The Journal of Physiology

TOPICAL REVIEW

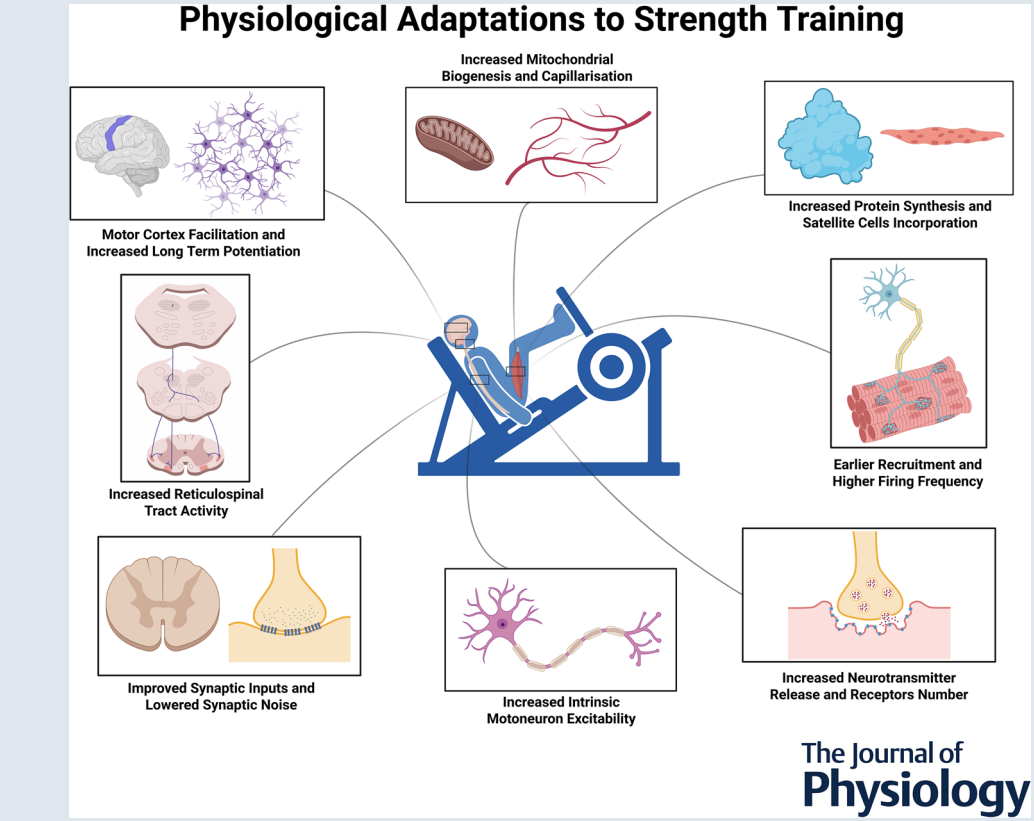
Resistance training-induced adaptations in the neuromuscular system: Physiological mechanisms and implications for human performance

Edoardo Lecce, Paolo Amoruso, Francesco Felici and Ilenia Bazzucchi

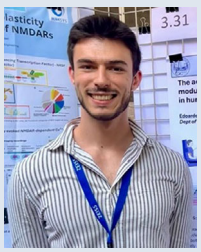
Department of Movement, Human and Health Sciences, University of Foro Italico, Rome, Italy

Handling Editors: Laura Bennet & Christopher Sundberg

The peer review history is available in the Supporting Information section of this article (https://doi.org/10.1113/JP289716#support-information-section).



Edoardo Lecce is a post-doc researcher at the University of Rome 'Foro Italico', where he obtained his PhD in human and exercise physiology. He specialised in electromyographic research on human motor units. His work includes non-invasive high-spatial-resolution electromyography to characterise the neural command across different populations. His research explores adaptations to resistance training and mechanical perturbations, aiming to expand the understanding of neuromuscular function and its practical applications in healthy individuals and those affected by chronic disorders.



