM al mejorar la activación neuronal de la maquinaria contráctil del músculo esquelético. Sin embargo, gran parte de la evidencia de adaptaciones neuronales es indirecta y los mecanismos específicos

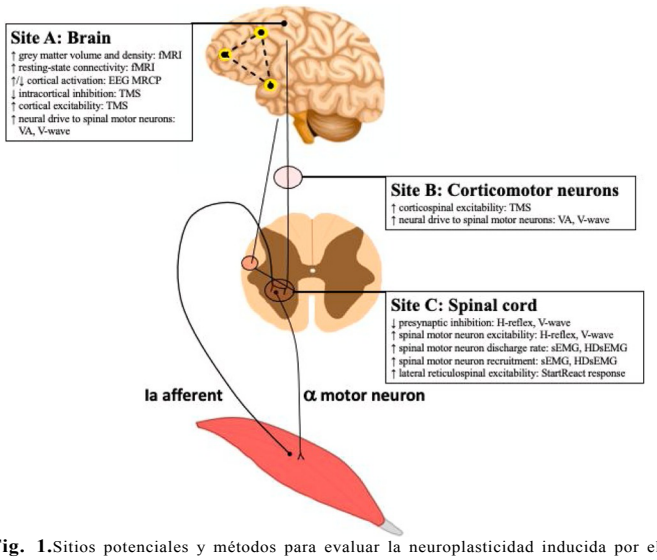


Fig. 1. Sitios potenciales y métodos para evaluar la neuroplasticidad inducida por el entrenamiento de resistencia. Abordamos la neuroplasticidad inducida por el entrenamiento de resistencia y su relevancia funcional en: Sitio A en las secciones 2.2, 2.3, 2.4 y 2.5; Sitio B en las secciones 2.2, 2.3 y 2.4, y en el Sitio C en las secciones 2.1 y 2.3. Las líneas discontinuas simbolizan la conectividad entre las áreas frontales (cognitivas), motoras y temporales (memoria) que se sabe que se modifican por el entrenamiento de resistencia. Las flechas verticales en el texto indican la dirección de los cambios (aumento, disminución, sin cambios). Este modelo simplificado no muestra varios sitios potenciales adicionales donde podrían ocurrir adaptaciones al entrenamiento de resistencia, como las conexiones corticorreticulares, las conexiones reticulares recíprocas, las proyecciones reticuloespinales a las interneuronas, las proyecciones corticoespinales a las interneuronas y las sinapsis corticomotoneuronales (véase Glover y Baker, 2020). fMRI, resonancia magnética funcional; EEG MRCP, potenciales corticales relacionados con el movimiento electroencefalográfico; TMS, estimulación magnética transcraneal; VA, activación voluntaria; onda V, onda voluntaria evocada por estimulación nerviosa periférica; reflejo H, reflejo de Hoffman; sEMG, electromiografía de superficie; HDsEMG, sEMG de alta densidad.

siguen siendo difíciles de determinar. Tampoco existe consenso sobre los mecanismos individuales ni evidencia sobre la importancia relativa de los diversos mecanismos adaptativos.

Críticamente para numerosas poblaciones como los atletas, el número cada vez mayor de adultos mayores y pacientes, la pregunta no abordada y oportuna es ¿cómo son funcionalmente relevantes las "adaptaciones neuronales"? Proponemos que la causa raíz de la falta de progreso en el campo es una interpretación y una confianza excesivas en los datos que muestran, en su mayor parte, cambios meramente paralelos en los índices de neuroplasticidad y las medidas de fuerza MVC o rendimiento motor grueso multiarticular. Nuestra hipótesis es que los cambios paralelos en los resultados neuronales y la fuerza MVC

o el rendimiento motor pueden ocurrir sin una asociación significativa o estadísticamente significativa. Sospechamos que las razones de los cambios no correlacionados después del EF son: 1) La especificidad de la tarea de las mediciones en reposo es baja en relación con el entrenamiento a altas fuerzas, pero técnicamente es difícil evaluar de manera confiable la neuroplasticidad durante las mediciones MVC y la interpretación de dichos datos es compleja (Lundbye-Jensen et al., 2005); 2) Selección de solo una o dos variables que cuantifiquen la neuroplasticidad, ninguna de las cuales por sí sola es informativa versus un análisis de red o un enfoque multivariado se esperaría conceptualmente que predijera aumentos en la fuerza MVC, y 3) Los cambios en la neuroplasticidad y la fuerza MVC ocurren con diferentes cursos de tiempo durante y después del EF (Csapo et al., 2011; Kubo et al., 2010) y en sitios que se han pasado por alto (Baker y Pérez, 2017; Choudhury et al., 2019; Fernández-Del-Olmo et al., 2014; Glover y Baker, 2020).

Si la asociación entre los aumentos de fuerza de la MVC inducidos por el EF y los cambios en los marcadores de neuroplasticidad es baja, no sorprende que dichas asociaciones sean casi inexistentes entre los cambios en las medidas de neuroplasticidad y los aumentos en el rendimiento motor grueso, como caminar, saltar y lanzar.

De hecho, hay escasez de estudios que examinen cómo las habilidades físicas recién adquiridas (es decir, el aumento de la fuerza MVC) pueden incorporarse, por ejemplo, en la marcha de adultos mayores y pacientes, permitiéndoles caminar más rápido y con seguridad (Beijersbergen et al., 2013). La neuroplasticidad asociada con el entrenamiento de fuerza (EF) sería funcional si actuara como mecanismo facilitador en los aumentos del rendimiento motor grueso en adultos sanos y en pacientes con enfermedad de Parkinson (PcPD), esclerosis múltiple (PcMS) y accidente cerebrovascular (PcS). Una posible razón para las correlaciones débiles o inexistentes entre los cambios en la fuerza MVC y el rendimiento motor grueso es la baja especificidad de la tarea entre los ejercicios de EF uniarticulares y las tareas de motor grueso compuestas por movimientos multiarticulares. El entrenamiento de fuerza monoarticular puede aumentar el tamaño y la fuerza muscular, pero podría no ser tan efectivo para aumentar el rendimiento motor grueso como lo serían los ejercicios que involucran movimientos multiarticulares que imitan de cerca la estructura espaciotemporal y los patrones de activación muscular de caminar, correr, saltar o movimientos de alcance con los brazos (Kraemer et al., 2002; Kraemer y Ratamess, 2004). En otras palabras, si el entrenamiento de fuerza incluye principalmente ejercicios monoarticulares, la transferencia a movimientos funcionales como caminar, correr y saltar es limitada, lo que puede explicarse mediante el principio de especificidad del entrenamiento. Este principio denota que el ejercicio de entrenamiento de fuerza aplicado debe asemejarse a la tarea de movimiento funcional para aumentar la probabilidad de transferir las ganancias de fuerza relacionadas con el entrenamiento de fuerza a la función (Reilly et al., 2009). Por lo tanto, existe la necesidad de pasar al siguiente nivel, es decir, más funcional, para comprender la relación entre las adaptaciones neuronales al entrenamiento de fuerza, los cambios potenciales en la función motora gruesa y los mecanismos subyacentes.

El propósito de esta revisión fue examinar 1) si las variaciones individuales en las ganancias inducidas por el EF en la fuerza MVC están asociadas con variaciones individuales en índices específicos de neuroplasticidad y 2) si dicha relación subyace a las mejoras en la fuerza MVC y, más ampliamente, en la función motora gruesa multiarticular en atletas, adultos mayores y pacientes. Claramente, la correlación no es causalidad. Sin embargo, argumentamos que la determinación de cambios correlativos llenaría el vacío en el conocimiento actual que se basa simplemente en cambios paralelos en los índices de neuroplasticidad y los resultados conductuales del EF. Una escasez crítica en la investigación previa es la falta de análisis correlativos de los cambios en los resultados conductuales (fuerza MVC, rendimiento motor) y medidas de neuroplasticidad subyacente.

Una forma de abordar esta brecha de conocimiento es mediante análisis de mediación causal que buscan obtener estimaciones sin factores de confusión de los efectos directos e indirectos del EF sobre el rendimiento motor (Zhang et al., 2016). En el contexto actual, la mediación es el proceso mediante el cual el EF provoca aumentos en el rendimiento motor. La hipótesis no probada es que parte o la totalidad del efecto total del EF sobre el rendimiento motor opera a través de un mediador, es decir, la neuroplasticidad. El efecto directo es el efecto del EF sobre el rendimiento motor sin el efecto del mediador. La vía indirecta es el efecto del EF sobre el resultado que opera a través de mediadores. Tras un número creciente de intentos utilizando análisis de mediación causal en kinesiología (Condello et al., 2019, 2016; Condello et al., 2017; Forte et al., 2013; Jekauc et al., 2017; Marcos-Pardo et al., 2020; Mavros et al., 2017; Tolla´r et al., 2019a, 2020), proporcionamos ejemplos ilustrativos de este enfoque para recomendar un examen más sistemático, mecanicista e impulsado por hipótesis de la relevancia funcional de la neuroplasticidad inducida por EF en la mejora del rendimiento motor en la salud y la enfermedad. Primero, examinamos la evidencia de la asociación entre los índices de neuroplasticidad informados con mayor frecuencia y los aumentos en la fuerza MVC generada por los músculos en una sola articulación. A continuación, revisamos la evidencia de cómo las adaptaciones neuronales al EF podrían mediar mejoras en la función motora gruesa en atletas, adultos mayores y grupos seleccionados de pacientes con discapacidades de movilidad. En cuanto a la inclusión de una población tan diversa, postulamos que la radioterapia de 2 a 12 semanas puede reducir la debilidad muscular mediante la inducción de neuroplasticidad, lo que aumenta la comprensión de la relevancia funcional de dichas adaptaciones neuronales, aplicable a todos los participantes en intervenciones de radioterapia, independientemente de su historial clínico. Concluimos con recomendaciones para futuras investigaciones y, con base en datos experimentales extraídos de artículos individuales incluidos en revisiones, proponemos modelos de ecuaciones estructurales mecanicistas basados en la evidencia que actualizan el modelo descriptivo clásico de Sale (Sale, 1988, 2003). Este modelo permite vincular causalmente los cambios inducidos por EF en los marcadores de neuroplasticidad y el rendimiento motor, como se revisó en detalle anteriormente (Nuzzo et al., 2019a; Steele et al., 2020; Tolla´r et al., 2019a).

2. Relevancia funcional de la plasticidad inducida por el entrenamiento de fuerza y la MVC

En este apartado, examinamos los cambios inducidos por el EF en los marcadores de neuroplasticidad que subyacen al aumento de la fuerza de la MVC. Los marcadores de activación muscular incluyen la actividad electromiográfica de superficie (sEMG) y la activación voluntaria (AV), las respuestas a la estimulación nerviosa periférica (reflejo Hoffman o H, onda voluntaria o V), las respuestas a la estimulación cerebral magnética transcraneal (EMT) y las pruebas de imagen (PET, fMRI).

2.1. Activación muscular: actividad sEMG y MVC

La fuerza MVC es el resultado de la fuerte activación de los músculos motores primarios individuales que forman el grupo muscular agonista, la desactivación coordinada de los músculos individuales que forman el grupo muscular antagonista y la activación coordinada de grupos musculares remotos para estabilizar la postura (Rutherford, 1988; Rutherford y Jones, 1986). La plasticidad inducida por el EF en la coordinación entre agonistas individuales y los cambios coordinativos entre estabilizadores rara vez se han examinado. En cambio, los estudios se han centrado en la medición de marcadores de neuroplasticidad en músculos individuales representativos de agonistas y la coordinación entre grupos musculares agonistas y antagonistas (Arnold y Bautmans, 2014; Hortoba'gyi et al., 2006; Remaud et al., 2007).

En cuanto a los marcadores de neuroplasticidad en músculos representativos de agonistas, la fuerza de la MVC está determinada por el reclutamiento de unidades motoras y la velocidad a la que las motoneuronas descargan potenciales de acción (Carroll et al., 2011; Folland y Williams, 2007). La salida neta (espinal y supraespinal) controla el reclutamiento y la velocidad de descarga de las unidades motoras durante la contracción muscular. Por lo tanto, los cambios estructurales y funcionales en los circuitos espinales o en las áreas cerebrales previas a las motoneuronas espinales podrían ser el origen de las adaptaciones neuronales al EF, lo que subyace a los aumentos en la fuerza de la MVC (Kidgell et al., 2017; Kidgell y Pearce, 2011; Siddique et al., 2019).

Los cambios en el tamaño muscular y la fuerza de la MVC ocurren de forma temporalmente disociada. La actividad sEMG se ha utilizado como medida sustitutiva de la neuroplasticidad. Esta suma los potenciales de acción de las neuronas motoras detectables reclutadas durante la contracción muscular. De hecho, los aumentos en la activación sEMG del músculo entrenado preceden a cambios detectables en la hipertrofia (Akima et al., 1999; Häkkinen et al., 2001a, b; Narici et al., 1989; Rutherford y Jones, 1986). Sin embargo, de los 25 estudios individuales analizados en las revisiones, solo encontramos 2 estudios que informaron asociaciones muy fuertes (r≈0,70) entre los aumentos en sEMG y la fuerza muscular después del

entrenamiento de fuerza (Häkkinen y Komi, 1986; Häkkinen et al.,1985a, b). Clasificamos los coeficientes de correlación de 0,1, 0,3, 0,5, 0,7 y 0,9 como correlaciones débiles, moderadas, fuertes, muy fuertes y extremadamente fuertes, respectivamente (Hopkins et al., 2009; Schober et al., 2018). La mayoría de los estudios no informaron ni encontraron una asociación entre las adaptaciones neuronales al EF indexadas por sEMG y las mejoras en la fuerza de la MVC. Si la reducción del impulso neural hacia los antagonistas podría explicar el aumento de la fuerza de la MVC sigue siendo controvertido, ya que un número igual de estudios informan de dichas reducciones (Carolan y Cafarelli, 1992; Ha¨kkinen et al., 1985a,b; Simoneau et al., 2007) y también de la ausencia de cambios en la sEMG del antagonista después del EF (de Boer et al., 2007; Holtermann et al., 2005; Reeves et al., 2005), pero ninguno informó cambios correlacionados en la fuerza de la MVC y la sEMG del antagonista. Las limitaciones de la sEMG, como los sesgos de cancelación del potencial de acción, restringen la amplitud de la sEMG como índice de neuroplasticidad. La medición de los componentes de la sEMG, es decir, el reclutamiento de unidades motoras y la velocidad a la que las neuronas motoras descargan potenciales de acción podría reducir este sesgo y existe la primera evidencia que indica una asociación entre estos parámetros y las ganancias de fuerza (Del Vecchio et al., 2019a).

Un factor adicional que complica muchos estudios es que la sEMG se registró a menudo en un solo músculo, mientras que la fuerza MVC es el resultado de varios músculos individuales que conforman el grupo muscular agonista y la desactivación coordinada del antagonista y la activación de estabilizadores remotos, factores que rara vez se miden (Rutherford, 1988; Rutherford y Jones, 1986). Incluso las mediciones de sEMG realizadas correctamente, es decir, normalizadas con Mmáx, pueden ser marcadores insensibles de adaptaciones neuronales a intervenciones de EF con composiciones drásticamente diferentes (Duchateau et al., 2020), lo que requiere el uso de métodos de sEMG más avanzados (Vieira y Botter, 2021). En resumen, la evidencia es, en el mejor de los casos, débil para la activación muscular indexada por sEMG como medida de neuroplasticidad que acompaña al EF. (Véanse las Recomendaciones 5.1 y 5.4).

2.2. Activación muscular: AV y MVC

En comparación con la sEMG, la interpolación de contracción proporciona más información para determinar la activación voluntaria (AV), que es una estimación sumada del número de neuronas motoras reclutadas y la velocidad a la que descargan potenciales de acción (Allen et al., 1998; Nuzzo et al., 2019b; Shield y Zhou, 2004). Presumiblemente, la AV medida por interpolación de contracción sobre el punto motor refleja la neuroplasticidad en un solo músculo agonista. Por lo tanto, es sorprendente que las revisiones sistemáticas relevantes del tema no incluyan estudios que utilicen estimulación nerviosa periférica para evaluar la AV. En cambio, algunos estudios reportan solo la AV medida por EMT (Carroll et al., 2011; Kidgell et al., 2017; Siddique et al., 2019). Contrariamente a lo esperado, se encontró que la fuerza de la MVC también aumenta después del EF sin cambios en la AV (Herbert et al., 1998; Tillin et al., 2011). No obstante, la fuerza de AV y MVC tendió a aumentar en paralelo después del EF (Behrens et al., 2016; Brown et al., 2017; Giboin et al., 2018) y, en algunos casos, de manera moderada a altamente correlacionada (r = 0,54-0,77) (Ema et al., 2018; Toien et al., 2018), lo que se ha atribuido a una baja AV al inicio, especialmente en adultos mayores (Arnold y Bautmans, 2014). Además, la evidencia limitada sugiere que la AV podría actuar como un mecanismo que permite la incorporación de una mayor fuerza de MVC en el rendimiento motor grueso. Por ejemplo, los aumentos en la AV y la velocidad de la marcha se correlacionaron fuertemente (r = 0,67) después del EF en adultos mayores con movilidad limitada (Hvid et al., 2016). Sin embargo, observamos que si la AV es una medida integral del impulso neural y alcanza el 100 % de las neuronas motoras disponibles en adultos sanos inicialmente sedentarios después del entrenamiento de fuerza, es bastante improbable que los atletas con entrenamiento de fuerza puedan mejorar aún más la AV. En cambio, es más probable que dichos atletas puedan mejorar la fuerza de la MVC a través de la hipertrofia muscular (Balshaw et al., 2019). Una posibilidad es que la medición de la AV en un músculo no represente adaptaciones en el resto de los músculos individuales que componen el grupo muscular agonista que produce la fuerza de la MVC, lo que resulta en una subestimación de la AV para todo el grupo muscular y, por lo tanto, resulta en correlaciones bajas o nulas con el rendimiento motor (Allen et al., 1998; Nuzzo et al., 2019b; Shield y Zhou, 2004). Los datos inconsistentes también están relacionados con las formas de medir la AV, incluyendo pulsos eléctricos periféricos simples, dobles y múltiples y la AV inducida por EMT. (Véanse las recomendaciones 5.2, 5.4).

2.3. Estimulación nerviosa periférica y MVC

La amplitud del reflejo H, producida por la estimulación nerviosa periférica en reposo, puede proporcionar una estimación de la excitabilidad de las neuronas motoras espinales y, por lo tanto, un marcador de neuroplasticidad después del EF. Un metaanálisis no encontró cambios en la amplitud del reflejo H medida en reposo en respuesta al EF (Siddique et al., 2019). La onda V es una variante del reflejo H evocada durante contracciones musculares enérgicas mediante la estimulación supramáxima de un nervio mixto periférico. Aunque la onda V está influenciada por todas las entradas sinápticas al conjunto de neuronas motoras, durante las contracciones máximas una gran parte de la entrada de la neurona motora proviene del impulso neural descendente y podría ser un marcador de adaptaciones neurales específicas de la tarea al EF (Aagaard et al., 2020, 2002). La evidencia metaanalítica de cinco estudios (n = 52 sujetos) sugirió un aumento consistente en la amplitud de la onda V después del EF; Sin embargo, solo un estudio mostró una correlación moderada (r = 0,45) entre los cambios en la fuerza de la MVC y la amplitud de la onda V tras el EF (Vila-Cha et al., 2012). El reflejo H y la onda V, como suele ocurrir con la AV, son medidas de un solo músculo y no representan a todos los músculos individuales del grupo agonista, ni pueden indicar cambios en la coordinación entre los músculos sinérgicos. (Véanse las recomendaciones 5.2 y 5.4).

2.4. Estimulación cerebral y MVC

La estimulación cerebral no invasiva, como la EMT de pulsos simples y pareados, puede medir los cambios en los circuitos excitatorios-inhibitorios producidos por cambios en la excitabilidad corticoespinal (CES) o cambios en la eficacia de las interneuronas inhibidoras o facilitadoras intracorticales tras el EF (Hallett, 2000). Dichos cambios producidos por el EF aumentarían hipotéticamente la magnitud y la eficacia de la orden motora, de modo que las neuronas motoras recibirían un mayor impulso, incrementando la fuerza de la CVM tras el EF. Los metaanálisis de datos de EMT respaldan la idea de que la CES aumenta y la inhibición intracortical disminuye tras el EF (Kidgell et al., 2017; Siddique et al., 2019). Esto es especialmente cierto cuando las mediciones de EMT se realizan utilizando una contracción de fondo (es decir, no en reposo). Los aumentos paralelos en la fuerza de la MVC y el CSE, y las disminuciones en la inhibición han llevado a algunos autores (Kidgell et al., 2017; Siddique et al., 2019) a suponer que estos procesos están vinculados mecánicamente, pero no todos los autores coinciden (Nuzzo et al., 2019a). De hecho, de los estudios que midieron el CSE (n = 22 estudios), el período silencioso contralateral (n = 7 estudios) y la inhibición intracortical de intervalo corto (n = 8 estudios) después del EF, solo dos informaron asociaciones significativas pero moderadas entre las disminuciones del período de silencio (una medida de inhibición cortical) y los aumentos en la fuerza de la MVC (r≈-0,50) (Hendy y Kidgell, 2013; Kidgell y Pearce, 2010). Una falta de correlación podría deberse en parte a la disimilitud entre las tareas de prueba y entrenamiento (es decir, descanso vs. contracción, intensidad y tipo de contracción). Este efecto de especificidad de la tarea parece ser más débil en el entrenamiento de fuerza que en el entrenamiento de equilibrio (Mouthon y Taube, 2019). Por ejemplo, incluso dentro del

mismo estudio, solo el entrenamiento de fuerza con ritmo externo, pero no interno, produjo cambios en el CSE y la inhibición cortical medidos durante la contracción, lo que implica que las adaptaciones en el CSE y la inhibición cortical no contribuyeron a las ganancias de fuerza (Leung et al., 2017). Los cambios neuroplásticos también estuvieron ausentes después del entrenamiento de fuerza cuando se midieron las respuestas a la EMT durante la contracción muscular en un músculo del brazo (Lundbye-Jensen et al., 2005). En resumen, la mayoría de los estudios no parecieron haber calculado, informado o encontrado asociaciones funcionalmente relevantes entre los cambios en los índices de neuroplasticidad derivados de la EMT y las mejoras en la fuerza de la MVC después del entrenamiento de fuerza. La evidencia de un vínculo funcional entre el aumento de fuerza y el aumento de la CSE o la disminución de la inhibición cortical en adultos sanos es limitada, lo que cuestiona el papel funcional de estas adaptaciones neuronales en el aumento de la fuerza de la MVC. (Véanse las recomendaciones 5.2 y 5.4).

2.5. Datos imágenes cerebrales y MVC

La neuroplasticidad que acompaña al EF rara vez se ha examinado mediante imágenes cerebrales. Datos de 18 estudios de imágenes cerebrales sugirieron que el EF puede aumentar el grosor y el volumen de la materia gris, así como mejorar la conectividad funcional y en reposo en diversas áreas cerebrales (Herold et al., 2019). Sin embargo, estos estudios se diseñaron para determinar la relación entre la plasticidad cerebral y la función cognitiva, más que el aumento del rendimiento motor. Es comprensible que estos estudios no describieran la asociación entre los cambios en el rendimiento motor y la plasticidad cerebral.

A corto plazo, de 2 a 12 semanas de EF produjeron adaptaciones cerebrales inconsistentes, medidas mediante resonancia magnética (RM). Doce semanas de EF aumentaron la densidad de materia gris en los lóbulos posterior y anterior del cerebelo, la circunvolución frontal superior del lóbulo frontal y la corteza cingulada anterior del lóbulo límbico en adultos mayores sanos. Sin embargo, los autores no evaluaron la relación entre estos cambios cerebrales y el rendimiento motor (Fontes et al., 2017). Dieciséis sesiones de 36 flexiones plantares isométricas unilaterales derechas mejoraron la fuerza de la CVM en la pierna entrenada (40 %) y no entrenada (30 %), y disminuyeron la difusividad media de la vía corticoespinal izquierda (tamaño del efecto = 1,4) y los volúmenes del putamen (Palmer et al., 2013). El aumento del 40 % en la fuerza de la CVM se correlacionó moderadamente (r = -0,55) con los cambios observados de aproximadamente el 2 % en la difusividad media, lo que refleja, según los autores, una mejora en la mielinización. Los cambios en el volumen del putamen podrían estar relacionados con una mejora en el aprendizaje motor. Los datos de difusividad podrían reflejar el componente de fuerza de las adaptaciones al entrenamiento. Sin embargo, el aumento del 30 % en el lado contralateral sin entrenamiento (educación cruzada) se produjo sin cambios en la estructura cerebral.

El entrenamiento con EF para desviación cubital unilateral derecha (n = 24 sesiones) mejoró la fuerza MVC de cada mano en un ~46 % (Farthing et al., 2007). Cuando los sujetos contrajeron la mano derecha entrenada dentro de la resonancia magnética después del entrenamiento con EF, la activación en la corteza motora primaria y somatosensorial izquierda, la corteza premotora dorsal y otras áreas aumentaron en comparación con la activación antes del entrenamiento con EF (n = 4 sujetos). Cuando los sujetos contrajeron la mano izquierda no entrenada después del entrenamiento con EF, la activación en la corteza sensoriomotora derecha y el lóbulo temporal izquierdo aumentaron en comparación con antes del entrenamiento con EF. El entrenamiento con EF de agarre unilateral evitó la pérdida de fuerza MVC en la extremidad opuesta inmovilizada (+0,8 %). La preservación de la fuerza se correlacionó con un mayor volumen de activación de la corteza motora izquierda. En los controles sin entrenamiento, la fuerza de agarre MVC de la extremidad inmovilizada disminuyó en un 11 % sin cambios en la activación de la corteza motora contralateral (Farthing et al., 2011). Sin embargo, no se realizaron más análisis de correlación entre las medidas de adaptaciones neuronales y los cambios en la fuerza MVC.

La actividad de la corteza cerebral medida con la frecuencia media del electroencefalograma (EEG) aumentó independientemente del tipo de intervención en PwPD (Carvalho et al., 2015), lo que sugiere un componente de aptitud física en los efectos del ejercicio en el flujo cerebral mejorado (Toll'ar et al., 2019a). La coherencia corticomuscular derivada del EEG medida en diferentes fuerzas MVC también fue independiente del historial de entrenamiento en el entrenamiento de fuerza y los atletas entrenados aeróbicamente (Dal Maso et al., 2017). Los efectos del entrenamiento de fuerza a corto plazo en la amplitud de los potenciales corticales relacionados con el movimiento (MRCP) en sujetos sanos no entrenados son inconsistentes. Tres semanas de entrenamiento de fuerza explosivo unilateral aumentaron la fuerza MVC, la tasa de desarrollo de tensión y la sEMG. Estos cambios fueron acompañados por disminuciones en la amplitud de los MRCP. Los autores no informaron si los cambios en las medidas de fuerza y EEG se correlacionaron entre sí. La interpretación fue que el entrenamiento de fuerza (EF) mejoró la economía neuronal, ya que la generación de fuerza submáxima se logró mediante un impulso cortical reducido (Falvo et al., 2010). Sin embargo, cuatro semanas de entrenamiento de fuerza excéntrico vs. concéntrico en piernas aumentaron los resultados de la MVC y también aumentaron las amplitudes de la MRCP registradas durante la contracción muscular submáxima en adultos mayores sanos (Kang et al., 2016). La imaginería motora de la flexión enérgica del codo durante 30 min en reposo aumentó la fuerza de la MVC y también la amplitud de la MRCP en un 20-22 % en los electrodos C3 y Cz (Yao et al., 2013). En consecuencia, el aumento en el comando descendente reclutaría unidades motoras previamente inactivas y/o tendría una mayor tasa de descarga de unidades motoras activas, aumentando así la fuerza de la MVC. El EF también podría haber reducido la inhibición del grupo de neuronas motoras de los músculos, aumentando la salida neta de neuronas motoras (Yao et al., 2013). Estos datos se interpretaron como evidencia de neuroplasticidad en la corteza motora, el cerebelo, el área motora suplementaria y la corteza premotora dorsal; sin embargo, los autores no informaron correlaciones entre EEG, sEMG y fuerza MVC (ver también (Liu et al., 2019). En conjunto, hay evidencia de que el EF produjo cambios favorables en la estructura y función del cerebro, pero hay poca evidencia de que dichos cambios se correlacionen con una mayor fuerza MVC. Además, no ha habido ningún intento de relacionar los datos de imágenes cerebrales con sEMG, EMT o datos de estimulación periférica después del EF; en consecuencia, los datos de imágenes actuales proporcionan poca evidencia mecanicista de cómo los cambios en las áreas y redes cerebrales putativas después del EF podrían aumentar el rendimiento motor. (Ver recomendaciones 5.3, 5.4).

3. Relevancia funcional de las adaptaciones nerviosas al entrenamiento de fuerza en el envejecimiento y condiciones neurológicas

Dado que el envejecimiento, especialmente en combinación con una enfermedad, reduce la capacidad de respuesta del músculo esquelético a los estímulos mecánicos (Drummond et al., 2008; Kumar et al., 2009), una comprensión más clara de cómo la neuroplasticidad podría mediar el aumento del rendimiento motor tras el entrenamiento de fuerza mejoraría la especificidad de la prescripción de ejercicio para adultos mayores y pacientes. En particular, los pacientes con enfermedades neurológicas y neurodegenerativas se beneficiarían, ya que el entrenamiento de fuerza podría aprovechar las áreas funcionales del sistema nervioso central para estimular la neuroplasticidad y las actividades de la vida diaria. (Véase para esta sección la Recomendación 5.5).