DOI: 10.1113/JP289716

Abstract figure legend Resistance training-induced adaptations involve multiple physiological pathways across the neuromuscular system. Plastic changes in the brain and spinal circuitries promote increased excitability, synaptic input transmission and lower synaptic noise, all producing a higher and more stable neural drive. In the skeletal muscle, mechanical and metabolic stresses activate contractile protein synthesis, structural repair by the satellite cells and improve endurance capacity using mitochondrial biogenesis and capillarisation.

(Received 11 August 2025; accepted after revision 12 November 2025; first published online 9 December 2025)
Corresponding author I. B.: Department of Movement, Human and Health Sciences, University of Foro Italico, Rome, Italy. Email: ilenia.bazzucchi@uniroma4.it

Introduction

Resistance training (RT) represents one of the most extensively practised forms of physical activity, eliciting well-characterised adaptations that enhance performance, health and overall well-being. The canonical responses to mechanical overloading, which include improved maximal force production, rate of force development (RFD) and muscle hypertrophy, are by now firmly established (del Vecchio et al., 2024; Moritani & deVries, 1979; Roberts et al., 2023; Škarabot et al., 2021). However structured RT regimens promote a broad range of benefits that extend far beyond mere gains in muscle size and strength. Such regimens have been recognised for the prevention and improvement of various conditions resulting from immobilisation, sedentary behaviour and metabolic dysfunction, such as sarcopenia (Aagaard et al., 2010; Cheng et al., 2024; Jones et al., 2022; Piasecki, 2024), diabetes-related complications (Andersen et al., 2004; Lecce, Bellini et al., 2025; Tian et al., 2023) and cardiovascular disorders (Braith & Stewart, 2006; Evans et al., 2018; Vincent & Vincent, 2006). Beneficial effects are mediated by multiple physiological processes, ranging from molecular signalling cascades to functional neuromuscular adaptations, all of which contribute to improvements in body composition, metabolic health and performance (Currier et al., 2023; Kraemer et al., 2002; Westcott, 2012).

Although previous reviews have elegantly addressed individual aspects of RT, covering functional, morphological and molecular mechanisms of such adaptations (Aagaard et al., 2020; Atkinson et al., 2022; Dai et al., 2024; del Vecchio, Casolo et al., 2019; Folland & Williams, 2007; Roberts et al., 2023; Škarabot et al., 2021), a single comprehensive source concurrently detailing the physiological pathways activated by specific structured protocols and the resulting adaptations is lacking.

Therefore the purposes of this topical review are (a) to summarise the most relevant and up-to-date evidence on the sites of putative neuromuscular adaptations and the molecular signalling pathways these engage; (b) to critically examine how these neuromuscular changes synergise with functional modifications to enhance performance; (c) to delineate how distinct RT modalities elicit specific physiological responses at the precise extent, thereby translating these insights into clear, evidence-based recommendations for optimising both performance and health outcomes. Together, these efforts aim to offer an integrated perspective on the multifaceted adaptations to structured RT, underscoring its enduring relevance for human adaptability in both everyday life and athletic performance.

Search string

For this *narrative review*, an extensive literature search was conducted in PubMed/MEDLINE, Scopus and Web of Science from database inception, updated in September 2025, using a combined set of MeSH terms and free-text keywords designed to capture the full spectrum of neuromuscular adaptations to RT at both the central and peripheral nervous systems, skeletal muscle, hormonal and molecular dimensions. The primary search string was constructed as follows: (‘Resistance training’ OR ‘strength training’ OR ‘weightlifting’) AND (‘Muscle, skeletal/physiology’ OR ‘neuromuscular adaptation’ OR ‘neural adaptation’ OR ‘brain/physiology’ OR ‘spinal cord/physiology’ OR ‘motor neurons/physiology’ OR ‘motor unit’ (Mesh) OR ‘motor unit recruitment’ OR ‘corticospinal’ OR ‘cortical plasticity’ OR ‘spinal excitability’ OR ‘synaptic plasticity’ OR ‘muscle hypertrophy’ OR ‘hormonal response’) AND (‘signal transduction’ OR ‘molecular pathway’ OR ‘gene expression’ OR ‘myogenic regulatory factors’ OR ‘neurotrophic factors’ OR ‘hormonal regulation’ OR ‘neuroendocrine adaptation’ OR ‘mTOR’ OR ‘Akt’ OR ‘MAPK’ OR ‘BDNF’ OR ‘IGF-1’ OR ‘testosterone’ OR ‘growth hormone’). In addition to database queries reference lists of key articles and recent reviews were manually searched to identify any pertinent publications that the keyword strategy may have overlooked. All identified records were screened by title and abstract, and full texts of potentially eligible articles were retrieved.

Neural adaptations

It is widely accepted that, during the initial weeks of a RT programme, most improvements in strength reflect neural adaptations because these changes occur without substantial increases in physiological cross-sectional area and early rises in muscle size have been attributed to oedema (Aagaard, 2003; Damas et al., 2016; Moritani & deVries, 1979; Škarabot et al., 2021). These adaptations involve changes in supraspinal regions, spinal circuitries, the neuromuscular junction (NMJ) and intrinsic motoneuron properties (Carroll et al., 2002; Deschenes, 2019; Folland & Williams, 2007; Gabriel et al., 2006; Perez & Cohen, 2008). Underlying these physiological modifications are molecular signalling cascades, including neurotrophic factors, ion-channel modulation and gene transcription, all contributing to synaptic remodelling and neuronal function.

Supraspinal circuitries. After a short-term RT intervention (≤4 weeks), the *primary motor cortex* (M1) typically exhibits changes in its excitatory–inhibitory balance (Perez et al., 2006; Siddique et al., 2020; Škarabot et al., 2021). Paired-pulse *transcranial magnetic stimulation* (TMS) studies consistently demonstrate a reduction in *short-interval intracortical inhibition* (SICI) following RT in young humans, indicating downregulation of *gamma-aminobutyric acid* $(GABA)_A$-mediated interneuronal activity (Kidgell et al., 2017; Weier et al., 2012). Concurrently, TMS-induced cortical *silent period* (SP), a transient interruption in the voluntary-evoked sEMG signal during contraction, is shorter after RT intervention (Gómez-Feria et al., 2023; Kidgell et al., 2017; Siddique et al., 2020), indicating a lower $GABA_B$-dependent suppression of the volitional drive from M1 onto the spinal motoneurons in recreationally active humans (Yacyshyn et al., 2016).

These modifications mirror those observed in motor learning (Carroll et al., 2002; Martin & Morris, 2002), suggesting that use-dependent synaptic plasticity underlies M1 adaptations. Specifically, *N*-methyl-D-aspartate $(NMDA)_R$-dependent long-term potentiation and *brain-derived neurotrophic factor* (BDNF)-mediated signalling likely contribute to these training-induced modifications (Carroll et al., 2002; Farmer et al., 2004; Neeper et al., 1995; Zuo et al., 2025). Additionally, several studies report enhanced intracortical facilitation after RT intervention in animals (Glover & Baker, 2020) and young humans (Falvo et al., 2010), implying a modification in the balance between GABAergic *inhibition* and glutamatergic *excitation* within M1 circuits (Coxon et al., 2018; Maddock et al., 2011, 2016; Stagg et al., 2011).