3.1. Neuroplasticidad inducida por el entrenamiento de fuerza para mejorar la velocidad de la marcha en ancianos

La velocidad de la marcha en la mediana edad tardía predice condiciones de salud, médicas y cognitivas más adelante en la vida, incluyendo mortalidad/supervivencia y morbilidad (Beijersbergen et al., 2013). Por lo tanto, comprender los mecanismos biomecánicos y neuronales para minimizar la pérdida de velocidad de la marcha relacionada con la edad es un elemento importante para diseñar y prescribir ejercicio para adultos mayores. En dichos estudios, el entrenamiento de fuerza (EF) de las extremidades inferiores mejoró la fuerza MVC de los músculos involucrados en la generación de fuerza en la fase de apoyo de la marcha (Hortoba´gyi et al., 2015). Sin embargo, los aumentos en la velocidad de la marcha y la fuerza MVC de los músculos involucrados en el empuje de propulsión se correlacionaron débilmente (Bei-jersbergen et al., 2017; Uematsu et al., 2018, 2014). Se asume que la neuroplasticidad inducida por el EF subyace a los aumentos en la velocidad de la marcha. De hecho, los cambios en la sEMG después del EF sugirieron que los adultos mayores utilizaron una fracción de los aumentos inducidos por el entrenamiento en la capacidad de activación muscular durante la marcha. Además, después del EF, los cambios en la coordinación interarticular evaluados a través de la cinemática de la marcha predijeron pobremente los aumentos en la velocidad de la marcha (Beijersbergen et al., 2013). Es decir, la activación muscular medida durante la marcha por sEMG después del EF tuvo poca o ninguna relevancia funcional para aumentar la velocidad de la marcha. Especulamos que cada sujeto se adaptó de manera diferente, "*eligiendo una solución diferente*", lo que descarta la aparición de un patrón adaptativo neuronal común. Cuando la prioridad funcional es aumentar la velocidad de la marcha, la administración independiente de un programa de EF tiene baja efectividad, que puede aumentarse combinando el EF con protocolos de reentrenamiento de la marcha en los ancianos (Gillespie et al., 2012).

Estos enfoques están diseñados para que la neuroplasticidad inducida por el entrenamiento de fuerza facilite la incorporación de la fuerza muscular recién adquirida a la cinética de la marcha. Sin embargo, aún no se ha esclarecido el papel funcional de la neuroplasticidad inducida por el entrenamiento de fuerza en la mejora de la velocidad de la marcha en adultos mayores.

3.2. Neuroplasticidad inducida por el entrenamiento de fuerza y función motora en personas con la enfermedad de Parkinson (EP)

La mayoría de las personas con enfermedad de Parkinson (EP) presentan niveles de fuerza más bajos y muestran tasas de desarrollo de fuerza más bajas en comparación con sujetos de control sanos de la misma edad (Inkster et al., 2003; Paasuke et al., 2004, 2002). A pesar de sus efectos sobre la MVC, la enfermedad de Parkinson puede afectar la conducción nerviosa del músculo y, por lo tanto, causar una menor AV (Huang et al., 2017) y una mayor inestabilidad de la fuerza voluntaria (Skinner et al., 2019).

Aunque se ha demostrado que la fuerza MVC se correlaciona fuertemente (r = 0,68-0,80) con el levantamiento de la silla y el rendimiento de levantarse y andar cronometrado en algunos estudios (Inkster et al., 2003; Schilling et al., 2009), las revisiones sistemáticas concluyeron que los aumentos inducidos por el EF en la fuerza MVC podrían no traducirse en mejoras funcionales en personas con EP (Cherup et al., 2019; Falvo et al., 2008; Ramazzina et al., 2017; Roeder et al., 2015; Tillman et al., 2015). El único indicio de que la neuroplasticidad inducida por el EF se correlaciona con la función motora surgió cuando los aumentos inducidos por el EF en la fuerza MVC y la activación muscular EMG predijeron la bradicinesia de las extremidades superiores después de 24 meses de EF (David et al., 2016). En resumen, las personas con EP responden al entrenamiento de fuerza (EF), pero las adaptaciones neuroplásticas y de fuerza no están correlacionadas y tienen efectos limitados o nulos en las actividades de la vida diaria. Esto podría estar relacionado con la baja especificidad del ejercicio de EF para los patrones de activación muscular presentes en las actividades de la vida diaria. Aún no está claro cómo, y si, la neuroplasticidad inducida por el EF podría actuar como mecanismos facilitadores para que las personas con EP mejoren las actividades de la vida diaria mediante el aumento de la fuerza de la MVC.

3.3. Neuroplasticidad inducida por el entrenamiento de fuerza y función motora en personas con esclerosis múltiple (EM)

Las personas con esclerosis múltiple (EM) suelen presentar una fuerza MVC baja en los músculos de las extremidades, lo que afecta la capacidad funcional (Kjolhede et al., 2015b). Se observó que la fuerza MVC del flexor de la rodilla (r ~0,5-0,7) se correlacionaba más fuertemente que la del extensor de la rodilla (r ~0,1-0,4) con la capacidad de caminar en las personas con EM (Broekmans et al., 2013). La interpretación clínica fue que las personas con EM se beneficiarían del entrenamiento de fuerza (EF) para mejorar la capacidad de caminar (Manca et al., 2019). De hecho, el EF aumentó la fuerza MVC hasta en un 36 % en las personas con EM (Cruickshank et al., 2015; Manca et al., 2019). Un metanálisis reveló aumentos en la fuerza MVC con tamaños de efecto pequeños a moderados, lo que se interpretó como una menor capacidad de respuesta de las personas con EM al EF (Jorgensen et al., 2017). No está claro si el aumento de la fuerza de la MVC también se traduce en una mejora de la función motora gruesa. Si bien existe una relación entre la velocidad de la marcha y la fuerza de la MVC en las piernas en personas con EM (Thoumie et al., 2005), el entrenamiento de fuerza solo mejoró la velocidad de la marcha con tamaños de efecto bajos (0,35) (Manca et al., 2019). Datos esporádicos sugieren que el EF también puede mejorar la capacidad de subir sillas, subir escaleras, la velocidad de la marcha de 10 metros y la distancia recorrida en 6 min (Dalgas et al., 2009). La evidencia de que el EF mejora la función de las extremidades superiores en personas con EM es más débil (Lamers et al., 2016).

En la literatura sobre EM, hasta el momento se ha prestado mínima atención a si la neuroplasticidad inducida por el EF podría ser la base de los aumentos en la fuerza de la MVC. Se observaron aumentos paralelos en la actividad sEMG de los extensores y flexores de la rodilla y en la fuerza de la MVC de estos músculos (Dalgas et al., 2013; Kjolhede et al., 2015a). Asimismo, la actividad sEMG y las amplitudes de las ondas V superpuestas en los flexores plantares del tobillo aumentaron después de 3 semanas de EF de intensidad máxima en pacientes con EM (Fimland et al., 2010). El control de la fuerza isométrica submáxima de los músculos de la pierna se correlacionó con la velocidad de la marcha en pacientes con EM, lo que sugiere que las disminuciones moderadas en el rendimiento de la marcha se asociaron más fuertemente con deficiencias en el control de la fuerza que con disminuciones en la fuerza de la MVC (Davis et al., 2020). En resumen, la evidencia limitada parece sugerir que el EF es un método eficaz para aumentar la salida motora eferente de las neuronas motoras espinales en pacientes con EM. Sin embargo, no se reportaron correlaciones entre los cambios en los resultados basados en sEMG y el aumento de la fuerza de la CVM. Asimismo, faltan datos sobre la relación entre los cambios en los marcadores de neuroplasticidad y los cambios en la función motora gruesa.

3.4. Neuroplasticidad inducida por el entrenamiento de fuerza y función motora en personas con ictus (IC)

La debilidad muscular limita la actividad motora en pacientes con ictus (IC) (Ada et al., 2006; Canning et al., 2004). La fuerza de la MVC en la extremidad afectada puede ser tan baja como la mitad de la de los controles sanos emparejados por edad y sexo (Neckel et al., 2006). La evidencia metaanalítica sugiere que el entrenamiento de fuerza (EF)

puede aumentar la fuerza de la MVC en las extremidades inferiores en pacientes con IC crónicos (Dorsch et al., 2018; Wist et al., 2016). La eficacia del EF para aumentar la fuerza de la MVC en las extremidades superiores en pacientes con PcS (Harris y Eng, 2010) y en el estado agudo (es decir, hasta tres meses después de un accidente cerebrovascular) es incierta (Salter et al., 2016).

Tampoco está claro si los aumentos inducidos por el EF en la fuerza de la MVC están relacionados con mejoras en la función motora. Si bien el EF mejoró sustancialmente la fuerza de la MVC en los músculos de las extremidades inferiores (tamaño del efecto = 1,1), no se produjeron mejoras en la función motora evaluada mediante la prueba cronometrada de levantarse y andar (tamaño del efecto = 0,4) (Dorsch et al., 2018). Los efectos del EF también fueron mínimos en las funciones de las extremidades superiores (tamaño del efecto = 0,2). Las revisiones concluyen que las ganancias inducidas por el EF en la fuerza de la MVC, en general, no se transfieren a mejoras funcionales en personas con IC (Tiozzo et al., 2015). Una excepción es la velocidad de la marcha (Wonsetler y Bowden, 2017), que mejoró (tamaño del efecto: 0,4-0,7) por encima de la diferencia mínimamente importante para la velocidad de marcha habitual (+0,11 m/s) y rápida (+0,18 m/s) después del EF (Clark y Patten, 2013). El entrenamiento de fuerza de alta intensidad de los músculos de las extremidades superiores, combinado con la práctica de tareas funcionales, también mejoró la fuerza de la MVC y, en paralelo, diversos resultados funcionales (Patten et al., 2013), lo que sugiere la posibilidad de que la combinación de tareas funcionales con entrenamiento de fuerza aumente la especificidad del entrenamiento de fuerza para las tareas cotidianas. Sin embargo, aún no se ha aclarado el papel de la neuroplasticidad inducida por el entrenamiento de fuerza en las mejoras de la fuerza de la MVC y el rendimiento motor grueso en pacientes con síndrome de Prader-Schneider.

4. Neuroplasticidad inducida por el entrenamiento de fuerza para incrementar el rendimiento atlético

Los atletas utilizan el entrenamiento de fuerza (EF) para mejorar la MVC con una expectativa basada en la suposición y la evidencia científica de que la fuerza contráctil y la velocidad están asociadas con el rendimiento deportivo. Sin embargo, según el principio de Adaptación Específica a las Demandas Impuestas (Fox y Mathhews, 1988) y el concepto de especificidad del entrenamiento (Sale y MacDougall, 1981), el EF normalmente no entrena explícitamente las habilidades deportivas (Sale, 1988). Examinamos esta suposición con respecto al rendimiento en carreras de velocidad y de fondo, en atletas con un alto nivel de fuerza, en quienes el modelo de Sale (Sale y MacDougall, 1981) predice poca o ninguna neuroplasticidad inducida por el EF, y en niños prepúberes que podrían mejorar su rendimiento deportivo tras el EF casi exclusivamente debido a cambios neuroplásticos. (Véase para esta sección la Recomendación 5.5).

4.1. Rendimiento en velocistas

Los velocistas utilizan el entrenamiento de fuerza (EF) para aumentar la velocidad de carrera (Haugen et al., 2019). Durante el sprint, los atletas aceleran la masa corporal aplicando rápidamente altas fuerzas al suelo. Los velocistas utilizan el EF de alta velocidad para aumentar la potencia muscular de las piernas mejorando la fuerza contráctil y la velocidad, a la vez que minimizan las ganancias de masa muscular (Behm et al., 2017; Delecluse, 1997). Las adaptaciones neuronales en evolución reducen el tiempo de generación de torque mediante un mayor reclutamiento y tasas de descarga de unidades motoras en los músculos agonistas (Del Vecchio et al., 2019a, b) y un reclutamiento más temprano de unidades motoras de alto umbral (Del Vecchio et al., 2019b). Un aumento en la excitabilidad de la neurona motora después del EF también aumentaría la fuerza de la MVC en respuesta a la entrada del impulso supraespinal y las aferencias espinales Ia, y aumentaría la rigidez de la unidad músculo-tendinosa, lo que favorece la producción de fuerza y reduce los tiempos de contacto con el suelo (Aagaard et al., 2002; Ross et al., 2001).

Actualmente, no existen estudios que muestren una relación entre los aumentos inducidos por el EF en la fuerza de la MVC, los marcadores de neuroplasticidad y los tiempos de sprint. Se espera que el EF aumente la amplitud del reflejo H, es decir, la excitabilidad de la neurona motora, y disminuya la inhibición presináptica (Aagaard et al., 2002), pero los velocistas, en comparación con los corredores de fondo, tuvieron una menor amplitud del reflejo H (Casabona et al., 1990; Maffiuletti et al., 2001). Dado que el reflejo H surge de la activación de neuronas motoras de umbral bajo, la menor amplitud del reflejo H puede resultar de la menor proporción de unidades motoras de umbral bajo frente a las de umbral alto, lo que resulta en la activación de menos neuronas motoras que contribuyen al reflejo H durante intensidades de estimulación en las que el reflejo H no se cancela por la propagación antidrómica del potencial de acción (Casabona et al., 1990). Se necesitan estudios longitudinales para responder a esta pregunta.

Si bien el entrenamiento de fuerza mejora la fuerza de la MVC de los velocistas y produce cambios neuroplásticos, estos cambios se correlacionan débilmente con mejores tiempos de sprint (Harris et al., 2000; Lyttle et al., 1996; McBride et al., 2002; Moir et al., 2007; Wilson et al., 1993). Las diferencias en el patrón de activación muscular durante el entrenamiento de fuerza y el sprint, así como ser un velocista principiante frente a uno de élite, podrían explicar esta escasa correlación (Barr et al., 2014; Styles et al., 2016). Por el contrario, el entrenamiento de sprint resistido en distancias cortas en comparación con el EF mejoró los tiempos de sprint de forma más efectiva, lo que sugiere que la estructura espaciotemporal del estímulo de entrenamiento es un factor importante para mejorar los tiempos de sprint (Bachero-Mena y Gonzalez-Badillo, 2014; Behm y Sale, 1993; Bolger et al., 2015; Petrakos et al., 2016; Rumpf et al., 2016). El grado de especificidad no está del todo claro porque el entrenamiento isométrico realizado en un cicloergómetro también mejoró la potencia máxima de las piernas de los ciclistas de clase mundial (Kordi et al., 2020). En conjunto, los datos sugieren que la similitud en la activación muscular durante el entrenamiento (sprint resistido) y las tareas objetivo (sprint sin resistencia, "de la vida real") proporciona la mayor especificidad y, por lo tanto, la eficacia del entrenamiento, pero no está claro si la neuroplasticidad inducida por el EF actúa como el mecanismo habilitador para mejorar los tiempos de sprint.