In contrast, measures of corticospinal excitability, such as resting *motor-evoked potential* (MEP) amplitude and input–output slope, have yielded heterogeneous responses (Gómez-Feria et al., 2023). In response to short-term interventions (≤4 weeks) in humans, some studies have reported increased MEP amplitudes following training (Griffin & Cafarelli, 2007; Kidgell & Pearce, 2010; Kidgell et al., 2010; Weier et al., 2012), whereas others have observed no changes or even reductions in these measures (Carroll et al., 2009; Christie & Kamen, 2014; Lee et al., 2009). Notably, when corticospinal output is probed using *transcranial electrical stimulation* (TES), which preferentially activates a larger proportion of corticospinal neurons than TMS (di Lazzaro et al., 1998), RT appears to alter spinal circuitry without substantially reorganising M1 in young humans following 4 weeks of RT (Carroll et al., 2002).

Concurrently, the reticulospinal system exhibits clear potentiation of its drive to spinal motoneurons. In non–human primates, high-load RT strengthens reticulospinal-motoneuron connections, thereby augmenting gross descending drive during maximal voluntary efforts (Glover & Baker, 2020; Riddle et al., 2009). This potentiation may arise via multiple pathways, including cortico-reticular inputs, intrinsic reticular interconnections, reticulospinal synapses onto spinal interneurons or direct reticulospinal projections to motoneurons (Škarabot et al., 2021). Although these contributions have not been directly observed in humans, evidence from *high-density surface electromyography* (HDsEMG) studies suggests that synaptic input to motoneurons increases when an auditory startling stimulus is provided (Škarabot et al., 2022), an effect attributed to reticulospinal facilitation of descending commands (Atkinson et al., 2022).

Spinal circuitries. Adaptations to RT also include spinal-level mechanisms, although determining their precise loci remains challenging due to both the complexity of spinal networks and methodological constraints. Two non–invasive measures commonly employed in human studies, the *Hoffmann* (H) reflex and the V-wave, offer complementary, albeit indirect, insights into spinal excitability and presynaptic modulation (McNeil et al., 2013; Škarabot et al., 2021). Although resting H-reflex amplitude usually remains unchanged after training, the H-reflex measured during maximal voluntary contractions improves significantly in young adults after short-term RT (7 weeks) (Duclay et al., 2008) and in both young and older adults after longer interventions (>14 weeks) (Aagaard et al., 2002a; Scaglioni et al., 2002), suggesting that spinal adaptations become evident primarily under functional loading conditions. Concurrently, human studies indicate that the V-wave tends to increase after a brief (4 weeks) (Fimland, Helgerud, Gruber et al., 2009) or longer (16 weeks) RT intervention (Aagaard et al., 2002a), suggesting either

an enhanced descending drive or suppressed spinal inhibition during force production (Škarabot et al., 2021).

However, interpreting these changes as purely 'spinal' adaptations warrants caution (Škarabot et al., 2021). The H–reflex is modulated by presynaptic gating of Ia afferents and by peripheral axonal excitability. Consequently, an increased H_{max}/M_{max} ratio may reflect reduced presynaptic inhibition or altered axonal membrane properties rather than intrinsic motor pathway plasticity (Theodosiadou et al., 2023). Although the V–wave is less prone to peripheral bias, both measures include polysynaptic contributions (e.g. interneuronal circuits), further complicating the assignment of adaptations to specific spinal loci (Burke et al., 1984; Grau et al., 2024; Kiehn, 2016). Moreover, eccentric–only training appears particularly effective at augmenting both H–reflex pathway excitability and V–wave amplitude. These effects are thought to result from reduced Ib inhibition and stronger supraspinal drive, even though some of the effects may also reflect altered descending input rather than purely spinal adaptations (Duclay et al., 2008; Vangsgaard et al., 2014).