4.2. Rendimiento en corredores de fondo

Los corredores de fondo también utilizan el entrenamiento de fuerza (EF) para mejorar sus tiempos en carreras de fondo (Trowell et al., 2019). Se asume que el EF mejora la MVC de los grupos musculares entrenados y la capacidad de los atletas para activar estos músculos. Una mejor activación aumentaría la aceleración angular de la pierna durante el balanceo, incrementando así la velocidad de carrera. Sin embargo, no existe correlación entre el aumento inducido por el entrenamiento en los torques extensores durante una MVC y la economía de carrera tras el EF, lo que implica que las mejoras en los torques de las articulaciones de la cadera y la rodilla podrían contribuir a aumentar la velocidad de carrera máxima, pero no la submáxima, utilizada durante las carreras de fondo (Alcaraz-Ibáñez y Rodríguez-Pérez, 2018; Macadam et al., 2019; Trowell et al., 2019; Young, 2006).

La neuroplasticidad inducida por el entrenamiento de fuerza podría permitir una carrera más rápida al modificar la coordinación intermuscular dentro de un grupo muscular y la coordinación interarticular en movimientos específicos y similares a los ejercicios de entrenamiento (Enoka, 1988; Folland y Williams, 2007). Las modificaciones incluyen aumentos en la activación muscular selectiva y sinérgica y disminuciones en la activación muscular antagonista. Dichos cambios podrían reducir el impulso neural necesario para las contracciones submáximas. El aumento en la excitabilidad de las neuronas

motoras después del entrenamiento de fuerza también podría reducir la tasa de descarga de las unidades motoras, compensada por el reclutamiento de unidades motoras durante el ejercicio submáximo prolongado (Vila-Cha et al., 2012). Por lo tanto, el entrenamiento de fuerza reduciría el coste metabólico de cada paso. Sin embargo, la activación muscular durante la carrera nunca se ha medido después del entrenamiento de fuerza en corredores de competición. Por lo tanto, se desconoce si el entrenamiento de fuerza podría mejorar la aplicación de la fuerza sobre el suelo mediante una coordinación alterada o si modificaría el reclutamiento de unidades motoras, lo que resultaría en una mejora del coste metabólico y la economía de carrera, la resistencia a la fatiga y, en última instancia, la velocidad de carrera.

De hecho, la evidencia parece favorecer un mecanismo mecánico, más que neuronal, del entrenamiento de fuerza (EF) para mejorar los tiempos en carreras de fondo. Aparentemente en contra del principio de especificidad del entrenamiento, el EF isométrico mejoró el rendimiento en carreras de fondo (Lum y Barbosa, 2019). Esto es posible porque, a medida que el tendón de Aquiles se estira en la fase de apoyo, las fibras musculares de los extensores de la rodilla y el tobillo se encuentran en un estado isométrico (Bohm et al., 2018; Roberts et al., 1997), aumentan la fuerza de despegue. El EF de las extremidades inferiores también mejora la economía de carrera en un 4% debido al aumento de la rigidez del tendón, lo que resulta en un aumento de la energía elástica y una redistribución de la producción muscular durante la carrera (Albracht y Arampatzis, 2013). Una combinación de entrenamiento de fuerza intenso y explosivo puede mejorar el control neural, la fuerza muscular y la elasticidad, lo que a su vez podría acortar los tiempos de contacto con el suelo y mejorar la economía de carrera (Balsalobre-Fernandez et al., 2016; Blagrove et al., 2018; Johnston et al., 1997; Paavolainen et al., 1999), aunque la relación entre estos cambios es inconsistente (Blagrove et al., 2018; Jung, 2003). Los corredores de fondo ciertamente experimentan mejoras con el entrenamiento de fuerza, aunque no se pueden descartar adaptaciones neuroplásticas, la evidencia de mejoras en el rendimiento a través de cambios mecánicos es más probable.

4.3. Neuroplasticidad inducida por el entrenamiento de fuerza en atletas entrenados

Sale sugirió que las adaptaciones neuronales al entrenamiento de fuerza se estabilizan tras las primeras semanas de entrenamiento, cuando la hipertrofia se convierte en el determinante predominante de las ganancias de fuerza (Sale, 1988). Los estudios transversales no abordan este problema, pero proporcionan indicios de que los cambios neuroplásticos continúan más allá del período inicial arbitrario. Por ejemplo, las reducciones en la fuerza provocada por la EMT durante la contracción muscular sugirieron que la neuroplasticidad inducida por el entrenamiento de fuerza era evidente en adultos sanos entrenados con entrenamiento de fuerza que continuaron con el entrenamiento de fuerza (del Olmo et al., 2006). Los adultos sanos entrenados crónicamente con entrenamiento de fuerza mostraron una inhibición cortical abolida provocada por la EMT durante fuerzas voluntarias de ≥40 % de la MVC (Lahouti et al., 2019). En los individuos entrenados con entrenamiento de fuerza que continuaron con el entrenamiento de fuerza, las adaptaciones de las neuronas motoras continuaron (Pearcey et al., 2014) y la activación muscular antagonista se redujo tras 4 años de entrenamiento de fuerza, lo que sugiere que la coordinación intermuscular es una adaptación neuronal a largo plazo (Balshaw et al., 2019). En contraste con estos datos que respaldan la persistencia de cambios neuroplasticos durante años tras el inicio del entrenamiento de fuerza (EF), la activación muscular agonista medida mediante sEMG no mostró diferencias tras 12 semanas o 4 años de EF; sin embargo, no se examinaron los cambios en la coactivación. Una serie de casos de dos levantadores de potencia y un levantador de pesas con muchos años de EF mostró mejoras de hasta un 10 % en la fuerza máxima en sentadilla sin hipertrofia muscular (Zourdos et al., 2016). Se demostró que los cambios inducidos por el EF en los marcadores de neuroplasticidad persistían en esquiadores júnior de élite (<15 años), quienes mejoraron su rendimiento en salto vertical junto con (aunque no se correlacionaron con) un aumento de la excitabilidad espinal, lo que sugiere un aumento de la producción neuronal motora con el EF de larga duración (Taube et al., 2007). La evidencia aquí presentada hace que la meseta propuesta por Sale parezca improbable.

4.4. Neuroplasticidad inducida por el entrenamiento de fuerza en atletas prepuberales

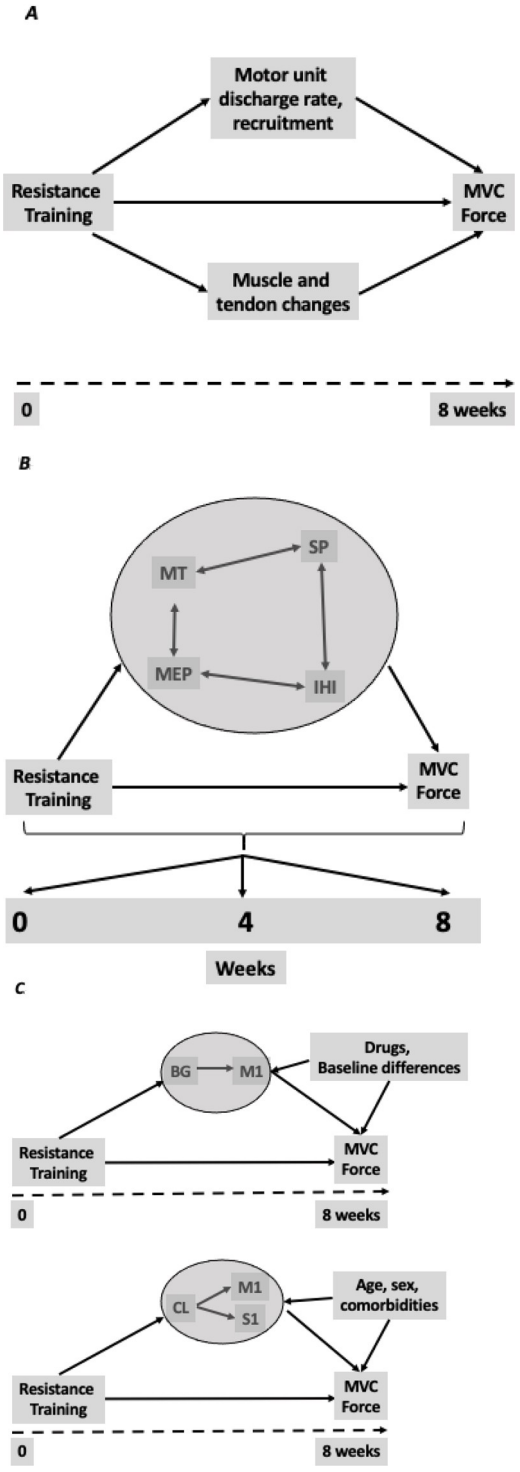
Debido a la falta de andrógenos circulantes en niños prepúberes, las ganancias inducidas por el EF en la fuerza de la MVC son causadas principalmente por factores neurales en lugar de musculares (Behringer et al., 2011; Granacher et al., 2011). Por ejemplo, el EF durante 20 semanas aumentó la activación voluntaria (AV) de los flexores del codo y los extensores de la rodilla medidos por interpolación de contracción en niños prepúberes de 9 a 11 años (Ramsay et al., 1990). Sin embargo, ningún estudio ha reportado cambios neuroplásticos correlacionados y aumentos concomitantes en la fuerza de la MVC y/o las habilidades motoras. No obstante, dado su perfil hormonal, es probable que los cambios neuroplásticos inducidos por el EF subyacen a los aumentos en el rendimiento atlético después del EF en estos niños. Estudios futuros podrían determinar la relación entre la neuroplasticidad inducida por el EF y el rendimiento funcional en estos niños en paradigmas que combinan el EF con la práctica específica del evento conocida por inducir neuroplasticidad (Behm et al., 2008).

5. Recomendaciones

Estudios históricos introdujeron la idea de que la neuroplasticidad subyace a los rápidos aumentos iniciales de la fuerza de la MVC y el rendimiento motor grueso tras el entrenamiento de fuerza (EF). Con el fin de actualizar esta idea, revisamos y extrajimos evidencia experimental de revisiones previas sobre la relevancia funcional de la neuroplasticidad inducida por el EF para aumentar el rendimiento motor. Si cambios neuroplásticos inducidos por el EF realmente tienen lugar, la mayoría de los estudios informaron de un aumento “paralelo” en los cambios en los marcadores de neuroplasticidad, fuerza de la MVC o rendimiento motor grueso. Sin embargo, encontramos poca evidencia de que las variaciones individuales en las mejoras de rendimiento inducidas por el EF se asociaran con variaciones individuales en los marcadores de neuroplasticidad. Por lo tanto, formulamos las siguientes recomendaciones para mejorar la eficacia del entrenamiento físico que realizan los atletas y la rehabilitación que reciben los pacientes. Estas recomendaciones se realizan entendiendo que la correlación no es causalidad, pero sirve como un importante punto de partida para los análisis de mediación (causal). Estos modelos podrían servir de base para una actualización del modelo descriptivo de Sale, en el que se ha basado este campo durante unos 40 años.

Recomendamos el uso de métodos avanzados para la identificación de la neuroplasticidad y su relevancia funcional. Estos podrían incluir la cuantificación de la coherencia sEMG-sEMG de la activación muscular sinergista y antagonista, la coherencia corticomuscular sEMG-EEG, la sinergia basada en sEMG y el análisis de wavelets, en lugar de utilizar métodos sEMG de detección de un solo músculo, para determinar la neuroplasticidad inducida por EF. Estos métodos podrían proporcionar nuevos conocimientos sobre la neuroplasticidad inducida por EF en forma de coordinación intra e intergrupos musculares, acoplamiento corticomuscular y la organización de la entrada sináptica a las neuronas motoras (Aagaard et al., 2020). Recomendamos el uso de registros de unidades motoras derivados de sEMG multimatriz para rastrear longitudinalmente los cambios en la activación de una sola unidad motora a lo largo de múltiples sesiones (Casolo et al., 2020; Del Vecchio et al., 2019a, b); (Vila-Cha et al., 2012, 2010). Recomendamos la determinación de los resultados de EMT y estimulación nerviosa periférica, especialmente durante la contracción muscular en lugar del reposo (Taube et al., 2020), la combinación de mediciones basadas en estimulación con EEG y MRI, proporcionando un nuevo marco metodológico-analítico (Raffin et al., 2020), y la exploración de vías

alternativas para la neuroplasticidad producida por EF, como el tracto reticuloespinal lateral (Baker y Pérez, 2017; Choudhury et al., 2019; Fernández-De-l-Olmo et al., 2014; Glover y Baker, 2020).



(explicación siguiente columna)

Fig. 2. Gráficos acíclicos dirigidos (GAD) que ilustran la actualización y extensión del modelo de Sale.

2A. Un GAD ilustra las vías causales entre los aumentos de la fuerza isométrica voluntaria máxima (FVM) tras el entrenamiento de resistencia. Los datos experimentales modifican el modelo descriptivo de Sale, asignando posibles funciones a factores neurales y musculotendinosos en los aumentos de la FVM durante las fases iniciales del entrenamiento de resistencia. Los mediadores teóricos incluyen la tasa de descarga de la unidad motora, el número de unidades motoras, los marcadores de hipertrofia y la rigidez tendinosa. No se muestran los posibles factores de confusión, pero podrían incluir la edad, la FVM inicial, el tamaño muscular inicial y el sexo. B. El GAD especifica con más detalle las vías mecanicistas ilustradas en 2A entre el entrenamiento de resistencia y los aumentos de la FVM. Las adaptaciones en el impulso central se evalúan determinando la relación entre los resultados de la estimulación cerebral magnética al inicio (0), durante (4) y después (8 semanas) del entrenamiento de resistencia a medida que los mediadores aumentan la FVM. Las mediciones repetidas ayudarían a determinar la contribución relativa de esos diferentes resultados al rendimiento motor en diferentes etapas del entrenamiento mediante el uso del análisis de mediación y si alguna adaptación causal a los cambios de EF con el tiempo. Resultados de la estimulación cerebral magnética: umbral motor (MT); tamaño del potencial evocado motor (MEP), inhibición intracortical (IHI), período silencioso (SP). El modelado de ecuaciones estructurales identifica la relación entre los resultados individuales de la estimulación cerebral subyacentes al curso temporal y el papel relativo de estos resultados en los aumentos de la fuerza MVC.2 C. DAG que ilustra las vías mecanicistas a través de las cuales el entrenamiento de resistencia puede mejorar la fuerza MVC y los síntomas clínicos a través de alteraciones de la red funcional y estructural en la enfermedad de Parkinson según (Bologna et al., 2020). El entrenamiento de resistencia activa las cortezas motora y sensoriomotora primaria, los ganglios basales y el cerebelo involucrados en la generación y el control de las secuencias lentas, débiles, de amplitud estrecha y propensas a errores en los movimientos voluntarios. Las variables del entrenamiento de resistencia (intensidad de la contracción, duración, frecuencia, repetición de movimientos individuales, variación en la fuerza inducida por perturbaciones, implementos sensoriales con peso en movimiento) (Toll'ar et al., 2019a, b) afectan la duración de la activación cerebral y muscular, variables que a su vez pueden ajustarse para reducir las disfunciones clínicas individuales. El DAG ilustra las vías compensatorias a través de las cuales el entrenamiento de resistencia podría actuar mientras está en estado de ON-dopamina. La forma ovalada identifica la supuesta red examinada para la activación y la conectividad mediante imágenes cerebrales y su relación ajustada por factores de confusión con los aumentos en la fuerza de la MVC. El DAG superior resalta el bucle motor y el DAG inferior representa la red cerebelo-tálamo-cortical involucrada en el bucle de retroalimentación del movimiento. Los factores de confusión son las diferencias en los síntomas clínicos y motores iniciales, los fármacos, las comorbilidades, la edad y el género. Los DAG extienden el modelo de Sale a las condiciones clínicas utilizando un enfoque mecanicista en lugar de uno descriptivo. M1, corteza motora primaria; S1, corteza sensoriomotora; BG, ganglios basales; CL, cerebelo; MVC, contracción voluntaria máxima.

Recomendamos incorporar los datos obtenidos mediante estos métodos en análisis de mediación para determinar los vínculos causales entre la neuroplasticidad inducida por el EF y las mejoras en la fuerza de la MVC o el rendimiento motor grueso en la salud y la enfermedad (Nuzzo et al., 2019a; Steele et al., 2020; Textor et al., 2016; Tolla'r et al., 2019a) (Figura 2A); dichos análisis deben realizarse antes, durante (es decir, mediciones longitudinales) y después del EF (Hortoba'gyi et al., 2011). Recomendamos estimar la contribución relativa de estos resultados al rendimiento motor antes, durante y después del EF mediante la prueba de hipótesis utilizando análisis de mediación (causal) (Fig. 2B).

Los análisis de la red cerebral serían altamente informativos después del EF incluso en adultos jóvenes sanos como controles

para contrastar con el papel funcional desempeñado por las adaptaciones de la red en la recuperación de la función motora en personas con Parkinson, esclerosis múltiple o ictus (August et al., 2006; Bajaj et al., 2015; James et al., 2009). Los cambios en la red después del EF podrían ser además informativos sobre la localización y el grado de neuroplasticidad en estos pacientes y esto podría evaluarse a través de análisis de mediación (causal) (Bologna et al., 2020; Hallett et al., 2020) (Fig. 2C). Esta recomendación está respaldada por datos que sugieren que la neuroplasticidad inducida por el EF podría reducir las desconexiones estructurales y funcionales causadas por lesiones en personas con ictus y que la conectividad mejorada por el EF predice cambios motores y conductuales (Salvalaggio et al., 2020).

Recomendamos examinar la retención y la transferencia de la habilidad desarrollada mediante el entrenamiento de fuerza (EF). A pesar de los datos obtenidos en animales (Remple et al., 2001) y la invariancia en la estructura espacial y temporal de los ejercicios monoarticulares y multiarticulares, el EF a menudo implica el aprendizaje de habilidades (Lundbye-Jensen et al., 2005). La retención y la transferencia son características del aprendizaje motor (Dayan y Cohen, 2011; Krakauer et al., 2019; Tablerion et al., 2020; Wanner et al., 2020). Dichos estudios son necesarios debido a la escasa información sobre la relación entre el desentrenamiento neuroplástico y el aumento de la especificidad de estas mediciones. La inclusión de un grupo de control activo podría confirmar que el estímulo del EF, y no solo la actividad contráctil inespecífica, da lugar a la neuroplasticidad. Esta recomendación está respaldada por la necesidad demostrada de examinar "…*cambios neuronales específicos que podrían resultar de las prescripciones de ejercicio diseñadas específicamente para inducir ciertos cambios funcionales*" en la salud y la enfermedad (Sandroff et al., 2020).

Recomendamos determinar los efectos del entrenamiento de fuerza (EF) en el rendimiento motor grueso. Algunos estudios sugieren que entrenar el movimiento objetivo con cargas o contra resistencia puede ser beneficioso, por ejemplo, para aumentar el rendimiento motor en adultos mayores con (Messa et al., 2019) y sin EP (Brach et al., 2017; Brach y Vanswearingen, 2013; Brach et al., 2020), mejorar el rendimiento atlético en judokas (Blais y Trilles, 2006; Helm et al., 2018a, b), rugby (Harrison y Bourke, 2009), kayak (Logan et al., 1997) y ciclismo de velocidad (Kordi et al., 2020). Por lo tanto, para mejorar el rendimiento motor grueso mediante EF, recomendamos entrenar los movimientos objetivo con cargas o contra resistencia. Esta modalidad de entrenamiento de fuerza garantiza que la neuroplasticidad resultante sea funcionalmente relevante, ya que las adaptaciones neuronales subyacentes se convierten en los mecanismos que permiten la incorporación de la fuerza muscular recién adquirida al movimiento objetivo. Esto es posible gracias a las similitudes entre 1) la estructura espacial y temporal del entrenamiento y los movimientos objetivo, y 2) entre los patrones de activación cerebral y muscular durante la preparación y ejecución del movimiento en el entrenamiento y los movimientos objetivo, como caminar, saltar, lanzar y alcanzar.

6. Conclusiones

El modelo de Sale sobre neuroplasticidad inducida por EF ha sido de gran utilidad durante décadas. Recomendamos actualizar el modelo con modelos analíticos de mediación (causal) basados en hipótesis. Se necesitan estudios que examinen la asociación entre los cambios en la función muscular, los marcadores de neuroplasticidad y los índices de la arquitectura muscular y tendinosa en respuesta al EF mediante análisis de mediación causal (Nuzzo et al., 2019a; Steele et al., 2020; Tolla'r et al., 2019a). De forma similar al entrenamiento aeróbico (Voss et al., 2020), es necesario determinar la relación entre los cambios en los resultados de rendimiento y los cambios en las medidas de conectividad funcional y efectiva (estructural) dentro del sistema nervioso. Esto podría explorarse mediante métodos electrofisiológicos e imágenes cerebrales antes y después del EF, y después de un período de desentrenamiento utilizando un grupo de control activo. Además, la relación entre los cambios en los índices de adaptaciones neuronales al EF y los aumentos en el rendimiento muscular podría complicarse por cambios tempranos en la estructura del músculo esquelético que ascienden a ~10 % (DeFreitas et al., 2011; Folland y Williams, 2007; Seynnes et al., 2007; Stock et al., 2016); por lo tanto, la inclusión de la arquitectura músculo-tendinosa está justificada en futuros estudios y modelos de mediación. Como la evolución temporal de las adaptaciones neuronales, tendinosas y musculares al EF difiere (Csapo et al., 2011; Kubo et al., 2010), solo los estudios que incorporen una combinación de dichas medidas tendrán éxito en determinar la imagen holística de cómo el EF mejora la función motora gruesa a lo largo de la vida en el rendimiento, la salud y la enfermedad.

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Review article

Functional relevance of resistance training-induced neuroplasticity in health and disease

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ABSTRACT

Repetitive, monotonic, and effortful voluntary muscle contractions performed for just a few weeks, i.e., resistance training, can substantially increase maximal voluntary force in the practiced task and can also increase gross motor performance. The increase in motor performance is often accompanied by neuroplastic adaptations in the central nervous system. While historical data assigned functional relevance to such adaptations induced by resistance training, this claim has not yet been systematically and critically examined in the context of motor performance across the lifespan in health and disease. A review of muscle activation, brain and peripheral nerve stimulation, and imaging data revealed that increases in motor performance and neuroplasticity tend to be uncoupled, making a mechanistic link between neuroplasticity and motor performance inconclusive. We recommend new approaches, including causal mediation analytical and hypothesis-driven models to substantiate the functional relevance of resistance training-induced neuroplasticity in the improvements of gross motor function across the lifespan in health and disease.

1. Introduction

A series of historical studies introduced the idea that structural and functional modifications in specific brain and spinal circuits (i.e., neuroplasticity) contribute to the rapid initial increase in maximal voluntary muscle (MVC) force following a period of resistance training (RT) in healthy humans (Sale and MacDougall, 1981; Sale et al., 1983, 1982). Broadly, neuroplasticity is 'the ability of the nervous system to respond to intrinsic and extrinsic stimuli by reorganizing its structure, function and connections' (p.1592, (Cramer et al., 2011). The gain in function, i.e., the increase in MVC force is a positive adaptation to RT as a result of modifications in the neural command to and the activation of the muscle. A figure in a review adopted by numerous textbooks depicts the relative roles of neural and muscular adaptations to RT (Fig. 11 in (Sale, 1988). The figure conceptualizes a sharp, initial rise in the contributions by the nervous system to strength gains, which plateau after a few weeks of RT when muscle hypertrophy becomes the determinant factor of strength gains. The review states that '…increases in peak force and rate

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Table 1
Definition of key terms and markers of plasticity.

Key term (abbreviation)	Definition
Corticospinal excitability, CSE	Likelihood and magnitude of responses to transcranial magnetic stimulation of excitable structures of the corticospinal tract, from the primary motor cortex to muscle.
Gross motor performance	Multi-joint functional activities such as walking, jumping, throwing.
Hoffman reflex, H-reflex	Response to weak peripheral electrical nerve stimulation, an estimate of the excitability of spinal motoneurons and Ia-afferent presynaptic inhibition.
Maximal compound muscle action potential, Mmax	Response to maximal intensity peripheral electrical nerve stimulation, representing the sum of dispersed action potentials of the motor units under the territory of a recoding electrode on the skin surface.
Maximal voluntary contraction force, MVC force	Force generated during a maximal effort muscle contraction at a single joint against a resistance with or without continuous feedback.
Motor unit discharge rate	Frequency at which motor units discharge action potentials during a muscle contraction.
Motor unit recruitment	Number of active motor units during a muscle contraction.
Movement related cortical potentials, MRCP	Negative surface potentials detected at the scalp during voluntary movements that reflect cortical activity.
Neuroplasticity / Neural adaptations	Structural and functional modifications in specific brain and spinal circuits.
Resting-state connectivity	Associations between the fluctuations in the hemodynamic signal of brain regions.
Short-interval intracortical inhibition	Response to paired pulse transcranial magnetic stimulation, reflecting the efficacy of intracortical inhibition mediated by low-threshold inhibitory GABA-a intracortical neurons.
Silent Period	Response to single pulse transcranial magnetic stimulation, reflecting the efficacy of inhibition mediated by GABA-b intracortical neurons.
Surface electromyograph-ic activity, sEMG	Sum of action potentials discharged by recruited motor units under the territory of EMG electrodes during a muscle contraction.
Volitional wave, V-wave	Response to supramaximal intensity peripheral nerve during a maximal voluntary contraction, reflecting the efferent spinal motoneuron output to muscle.
Voluntary activation, VA	Computed response to maximal intensity, millisecond-duration peripheral nerve stimulation at rest and during maximal voluntary muscle contraction, reflecting the ability to of skeletal muscle to become activated by voluntary command.

of force development *are associated with* increased activation of prime mover muscles' (p. s135, (Sale, 1988). Sale later revised this scheme and postulated that RT-induced muscle adaptations (hypertrophy) do occur already after one session of RT in untrained subjects, as evidenced by muscle fiber damage and a subsequent stimulation of protein synthesis (Fig. 11, p. 305) (Sale, 2003).

Since the publication of these seminal papers over 30 years ago, nearly 20 reviews have highlighted several structural and functional adaptations at the spinal and supraspinal level with a role in strength gains during the initial 2–12 weeks of RT (Table 1, Figure 1) (Aagaard, 2003, 2018; Aagaard et al., 2010; Carroll et al., 2001, 2011; Cormie et al., 2011a, b; Duchateau et al., 2006; Enoka, 1988; Folland and Williams, 2007; Gabriel et al., 2006; Hedayatpour and Falla, 2015; Hortobágyi and Maffiuletti, 2011; Kidgell et al., 2017; Kidgell and Pearce, 2011; Kraemer et al., 1988; Markovic and Mikulic, 2010; Mason et al., 2019; Oranchuk et al., 2019; Siddique et al., 2019). The assumption was that these adaptations increase MVC force by improving neural activation of skeletal muscle's contractile machinery. However, much evidence of neural adaptations is indirect and the specific mechanisms

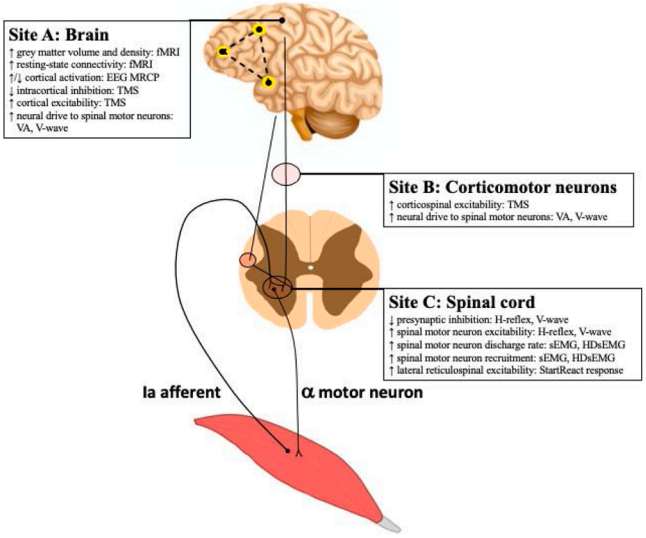

Fig. 1. Potential sites of and methods to assess neuroplasticity induced by resistance training. We address resistance training induced neuroplasticity and its functional relevance at: Site A in sections 2.2, 2.3, 2.4 and 2.5; Site B in sections 2.2, 2.3, and 2.4, and at Site C in sections 2.1 and 2.3. Dashed lines symbolize connectivity between frontal (cognitive), motor, and temporal (memory) areas known to become modified by resistance training. The vertical arrows in the text denote the direction of changes (increase, decrease, no change). This simplified model does not show several additional potential sites where adaptations to resistance training could occur such as corticoreticular connections, reciprocal reticular connections, reticulospinal projections to interneurons, corticospinal projections to interneurons, and corticomotoneuronal synapses (see Glover and Baker, 2020). fMRI, functional resonance imaging; EEG MRCP, electroencephalographic movement related cortical potentials; TMS, transcranial magnetic stimulation; VA, voluntary activation; V-wave, voluntary wave evoked by peripheral nerve stimulation; H-reflex, Hoffman-reflex; sEMG, surface electromyography; HDsEMG, high-density sEMG.

remain elusive. There is also no consensus on individual mechanisms nor evidence on the relative significance of the various adaptive mechanisms.

Critically for numerous populations such as athletes, the steadily increasing number of older adults, and patients, the unaddressed and timely question is how, 'neural adaptations' are functionally relevant? We propose that the root cause of a lack of progress in the field is an over interpretation of and over-reliance on the data showing, for the most part, merely parallel changes in indices of neuroplasticity and measures of MVC force or multi-joint, gross motor performance. We hypothesize that the parallel changes in neural outcomes and MVC force or motor performance can occur without a meaningful or statistically significant association. We suspect that the reasons for the uncorrelated changes after RT are: 1) The task-specificity of measurements at rest is low relative to training at high forces but technically it is challenging to reliably assess neuroplasticity during MVC measurements and the interpretation of such data is complex (Lundbye-Jensen et al., 2005); 2) Selection of only one or two variables quantifying neuroplasticity none of which on its own versus a network analysis or multivariate approach would be conceptually expected to predict increases in MVC force, and 3) Changes in neuroplasticity and MVC force occur with different time courses during and after RT (Csapo et al., 2011; Kubo et al., 2010) and at sites that have been overlooked (Baker and Perez, 2017; Choudhury et al., 2019; Fernandez-Del-Olmo et al., 2014; Glover and Baker, 2020).