RT elicits spinal-level adaptations that have been attributed to a different distribution of synaptic input to motoneurons, a modification hypothesised to directly influence motor unit (MU) recruitment threshold in humans (Dideriksen & del Vecchio, 2023; Johnson et al., 2017; Lecce et al., 2025). Concurrently, RT has been shown to reduce synaptic noise in young male and female individuals (Lecce et al., 2025). Synaptic noise, defined as stochastic fluctuations in synaptic input to motoneurons, is thought to be suppressed through a more balanced presynaptic excitatory–inhibitory drive, more reliable neurotransmitter release and stabilised synaptic conductance, thereby reducing firing variability within the active motoneuron pool (Calvin & Stevens, 1968; Hubbard et al., 1967; Rusakov et al., 2020; Sturm et al., 1997; Yarom & Hounsgaard, 2011). Additional spinal adaptations include potentiation of propriospinal interneuron circuits and strengthening of bilaterally projecting reticulospinal pathways (Atkinson et al., 2022; Laliberte et al., 2019), though direct evidence in humans is lacking. These modifications may impact discharge behaviour of spinal motoneurons, leading to earlier spike initiation and higher peak discharge rates (Dideriksen & del Vecchio, 2023; Johnson et al., 2017), effects that have been documented in response to short-term RT in both young (del Vecchio, Casolo et al., 2019; Lecce et al., 2025) and older adults (Orssatto, Rodrigues et al., 2023).

Inhibitory pathways. Spinal circuitry modifications, manifesting as enhanced excitability, may also stem from changes in spinal inhibitory mechanisms, which include Ib afferent feedback, homosynaptic depression and reciprocal and recurrent inhibition (Aagaard et al., 2000; Grau et al., 2024; Jami, 1992; Kiehn, 2016; Proske & Gandevia, 2012).

Ib afferent feedback originates from Golgi tendon organs, encapsulated mechanoreceptors at the muscle-tendon junction, whose Ib endings wrap collagen fibrils. Rising tendon tension deforms these endings and triggers autogenic inhibition via inhibitory interneurons, thereby limiting motoneuron output (Jami, 1992; Proske, 1979). Homosynaptic depression refers to the progressive decline in H–reflex amplitude with repeated Ia afferent stimulation, commonly attributed to the transient depletion of neurotransmitters at the Ia spinal motoneuron synapse. Reciprocal inhibition occurs when Ia afferents from an agonist muscle excite Ia inhibitory interneurons, which, in turn, suppress α–motoneurons of the antagonist muscle, facilitating co-ordinated movement and protecting against co–contraction. Recurrent inhibition is mediated by Renshaw cells (and related GABAergic interneurons) that receive collateral input from active α–motoneurons and feedback inhibitory signals onto the same and adjacent motoneurons, thereby regulating firing rates and preventing excessive excitation (Alvarez et al., 2013; Grau et al., 2024; Katz & Pierrot-Deseilligny, 1999; Kiehn, 2016; Rekling et al., 2000).

RT appears to attenuate several inhibitory spinal mechanisms converging on α–motoneurons, including autogenic Ib inhibition, reciprocal Ia inhibition and recurrent Renshaw-mediated inhibition, although evidence in humans is based primarily on indirect estimates derived from H-reflex measurements (Aagaard, 2018; Duclay et al., 2011; Hultborn & Pierrot-Deseilligny, 1979). Use-dependent plasticity is evident in Ia-mediated reciprocal inhibition: short-term RT (12 sessions) enhances disynaptic Ia inhibition in recreationally active humans (Geertsen et al., 2008). Notably, long-term strength-trained athletes present even greater Ia disynaptic reciprocal inhibition than recreationally active individuals (Koceja et al., 2004), potentially influencing the marked differences in discharge rate profiles between these populations (del Vecchio et al., 2018; Škarabot et al., 2024). These spinal-level adaptations likely contribute to the well-documented reduction in agonist–antagonist co-contraction following both acute and chronic RT observed in young humans (Balshaw et al., 2019; Bazzucchi et al., 2008; Pearcey et al., 2014, 2021). Moreover, the type of muscle contraction further modulates inhibitory tone: eccentric contractions evoke more pronounced recurrent inhibition compared to isometric or concentric actions (Barrué-Belou et al., 2018), suggesting that contraction-specific spinal gating may impact force production and motor control adaptations (Aagaard, 2018).