If the association between RT-induced increases in MVC force and changes in markers of neuroplasticity is low, it is not surprising that such associations are nearly non-existent between changes in measures of neuroplasticity and increases in gross motor performance such as walking, jumping, and throwing. There is indeed a paucity of studies

examining how newly acquired physical abilities (i.e., increase in MVC force) can be incorporated into, for example, older adults' and patients' gait, allowing them to walk safely faster (Beijersbergen et al., 2013). Neuroplasticity associated with RT would be functional if it acted as the enabling mechanism in the increases in gross motor performance in healthy adults and in patients with Parkinson's disease (PwPD), multiple sclerosis (PwMS), and stroke (PwS). A potential reason for the weak or non-existing correlations between changes in MVC force and gross motor performance is the low task specificity between single-joint RT exercises and gross motor tasks made up of multi-joint movements. Single joint RT can increase muscle size and strength but might not be as effective to increase gross motor performance as would exercises involving multi-joint movements that closely mimic the spatiotemporal structure and muscle activation patterns of walking, running, jumping, or reaching with the arms (Kraemer et al., 2002; Kraemer and Ratamess, 2004). In other words, if RT primarily includes single-joint exercises, transfer to functional movements such as walking, running, and jumping are limited which can be explained through the principle of training specificity. This principle denotes that the applied RT exercise should resemble the functional movement task to increase the likelihood of transferring RT-related strength gains to function (Reilly et al., 2009). Thus, there is a need to move to the next, i.e., more functional level in understanding the relation between neural adaptations to RT, the potential changes in gross motor function, and the underlying mechanisms.

The purpose of this review was to examine 1) if individual variations in RT-induced gains in MVC force are associated with individual variations in specific indices of neuroplasticity and 2) if such a relationship underlies improvements in MVC force and, more broadly, multi-joint, gross motor function in athletes, older adults, and patients. Clearly, correlation is not causation. However, we argue that the determination of correlative changes would fill the gap in current knowledge which is based on merely parallel changes in indices of neuroplasticity and behavioral outcomes of RT. A critical shortage in previous research is a lack of correlative analyses of changes in behavioral outcomes (MVC force, motor performance) and measures of underlying neuroplasticity.

One way to address this knowledge gap is through causal mediation analyses that aim to obtain unconfounded estimates of the direct and indirect effects of RT on motor performance (Zhang et al., 2016). In the current context, mediation is the process through which RT causes increases in motor performance. The untested hypothesis is that some or all of the total effect of RT on motor performance operates through a mediator, i.e., neuroplasticity. The direct effect is the effect of RT on the motor performance free of the mediator's effect. The indirect path is the effect of RT on the outcome operating through mediator(s). Following an increasing number of attempts using causal mediation analyses in kinesiology (Condello et al., 2019, 2016; Condello et al., 2017; Forte et al., 2013; Jekauc et al., 2017; Marcos-Pardo et al., 2020; Mavros et al., 2017; Tollár et al., 2019a, 2020), we provide illustrative examples for this approach to recommend a more systematic, mechanistic, and hypothesis-driven examination of the functional relevance of RT-induced neuroplasticity in improving motor performance in health and disease. First, we examine evidence for the association between the most often reported indices of neuroplasticity and increases in MVC force generated by muscles at a single joint. Next, we review exemplary evidence how neural adaptations to RT could mediate improvements in gross motor function in athletes, older adults, and selected groups of patients with mobility impairments. Concerning the inclusion of such a diverse array of population, we posit that RT for 2–12 weeks can reduce muscle weakness through induction of neuroplasticity hence an increased understanding of the functional relevance of such neural adaptations are applicable to all participants of RT interventions regardless of clinical background. We conclude with recommendations for future research and, based on experimental data extracted from individual papers listed in reviews, we propose evidence-based, mechanistic structural equation models that update Sale's classical, descriptive model (Sale, 1988, 2003). Such modeling makes it possible to causally link RT-induced changes in markers of neuroplasticity and motor performance, as reviewed in detail previously (Nuzzo et al., 2019a; Steele et al., 2020; Tollár et al., 2019a).

2. Functional relevance of RT-induced neuroplasticity to increase MVC force

Here, we examine changes induced by RT in markers of neuroplasticity underlying the increases MVC force. Markers of muscle activation include surface electromyographic activity (sEMG) and voluntary activation (VA), responses to peripheral nerve stimulation (Hoffman or H-reflex, voluntary or V-wave), responses to transcranial magnetic brain stimulation (TMS), and imaging.

2.1. Muscle activation: sEMG activity and MVC force

MVC force is the result of the strong activation of prime mover individual muscles forming the agonist muscle group, the coordinated deactivation of individual muscles forming the antagonist muscle group, and coordinated activation of remote muscle groups to stabilize posture (Rutherford, 1988; Rutherford and Jones, 1986). RT-induced plasticity in the coordination among individual agonists and the coordinative changes among stabilizers have been rarely examined. Studies instead have focused on measuring markers of neuroplasticity in representative individual muscles of agonists and coordination between agonist and antagonist muscle groups (Arnold and Bautmans, 2014; Hortobágyi et al., 2006; Remaud et al., 2007).

Concerning markers of neuroplasticity in representative individual muscles of agonist, MVC force is determined by motor unit recruitment and the rate at which motor neurons discharge action potentials (Carroll et al., 2011; Folland and Williams, 2007). The net output (spinal and supraspinal) controls motor unit recruitment and discharge rate during muscle contraction. Thus, structural and functional changes in spinal circuits or within brain areas upstream to the spinal motor neurons could be the locus of neural adaptations to RT, underlying increases in MVC force (Kidgell et al., 2017; Kidgell and Pearce, 2011; Siddique et al., 2019).

Changes in muscle size and MVC force occur in a temporally dissociated manner. sEMG activity has been used as a surrogate measure of neuroplasticity. It summates the action potentials of detectable motor neurons recruited during muscle contraction. Indeed, increases in sEMG activation of the trained muscle precede detectable changes in hypertrophy (Akima et al., 1999; Häkkinen et al., 2001a, b; Narici et al., 1989; Rutherford and Jones, 1986). However, of the 25 individual studies analyzed in reviews, we found only 2 studies reporting very strong associations ($r \approx 0.70$) between increases in sEMG and muscle strength following RT (Häkkinen and Komi, 1986; Häkkinen et al., 1985a,b). We classify correlation coefficients of 0.1, 0.3, 0.5, 0.7, and 0.9 as weak, moderate, strong, very strong and extremely strong correlations, respectively (Hopkins et al., 2009; Schober et al., 2018). The majority of studies either did not report or find an association between sEMG-indexed neural adaptations to RT and improvements in MVC force. Whether reduced neural drive to antagonists could explain increased MVC force remains controversial, as an equal number of studies report such reductions (Carolan and Cafarelli, 1992; Häkkinen et al., 1985a,b; Simoneau et al., 2007) and also no changes in antagonist sEMG after RT (de Boer et al., 2007; Holtermann et al., 2005; Reeves et al., 2005), but none reported correlated changes in MVC force and antagonist sEMG. Limitations with sEMG, such as action potential cancellation biases, constrains sEMG amplitude as an index of neuroplasticity. Measuring sEMG constituents, i.e., motor unit recruitment and the rate at which motor neurons discharge action potentials could reduce this bias and there is first evidence indicating an association between these parameters and strength gains (Del Vecchio et al., 2019a). An additional complicating factor in many studies is that sEMG was often recorded in a single muscle, whereas MVC force is the result of

several individual muscles making up the agonist muscle group and the coordinated de-activation of antagonist and activation of remote stabilizers, factors rarely measured (Rutherford, 1988; Rutherford and Jones, 1986). Even properly, i.e., Mmax-normalized, sEMG measures can be insensitive markers of neural adaptations to RT interventions of drastically different compositions (Duchateau et al., 2020), necessitating the use of more advanced sEMG methods (Vieira and Botter, 2021). In total, the evidence is, at best, weak for sEMG-indexed muscle activation as a measure of neuroplasticity accompanying RT. (See Recommendations 5.1, 5.4).

2.2. Muscle activation: VA and MVC force

Compared with sEMG, twitch interpolation provides greater insights to determine VA, which is a summed estimate of the number of motor neurons recruited and the rate at which they discharge action potentials (Allen et al., 1998; Nuzzo et al., 2019b; Shield and Zhou, 2004). Presumably, VA measured by twitch interpolation over the motor point reflects the neuroplasticity in a single agonist muscle. It is therefore surprising that the relevant systematic reviews of the topic did not include studies using peripheral nerve stimulation to assess VA. Instead, some studies reported only VA measured by TMS (Carroll et al., 2011; Kidgell et al., 2017; Siddique et al., 2019). Counterintuitively, MVC force was found to also increase after RT without changes in VA (Herbert et al., 1998; Tillin et al., 2011). Notwithstanding, VA and MVC force tended to increase in parallel after RT (Behrens et al., 2016; Brown et al., 2017; Giboin et al., 2018) and, in some cases, in a moderately to highly correlated manner ($r = 0.54–0.77$) (Ema et al., 2018; Toien et al., 2018), which has been attributed to low VA at baseline, especially in older adults (Arnold and Bautmans, 2014). Furthermore, the limited evidence suggest that VA might act as a mechanism enabling the incorporation of increased MVC force into gross motor performance. For example, increases in VA and gait speed correlated strongly ($r = 0.67$) after RT in mobility-limited older adults (Hvid et al., 2016). However, we note that if VA is a comprehensive measure of neural drive and reaches 100 % of available motor neurons in initially sedentary healthy adults after RT, it is rather unlikely that highly-resistance trained athletes can further improve VA. Instead, it is more likely that such athletes can improve MVC force through muscle hypertrophy (Balshaw et al., 2019). One possibility is that measuring VA in one muscle does not represent adaptations in the rest of the individual muscles making up the agonist muscle group that produces MVC force, resulting in an underestimation of VA for the whole muscle group and thus resulting in low or no correlations with motor performance (Allen et al., 1998; Nuzzo et al., 2019b; Shield and Zhou, 2004). The inconsistent data are also related to the forms of measuring VA, including single, double, and multiple peripheral electrical pulses and TMS-induced VA. (See recommendations 5.2, 5.4).

2.3. Peripheral nerve stimulation and MVC force

The H-reflex amplitude, produced by peripheral nerve stimulation at rest, can provide an estimate of the excitability of spinal motor neurons, and hence a marker of neuroplasticity after RT. A meta-analysis found no changes in H-reflex amplitude measured at rest in response to RT (Siddique et al., 2019). The V-wave is an H-reflex variant evoked during forceful muscle contractions by supramaximally stimulating a peripheral mixed nerve. Although the V-wave is influenced by all of the synaptic inputs to the motor neuron pool, during maximal contractions a large part of the motor neuron input comes from the descending neural drive and could be a marker of task-specific neural adaptations to RT (Aagaard et al., 2020, 2002). Meta-analytical evidence of five studies ($n = 52$ subjects) suggested a consistent increase in V-wave amplitude after RT; however, only one study showed a moderate correlation ($r = 0.45$) between changes in MVC force and V-wave amplitude after RT (Vila-Cha et al., 2012). The H-reflex and V-wave, like most often VA, is a single muscle measure and does not represent all of the individual muscles in the agonist group nor can these outcomes indicate changes in coordination among the synergistic muscles. (See recommendation 5.2, 5.4).

2.4. Brain stimulation and MVC force

Non-invasive brain stimulation such as single and paired pulse TMS can measure changes in the excitatory-inhibitory circuits produced by changes in corticospinal excitability (CSE) and/or changes in the efficacy of intracortical inhibitory or facilitatory interneurons after RT (Hallett, 2000). Such changes produced by RT would hypothetically increase the magnitude and efficacy of the motor command so that the motor neurons would receive a greater drive, increasing MVC force after RT. Meta analyses of TMS data support the idea that CSE increases and intracortical inhibition decreases after RT (Kidgell et al., 2017; Siddique et al., 2019). This is particularly true when the TMS measurements are done using a background contraction (i.e., not at rest). The parallel increases in MVC force and CSE, and decreases in inhibition have led to the assumption by some (Kidgell et al., 2017; Siddique et al., 2019), that these processes are mechanistically linked, but not all authors concur (Nuzzo et al., 2019a). Indeed, of the studies that measured CSE ($n = 22$ studies), contralateral silent period ($n = 7$ studies), and short-interval intracortical inhibition ($n = 8$ studies) after RT, only two reported significant but moderate associations between decreases in silent period (a measure of cortical inhibition) and increases in MVC force ($r \approx -0.50$) (Hendy and Kidgell, 2013; Kidgell and Pearce, 2010). A lack of correlation could in part be due to the dissimilarity between the test and training tasks (i.e., rest vs. contraction, intensity and type of contraction). This task-specificity effect seems to be weaker in RT than in balance training (Mouthon and Taube, 2019). For example, even within the same study only externally but not internally paced RT produced changes in CSE and cortical inhibition measured during contraction, implying that the adaptations in CSE and cortical inhibition did not contribute to strength gains (Leung et al., 2017). Neuroplastic changes were also absent after RT when responses to TMS were measured during muscle contraction in an arm muscle (Lundbye-Jensen et al., 2005). In sum, most studies did not seem to have computed, reported, or found functionally relevant associations between changes in TMS-derived indices of neuroplasticity and improvements in MVC force after RT. The evidence for a functional link between strength gains and increases in CSE or decreases in cortical inhibition in healthy adults is modest, questioning the functional role of these neural adaptations in increasing MVC force. (See recommendations 5.2, 5.4).

2.5. Imaging data and MVC force

Neuroplasticity accompanying RT has been rarely examined by brain imaging. Data from 18 brain imaging studies suggested that RT can increase gray matter thickness and volume, and improve functional and resting-state connectivity in several brain areas (Herold et al., 2019). However, these studies were designed to determine the relationship between brain plasticity and cognitive function rather than increases in motor performance. Understandably, these studies did not describe association between changes in motor performance and brain plasticity.

Short term, 2–12 weeks of RT produced inconsistent brain adaptations as measured by magnetic resonance imaging (MRI). Twelve weeks of RT increased gray matter density in the posterior and anterior lobe of the cerebellum, the superior frontal gyrus in the frontal lobe, and in the anterior cingulate cortex of the limbic lobe in healthy older adults. However, the authors did not assess the relation between these brain changes and motor performance (Fontes et al., 2017). Sixteen sessions of 36 right-unilateral isometric plantarflexions improved MVC force in the trained (40 %) and untrained (30 %) leg and decreased mean diffusivity of the left corticospinal track (effect size = 1.4) and decreased putamen volumes (Palmer et al., 2013). The 40 % increase in MVC force correlated moderately, $r = -0.55$, with the observed ~2% changes in mean

diffusivity, reflecting, according to the authors, improved myelination. The changes in putamen volume might be related to improved motor learning. The diffusivity data could reflect the strength element of the training adaptations. However, the 30 % increase in the untrained contralateral side (cross-education) occurred without any changes in brain structure.

Right-unilateral ulnar deviation RT (n = 24 sessions) improved each hand's MVC force by ~46 % (Farthing et al., 2007). When subjects contracted the right-trained hand in the magnet after RT, the activation in left primary motor and somatosensory cortex, dorsal premotor cortex, and other areas increased compared with the activation before RT (n = 4 subjects). When subjects contracted the left-untrained hand after RT, activation in the right sensorimotor cortex and left temporal lobe increased compared to before RT. Unilateral handgrip RT spared the opposite immobilized limb from MVC force loss (+0.8 %). The force-sparing correlated with increased left motor cortex volume of activation. In the non-training controls, MVC grip force of the immobilized limb decreased by 11 % without changes in the contralateral motor cortex activation (Farthing et al., 2011). However, there were no further correlation analyses performed between measures of neural adaptations and changes in MVC force.

The activity of the cerebral cortex measured with the mean frequency of the electroencephalogram (EEG) increased independent of intervention type in PwPD (Carvalho et al., 2015), suggesting a fitness component in the exercise effects on improved brain flow (Tollár et al., 2019a). EEG-derived corticomuscular coherence measured at different MVC forces was also independent of training history in RT and aerobically trained athletes (Dal Maso et al., 2017). The effects of short-term RT on the amplitude of the movement related cortical potentials (MRCPs) in healthy untrained subjects are inconsistent. Three weeks of unilateral explosive RT increased MVC force, rate of tension development, and sEMG. These changes were accompanied by *decreases* in the amplitude of the MRCPs. The authors did not report if the changes in force and EEG measures correlated with each other. The interpretation was that RT improved neural economy, as submaximal force generation was achieved by reduced cortical drive (Falvo et al., 2010). However, four weeks of eccentric vs. concentric leg RT increased MVC outcomes and also *increased* MRCP amplitudes recorded during submaximal muscle contraction in healthy older adults (Kang et al., 2016). Motor imagery of forceful elbow flexion for 30 min at rest increased MVC force and also MRCP amplitude by 20–22 % at C3 and Cz electrodes (Yao et al., 2013). Accordingly, the increase in descending command would recruit previously inactive motor units and/or have higher discharge rate of active motor units, thereby increasing MVC force. RT might have also lowered inhibition to the motor neuron pool of the muscles, increasing net motor neuron output (Yao et al., 2013). These data were interpreted as evidence for neuroplasticity in motor cortex, cerebellum, supplementary motor area, and dorsal premotor cortex; however, the authors did not report correlations between EEG, sEMG, and MVC force (see also (Liu et al., 2019). Collectively, there is evidence that RT produced favorable changes in brain structure and function, but there is little evidence for such changes to correlate with increased MVC force. Additionally, there has been no attempt to relate brain imaging data to sEMG, TMS, or peripheral stimulation data following RT; consequently, current imaging data provide little mechanistic evidence for how changes in putative brain areas and networks after RT could increase motor performance. (See recommendations 5.3, 5.4).

3. Functional relevance of neural adaptations to RT in aging and neurological conditions

In light that aging, especially in combination with a disease, reduces the responsiveness of skeletal muscle to mechanical stimuli (Drummond et al., 2008; Kumar et al., 2009), a clearer understanding of how neuroplasticity could mediate increases in motor performance after RT would improve the specificity of exercise prescription for older adults and patients. In particular, patients with neurological and neurodegenerative conditions would benefit, as RT could exploit well-functioning areas of the central nervous system to stimulate neuroplasticity and activities of daily living. (See for this section Recommendation 5.5).

3.1. RT-induced neuroplasticity for improving older adults' walking speed

Gait speed in late mid-life predicts health, medical, and cognitive conditions later in life, including mortality/survival and morbidity (Beijersbergen et al., 2013). Understanding the biomechanical and neural mechanisms of minimizing age-related loss of gait speed is thus an important element of designing and prescribing exercise for older adults. In such studies, lower extremity RT improved MVC force of muscles involved in force generation in the stance phase of gait (Hortobágyi et al., 2015). However, increases in gait speed and MVC force of muscles involved in the propulsion thrust correlated weakly (Beijersbergen et al., 2017; Uematsu et al., 2018, 2014). The assumption is that RT-induced neuroplasticity underlies increases in gait speed. Indeed, changes in sEMG after RT suggested that older adults used a fraction of the training-induced increases in muscle activation-capacity during walking. Moreover, after RT, the changes in inter-joint coordination assessed through gait kinematics, poorly predicted the increases in gait speed (Beijersbergen et al., 2013). That is, muscle activation measured during gait by sEMG after RT had no or only limited functional relevance for increasing gait speed. We speculate each subject adapted differently, 'choosing a different solution', precluding the emergence of a common neural adaptive pattern. When the functional priority is to increase gait speed, the stand-alone administration of a RT program has low effectiveness, which can be increased by combining RT with gait re-training protocols in the elderly (Gillespie et al., 2012). Such approaches are designed so that RT-induced neuroplasticity could facilitate the incorporation of newly acquired muscle strength into gait kinetics. However, the functional role of RT-induced neuroplasticity in improving older adults' walking speed remains unclear.

3.2. RT-induced neuroplasticity and motor function in PwPD

Most PwPD have lower strength levels and display lower rates of force development compared to healthy age-matched control subjects (Inkster et al., 2003; Paasuke et al., 2004, 2002). Notwithstanding its effects on MVC, Parkinson's disease can impair the neural drive to the muscle and thereby cause a lower VA (Huang et al., 2017) and a higher unsteadiness of voluntary force (Skinner et al., 2019).

While MVC force has been shown to correlate strongly (r = 0.68−0.80) with chair rise and timed-up-and-go performance in a few studies (Inkster et al., 2003; Schilling et al., 2009), systematic reviews concluded that RT-induced increases in MVC force might not translate into functional improvements in PwPD (Cherup et al., 2019; Falvo et al., 2008; Ramazzina et al., 2017; Roeder et al., 2015; Tillman et al., 2015). The only hint for RT-induced neuroplasticity to correlate with motor function emerged when RT-induced increases in MVC force and EMG muscle activation predicted upper limb bradykinesia after 24 months of RT (David et al., 2016). In sum, PwPD respond to RT but the neuroplastic and strength adaptations are uncorrelated and have limited or no effects on activities of daily living. This may be related to the low specificity of RT exercise to the muscle activation patterns present in activities of daily living. It remains unclear how and if the RT-induced neuroplasticity could act as enabling mechanisms for PwPD to improve activities of daily living through the increased MVC force.

3.3. RT-induced neuroplasticity and motor function in PwMS

PwMS often have low MVC force in limb muscles, affecting functional capacity (Kjolhede et al., 2015b). MVC force of the knee flexor (r ~0.5−0.7) was found to correlate more strongly than knee extensor (r

~0.1−0.4) with walking capacity in PwMS (Broekmans et al., 2013). The clinical interpretation was that PwMS would benefit from RT to improve walking ability (Manca et al., 2019). Indeed, RT increased MVC force by up to 36 % in PwMS (Cruickshank et al., 2015; Manca et al., 2019). Meta-analysis revealed increases in MVC force with small-to-moderate effect sizes, which was interpreted as diminished responsiveness of PwMS to RT (Jorgensen et al., 2017). Whether the increases in MVC force also translate into improved gross-motor function is unclear. While there is a relationship between walking speed and leg MVC force in PwMS (Thoumie et al., 2005), RT improved walking speed only with low effect sizes (0.35) (Manca et al., 2019). Sporadic data suggest that RT can also improve chair rise, stair ascent, and 10-m walking speed, and distance walked in 6 min (Dalgas et al., 2009). The evidence is weaker for RT to improve upper extremity function in PwMS (Lamers et al., 2016).

In the MS literature minimal attention has been devoted so far to whether or not RT-induced neuroplasticity could underlie the increases in MVC force. There were parallel increases in sEMG activity of the knee extensors and flexors and MVC force of these muscles (Dalgas et al., 2013; Kjolhede et al., 2015a). Likewise, sEMG activity and superimposed V-wave amplitudes in ankle plantarflexors increased after 3 weeks of maximal intensity RT in PwMS (Fimland et al., 2010). Control of submaximal leg muscle isometric force correlated with walking speed in PwMS suggesting that moderate declines in the walking performance were more strongly associated with impairments in force control rather than decreases in MVC force (Davis et al., 2020). In sum, the limited evidence seems to suggest that RT is an effective method to increase efferent motor output of spinal motor neurons in PwMS. However, correlations between changes in sEMG-based outcomes and increases in MVC force were not reported. Likewise, there is a lack of data on the relationship between changes in markers of neuroplasticity and changes in gross motor function.

3.4. RT-induced neuroplasticity and motor function in PwS

Muscle weakness limits motor activity in PwS (Ada et al., 2006; Canning et al., 2004). MVC force in the affected limb can be as low as one half of healthy age- and sex-matched controls (Neckel et al., 2006). Meta-analytical evidence suggests that RT can increase MVC force in the lower extremities of chronic PwS (Dorsch et al., 2018; Wist et al., 2016). The efficacy of RT to increase MVC force in the upper extremity in PwS (Harris and Eng, 2010) and in the acute state (i.e., up to three months after a stroke) is uncertain (Salter et al., 2016).

It is also unclear if RT-induced increases in MVC force are related to improvements in motor function. While RT improved MVC force in lower extremity muscles substantially (effect size = 1.1), no improvements occurred in motor function assessed by the timed-up-and-go test (effect size = 0.4) (Dorsch et al., 2018). The RT effects were also minimal on upper limb functions (effect size = 0.2). Reviews conclude that RT-induced gains in MVC force, in general, do not transfer to functional improvements in PwS (Tiozzo et al., 2015). One exception is gait speed (Wonsetler and Bowden, 2017), which improved (effect size: 0.4−0.7) above the minimally important difference for habitual (+0.11 m/s) and fast walking speed (+0.18 m/s) after RT (Clark and Patten, 2013). High-intensity RT of upper extremity muscles combined with functional task practice also improved MVC force and a number of functional outcomes in parallel (Patten et al., 2013), alluding to the possibility that a combination of functional tasks with RT would increase the task-specificity of RT to daily tasks. However, the role of RT-induced neuroplasticity remains unclear in improvements in MVC force and gross motor performance in PwS.

4. RT-induced neuroplasticity for increasing athletic performance

Athletes use RT to improve MVC force with an expectation based on the assumption and research evidence that contractile force and speed are associated with athletic performance. However, based on the principle of Specific Adaptation to Imposed Demands (Fox and Mathhews, 1988) and the concept of training specificity (Sale and MacDougall, 1981), RT normally does not explicitly train athletic skills (Sale, 1988). We examine this assumption with respect to sprint and distance running performance, in highly resistance-trained athletes in whom the Sale model (Sale and MacDougall, 1981) predicts little or no RT-induced neuroplasticity and in prepubertal children who could improve athletic performance after RT almost exclusively due to neuroplastic changes. (See for this section Recommendation 5.5.)

4.1. Sprint running performance

Sprinters use RT to increase running speed (Haugen et al., 2019). During sprinting, athletes accelerate body mass by rapidly applying high forces to the ground. Sprinters use high-speed RT to increase leg muscle power by improving contractile force and velocity while minimizing muscle mass gains (Behm et al., 2017; Delecluse, 1997). The evolving neural adaptations reduce torque generation time through heightened motor unit recruitment and discharge rates in the agonist muscles (Del Vecchio et al., 2019a, b) and an earlier recruitment of high threshold motor units (Del Vecchio et al., 2019b). An increase in motor neuron excitability after RT would also increase MVC force in response to input from supraspinal drive and spinal Ia afferents, and would increase the stiffness of the muscle-tendon unit, aiding force production and reducing ground contact times (Aagaard et al., 2002; Ross et al., 2001).

Currently, there are no studies showing a relation between RT-induced increases in MVC force, markers of neuroplasticity, and sprint times. RT is expected to increase H-reflex amplitude, i.e., motor neuron excitability, and decrease presynaptic inhibition (Aagaard et al., 2002) but sprinters compared with distance runners had a *lower* H-reflex amplitude (Casabona et al., 1990; Maffiuletti et al., 2001). Because H-reflex arises from the activation of low threshold motor neurons, the lower H-reflex amplitude may result from the lower proportion of low- vs. high-threshold motor units, resulting in the activation of fewer motor neurons contributing to the H-reflex during stimulation intensities at which the H-reflex is not cancelled by the antidromic propagation of the action potential (Casabona et al., 1990). Longitudinal studies are needed to answer this question.

While RT improves sprinters' MVC force and produces neuroplastic changes, these changes weakly correlate with improved sprint times (Harris et al., 2000; Lyttle et al., 1996; McBride et al., 2002; Moir et al., 2007; Wilson et al., 1993). Differences in the pattern of muscle activation during RT and sprinting and being a novice vs. elite sprinter might explain the poor relationship (Barr et al., 2014; Styles et al., 2016). In contrast, resisted sprint training over short distances compared with RT improved sprint times more effectively, suggesting that the spatiotemporal structure of training stimulus is an important factor to improve sprint times (Bachero-Mena and Gonzalez-Badillo, 2014; Behm and Sale, 1993; Bolger et al., 2015; Petrakos et al., 2016; Rumpf et al., 2016). The extent of specificity is not entirely clear because isometric training conducted on a cycle ergometer also improved world class cyclists' peak leg power output (Kordi et al., 2020). Together, the data suggest that similarity in muscle activation during the training (resisted sprinting) and the target tasks (unresisted, 'real life' sprinting) affords the greatest specificity hence effectiveness of training but it is unclear if RT-induced neuroplasticity acts as the enabling mechanism to improve sprint times.

4.2. Distance running performance

Distance runners also use RT to improve distance-running times (Trowell et al., 2019). The assumption is that RT improves trained muscle groups' MVC force and athletes' ability to activate these muscles. Improved activation would increase angular acceleration of the leg during swing, increasing running speed. However, there is no

correlation between training-induced increases in MVC extensor torques and running economy following RT, implying that improvements in hip and knee joint torques might contribute to increase maximal but not submaximal running speed used during distance races (Alcaraz-Ibanez and Rodriguez-Perez, 2018; Macadam et al., 2019; Trowell et al., 2019; Young, 2006).

RT-induced neuroplasticity could enable faster running by modifying inter-muscular coordination within a muscle group and inter-joint coordination in movements that are specific for, and similar to, the training exercises (Enoka, 1988; Folland and Williams, 2007). The modifications include increases in selective and synergistic muscle activation and decreases in antagonist muscle activation. Such changes could reduce the neural drive needed for submaximal contractions. Increases in motor neuron excitability after RT could also reduce motor unit discharge rate compensated by motor unit recruitment during prolonged submaximal exercise (Vila-Cha et al., 2012). RT would thus reduce the metabolic cost of each step. However, muscle activation during running has never been measured after RT in competitive runners. It is therefore unknown if RT could improve ground force application through altered coordination or would modify motor unit recruitment, leading to improved metabolic cost and running economy, fatigue resistance, and ultimately running speed.