Evidence also suggests that local spinal inhibitory circuits can counteract the facilitatory actions of descending monoaminergic drive on dendritic *persistent inward currents* (PICs), potentially limiting the active dendritic integration of excitatory inputs (Hyngstrom et al., 2007; Kuo et al., 2003; Mesquita et al., 2022). Experimental work in animal models has shown that sustained excitatory inputs to motoneurons are markedly amplified by dendritic PICs, whose activation depends on monoaminergic input from the brainstem (Heckman et al., 2003; Rekling et al., 2000). When inhibitory inputs from antagonist muscle afferents are concurrently activated, they can substantially reduce PIC amplitude, with the degree of suppression being proportional to the strength of the inhibitory input (Kuo et al., 2003).

Under conditions of minimal monoaminergic activity, PICs are substantially diminished, and additional inhibition exerts little further effect. This interaction highlights the dynamic balance between descending neuromodulatory facilitation and local inhibitory control within spinal motoneurons, which together regulate the overall excitability and output of the motoneuron pool. By reducing inhibitory tone, RT may indirectly enhance intrinsic motoneuron excitability through increased PIC contribution, resulting in greater net neural drive to muscle, as observed following a short-term RT in recreationally active young individuals (del Vecchio, Casolo et al., 2019; Lecce, Conti et al., 2025) and in chronically strength-trained individuals (Casolo et al., 2021; Škarabot et al., 2024). Although direct assessment of these spinal-circuit adaptations in humans is currently unfeasible, converging evidence supports the notion that adaptive changes within inhibitory interneuronal networks play a central role in the neural plasticity underlying RT-induced improvements in both motoneuron function and performance outcomes (Abbasi et al., 2022; Gómez-Feria et al., 2023; Latella et al., 2012; Ramírez-Jarquín & Tapia, 2018; Siddique et al., 2020; Škarabot et al., 2021; Tallent et al., 2021).

Motoneuron intrinsic properties. The extent to which RT directly modulates the intrinsic motoneuron excitability in humans remains unclear. On one hand, mechanical overloading (or conversely unloading) has been shown to elicit specific changes in motoneuron properties that translate into altered force production in both young and older humans (Christie & Kamen, 2010; Lecce et al., 2025; Martino et al., 2024; Orssatto, Rodrigues et al., 2023; Piasecki, 2024; Valli et al., 2024). On the contrary, other human studies suggest minimal or inconsistent effects of RT on intrinsic motoneuron excitability (Ansdell et al., 2020; Kim et al., 2019; Nuzzo et al., 2017; Škarabot et al., 2021).

Animal models provide clearer evidence: short-term RT (5 and 12 weeks) induces a shortened action–potential duration, increased input resistance, lower rheobase, reduced *afterhyperpolarisation* (AHP) amplitude and decreased current threshold for rhythmic firing initiation (Krutki et al., 2015, 2017). Given the roles of voltage-gated sodium channels (Hodgkin & Huxley, 1952) and L–type calcium channels (Gorassini et al., 1998; Schwindt & Crill, 1980) in human motoneuron excitability (Mesquita et al., 2024), a growing body of evidence suggests that RT induces biophysical alterations in these channels (Cormery et al., 2005; Dai et al., 2024; Krutki et al., 2015, 2017; Lecce et al., 2025; Orssatto, Blazevich et al., 2023). Consequently, it is plausible that RT–driven enhancements in intrinsic motoneuron excitability arise from upregulated sodium (I_{NaP}) and calcium (I_{CaP}) conductances and/or modified monoaminergic modulation, as serotonergic and noradrenergic inputs are known to amplify these currents (Gardiner et al., 2006; Heckman et al., 2003, 2009).