Indeed, the evidence seems to favor a mechanical rather than a neural mechanism of RT improving distance-running times. Seemingly against the principle of training specificity, *isometric* RT improved distance-running performance (Lum and Barbosa, 2019). This is possible because as the Achilles tendon becomes stretched in the stance phase and muscle fibers of the knee and ankle extensors are in an isometric state (Bohm et al., 2018; Roberts et al., 1997), thereby increasing push-off force. Lower extremity RT also improves running economy by 4% due to increased tendon stiffness that results in increase in elastic energy and a redistribution of muscular output while running (Albracht and Arampatzis, 2013). A combination of heavy and explosive RT training can improve neural control, muscle force, and elasticity, which in turn could shorten ground contact times and improve running economy (Balsalobre-Fernandez et al., 2016; Blagrove et al., 2018; Johnston et al., 1997; Paavolainen et al., 1999), although the relationship between these changes is inconsistent (Blagrove et al., 2018; Jung, 2003). Distance runners certainly experience improvements from RT, even though neuroplastic adaptations cannot be ruled out, the evidence for performance improvements through mechanical changes is more likely.

4.3. RT-induced neuroplasticity in trained athletes

Sale suggested that neural adaptations to RT plateau after the initial weeks of RT when hypertrophy becomes the predominant determinant of strength gains (Sale, 1988). Cross-sectional studies do not address this issue, but provide clues that neuroplastic changes continue past the arbitrary initial period. For example, reductions in the force evoked by TMS during muscle contraction suggested that RT-induced neuroplasticity was evident in RT-trained healthy adults who continued RT (del Olmo et al., 2006). Chronically RT-trained healthy adults displayed abolished TMS-evoked cortical inhibition during voluntary forces of ≥40 % MVC (Lahouti et al., 2019). In RT-trained individuals who continued RT, motor neuron adaptations continued (Pearcey et al., 2014) and antagonist muscle activation was reduced after 4 years of RT, suggesting that inter-muscular coordination is a longer-term neural adaptation (Balshaw et al., 2019). In contrast to these data in support of neuroplastic changes extending over years after the start of RT, agonist muscle activation measured by sEMG did not differ after 12 weeks or 4 years of RT, however changes in co-activation were not examined. A case series of two power lifters and one weight lifter with many years of RT showed improvements of up to 10 % in maximal back squat strength without muscle hypertrophy (Zourdos et al., 2016). RT-induced changes in markers of neuroplasticity were shown to continue in elite junior skiers (<15 years) who improved vertical jump performance alongside (but not correlated with) increase in spinal excitability, suggesting increases in motor neuronal output with long-lasting RT (Taube et al., 2007). The evidence shown here makes the plateau proposed by Sale seem unlikely.

4.4. RT-induced neuroplasticity in prepubertal athletes

Due to a lack of circulating androgens in prepubertal children, RT-induced gains in MVC force are primarily caused by neural rather than muscular factors (Behringer et al., 2011; Granacher et al., 2011). For example, RT for 20 weeks increased VA of the elbow flexors and knee extensors measured by twitch interpolation in 9−11-year-old prepubertal boys (Ramsay et al., 1990). However, no study has reported correlated neuroplastic changes and concomitant increases in MVC force and/or motor skills. Nonetheless, given their hormonal profile, it is likely that RT-induced neuroplastic changes underlie the increases in athletic performance after RT in these children. Future studies could determine the relationship between RT-induced neuroplasticity and functional performance in these children in paradigms that combine RT with event-specific practice known to induce neuroplasticity (Behm et al., 2008).

5. Recommendations

Historical studies introduced the idea that neuroplasticity underlies the rapid initial increases in MVC force and gross motor performance after RT. In an effort to provide an update of this idea, we reviewed and extracted experimental evidence from previous reviews concerning the functional relevance of RT-induced neuroplasticity in increasing motor performance. If RT-induced neuroplastic changes did occur, the majority of studies reported a 'parallel' increase in changes in markers of neuroplasticity, MVC force, or gross motor performance. However, we found little evidence that individual variations in RT-induced performance gains were associated with individual variations in markers of neuroplasticity. We therefore make the following recommendations to improve the efficacy of exercise training athletes perform and rehabilitation patients receive. We make these recommendations with the understanding that correlation is not causation yet it serves as an important starting point for (causal) mediation analyses. Such models could serve as basis for an update of the descriptive Sale model the field has been relying on for some 40 years.

We recommend the use of advanced methods for the identification of neuroplasticity and its functional relevance. These could include the quantification of synergist and antagonist muscle activation sEMG-to-sEMG coherence, sEMG-EEG cortico-muscular coherence, sEMG-based synergy and wavelet analyses instead of the use of single-muscle detection sEMG approaches, to determine RT-induced neuroplasticity. These methods might provide new insights into RT-induced neuroplasticity in the form of intra- and inter muscle-group coordination, corticomuscular coupling, and in the organization of synaptic input to motor neurons (Aagaard et al., 2020). We recommend the use of multi-array sEMG-derived motor unit recordings to longitudinally track changes in single motor unit activation across multiple sessions (Casolo et al., 2020; Del Vecchio et al., 2019a, b);(Vila-Cha et al., 2012, 2010). We recommend the determination of TMS and peripheral nerve stimulation outcomes especially during muscle contraction instead of rest (Taube et al., 2020), the combination of stimulation-based measurements with EEG and MRI, providing a new methodological-analytical framework (Raffin et al., 2020), and the exploration of alternative paths for RT-produced neuroplasticity such as the lateral reticulospinal tract (Baker and Perez, 2017; Choudhury et al., 2019; Fernandez-Del-Olmo et al., 2014; Glover and Baker, 2020).

We recommend to place the data derived by these methods into mediation analyses to determine the causative links between RT-induced neuroplasticity and improvements in MVC force or gross motor performance in health and disease (Nuzzo et al., 2019a; Steele

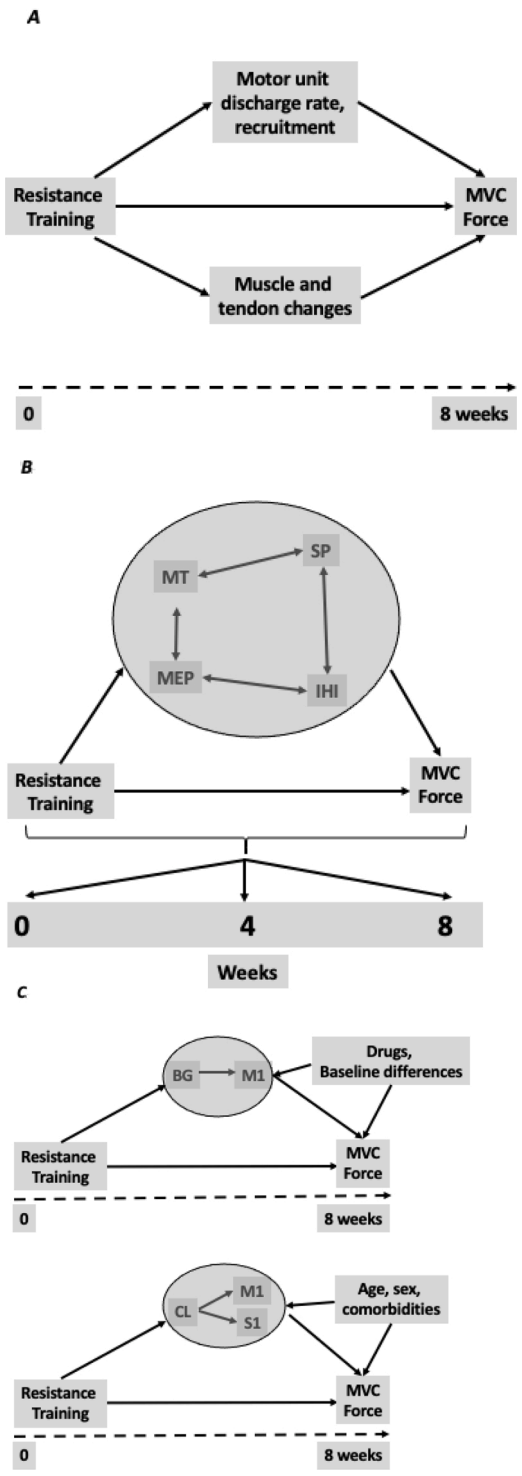

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Fig. 2. Directed acyclic graphs (DAG) illustrating the update and extension of the Sale model.

2A. A DAG, illustrating causal paths between increases in maximal voluntary isometric (MVC) force after resistance training. Experimental data modify the descriptive Sale model, assigning putative roles to neural and musculotendinous factors in the increases in MVC force during the initial phases of resistance training. Theory-based mediators include motor unit discharge rate, motor unit number, hypertrophy markers, and tendon stiffness. Potential confounders are not shown but might include age, baseline MVC force, baseline muscle size, and gender.2 B. DAG further specifying mechanistic paths illustrated in 2A, between resistance training and increases in MVC force. Adaptations in central drive are assessed by determining the relationship among magnetic brain stimulation outcomes at baseline (0), during (4), and after (8 weeks of) resistance training as mediators increases in MVC force. Repeated measurements would help to determine the relative contribution of those different outcomes to motor performance at different stages of training by using mediation analysis and if any causative adaptation to RT changes with time. Magnetic brain stimulation outcomes: Motor threshold (MT); motor evoked potential (MEP) size, intracortical inhibition (IHI), silent period (SP). Structural equation modeling identifies the relationship between individual brain stimulation outcomes underlying the time course and relative role of these outcomes in increases in MVC force.2 C. DAG illustrating mechanistic paths through which resistance training can improve MVC force and clinical symptoms through functional and structural network alterations in Parkinson's disease based on (Bologna et al., 2020). Resistance training activates the primary motor and sensorimotor cortices, basal ganglia, and cerebellum involved in generating and controlling the slowed, weak, narrow amplitude, and error-prone sequences in voluntary movements. Resistance training variables (contraction intensity, duration, frequency, repetition of individual movements, variation in force induced by perturbations, moving weighted sensory implements) (Tollár et al., 2019a, b) affect brain and muscle activation duration, variables that can in turn be tuned to reduce individual clinical dysfunctions. The DAG illustrates compensatory paths through which resistance training could act while ON-dopamine. The oval shape identifies the putative network examined for activation and connectivity by brain imaging and its confounder-adjusted relationship with increases in MVC force. The upper DAG highlights the motor loop and lower DAG depicts cerebello-thalamo-cortical network involved in movement feedback loop. Confounders are differences in baseline clinical and motor symptoms, drugs, comorbidities, age, and gender. The DAGs extend the Sale model to clinical conditions using a mechanistic instead of a descriptive approach. M1, primary motor cortex; S1, sensorimotor cortex; BG, basal ganglia; CL, cerebellum; MVC, maximal voluntary contraction.

et al., 2020; Textor et al., 2016; Tollár et al., 2019a) (Figure 2 A); such analyses should be performed before, during (i.e., longitudinal measurements), and after RT (Hortobágyi et al., 2011). We recommend to estimate the relative contribution of these outcomes to motor performance before, during, and after RT through hypotheses testing using (causal) mediation analyses (Fig. 2B).

5.3 Brain network analyses would be highly informative after RT even in healthy young adults as controls to contrast with the functional role played by network adaptions in the recovery of motor function in PwPD, PwMS, and PwS (August et al., 2006; Bajaj et al., 2015; James et al., 2009). Network changes following RT could additionally be informative about the localization and extent of neuroplasticity in these patients and this could be assessed through (causal) mediation analyses (Bologna et al., 2020; Hallett et al., 2020) (Fig. 2C). This recommendation is supported by data suggesting that RT-induced neuroplasticity could reduce structural and functional disconnections caused by lesions in PwS and that RT-improved connectivity predicts motor and behavioral changes (Salvalaggio et al., 2020).

We recommend to examine retention and transfer of the skill developed by RT. Notwithstanding animal data (Remple et al., 2001) and the invariance in the spatial and temporal structure of single and multi-joint exercises, RT often involves skill learning (Lundbye-Jensen et al., 2005). Retention and transfer are hallmarks of motor learning (Dayan and Cohen, 2011; Krakauer et al., 2019; Tablerion et al., 2020; Wanner et al., 2020). Such studies are needed because there is very little data on the relationship between neuroplastic detraining,

mal-adaptation, and strength loss following a retention period. To increase the specificity of these measurements, the inclusion of an active control group could confirm that the RT stimulus and not just non-specific contractile activity giving rise to neuroplasticity. This recommendation is supported by a demonstrated need to examine '… specific neural changes that might result from exercise prescriptions that are specifically designed to induce certain functional changes' in health and disease (Sandroff et al., 2020).

We recommend to determine the effects of RT on gross motor performance. Some studies suggest that training the target movement itself with loads or against resistance may be beneficial for example, to increase motor performance in older adults with (Messa et al., 2019) and without PD (Brach et al., 2017; Brach and Vanswearingen, 2013; Brach et al., 2020), improve athletic performance in judoka (Blais and Trilles, 2006; Helm et al., 2018a, b), rugby (Harrison and Bourke, 2009), kayaking (Logan et al., 1997), and sprint cycling (Kordi et al., 2020). Therefore, to improve gross motor performance by RT, we recommend to train target movements with loads or against resistance. Such a RT modality ensures that the ensuing neuroplasticity is functionally relevant because the underlying neural adaptations become the enabling mechanisms for the incorporation of newly acquired muscle strength in the target movement. This is possible due to the similarities between 1) the spatial and temporal structure of the training and the target movements, and 2) between brain and muscle activation patterns during movement preparation and execution in the training and target movements such as walking, jumping, throwing, and reaching.

6. Conclusions

Sale's model of RT-induced neuroplasticity has served outstandingly for many decades. We Sale's model of RT-induced neuroplasticity has served outstandingly for many decades. We recommend updating the model with (causal) mediation analytical, hypothesis-driven models. There is a need for studies that examine the association between changes in muscle function, markers of neuroplasticity, and indices of muscle and tendon architecture in response to RT through causal mediation analysis(Nuzzo et al., 2019a; Steele et al., 2020; Tollár et al., 2019a). Akin to aerobic training (Voss et al., 2020), there is a need to determine the relationship between changes in performance outcomes and changes in functional and effective (structural) connectivity measures within the nervous system. This could be explored using electrophysiological methods and brain imaging before and after RT, and after a period of detraining using an active control group. In addition, the relationship between changes in indices of neural adaptations to RT and the increases in muscular performance could be complicated by early changes in skeletal muscle structure that amount to ~10 % (DeFreitas et al., 2011; Folland and Williams, 2007; Seynnes et al., 2007; Stock et al., 2016); therefore, inclusion of muscle-tendon architecture is warranted in future studies and mediation models. As the time-course of neural, tendon and muscle adaptations to RT differ (Csapo et al., 2011; Kubo et al., 2010) only studies incorporating a combination of such measures will be successful in determining the holistic picture of how RT improves gross motor function across the lifespan in performance, health and disease.

Declaration of Competing Interest

The authors report no declarations of interest.

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