PICs influence motoneuron behaviour using two complementary mechanisms. *Subthreshold activation* lowers the membrane potential threshold for action-potential initiation, thereby reducing the recruitment threshold of motoneurons: larger subthreshold PICs imply motoneurons being recruited over a narrower voltage input (Johnson et al., 2017; Power et al., 2012; Rekling et al., 2000). *Suprathreshold amplification* increases depolarisation during ongoing firing: persistent Na^+ and gradually recruited L–type Ca^{2+} channels amplify incoming synaptic drive, sustaining and accelerating discharge in the *secondary range* of the *f–I* curve (Cantrell & Catterall, 2001; Heckman, 1994; Prescott & de Koninck, 2005; Shapiro & Lee, 2007).

Adaptations in intrinsic excitability thus likely reflect changes in the expression or kinetics of these ionic conductances: upregulated I_{NaP} and L–type I_{CaP} for initiation and amplification, downregulated delayed-rectifier K^+ currents (K_{DR}) to prolong depolarisation and reduced Ca^{2+}-activated K^+ currents (K_{Ca}) to shorten the AHP phase. Although briefer AHPs have been observed in both young and older humans in response to a short-term (2 weeks) RT intervention (Christie & Kamen, 2010), direct evidence for RT-induced changes in channel expression underlying AHP modifications remains to be established (Dai et al., 2024).

Although direct evidence for RT-induced modulation of Na^+ and Ca^{2+} channels in humans is still lacking, data from *in vitro* animal models of endurance exercise demonstrate the upregulation of I_{NaP} and L–type I_{CaP}, alongside dendritic hypertrophy (Chen & Dai, 2022; Ge & Dai, 2020). Enhanced I_{NaP} increases subthreshold depolarising drive, lowering rheobase and supporting firing amplification, whereas enhancement of dendritic

L–type I_{CaP} promotes plateau potentials and firing bistability under strong synaptic inputs (Binder et al., 2020; Heckman et al., 2003; Lee & Heckman, 1998; Power et al., 2012).

Downregulation of K_{DR} has been associated with a decreased spiking initiation threshold and steeper *f–I* slope, thereby enhancing intrinsic motoneuron excitability following RT in animal models (Dai et al., 2002; Lombardo & Harrington, 2016). However, findings for K_{Ca} channels remain less consistent. Computational models indicate that reduced K_{Ca} conductance implicates a steeper *f–I* slope and enhances motoneuron recruitment (Dai et al., 2002; Zhang & Dai, 2020). Chronic exercise has been associated with a lower K_{Ca}-channel gene expression in rodent models (Woodrow et al., 2013), a mechanism responsible for reduced AHP in both animals (MacDonell et al., 2015) and humans (Christie & Kamen, 2010). Nonetheless, other animal investigations show increased AHP amplitude following 5–12 weeks of muscle overloading or voluntary wheel running (Beaumont & Gardiner, 2002; Krutki et al., 2015). These conflicting results may reflect activity–dependent suppression of PICs as a fatigue–resistance mechanism (Dai et al., 2024), although future investigations in humans are warranted to confirm these hypotheses.

Neuromodulatory input. RT induces adaptations in motoneuron pools by increasing serotonergic innervation and upregulating facilitatory 5-HT_2 and α_1-adrenergic receptors, while concurrently downregulating inhibitory 5-HT_1A and $GABA_A$ receptors (Dai et al., 2024; Rekling et al., 2000; Thorstensen et al., 2024). These receptor-level adaptations amplify monoaminergic facilitation of both persistent I_{NaP} and I_{CaP}, thereby increasing motoneuron gain and broadening the hysteresis window during voluntary force exertion (Heckman et al., 2003, 2009; Rekling et al., 2000). Although intrinsic motoneuron excitability is mainly dependent on neuromodulatory input from the raphe nuclei (*serotonin* (5-HT)) and locus coeruleus (*norepinephrine* (NE)), as well as by intrinsic spinal monoaminergic neurons (Heckman et al., 2003, 2009; Rekling et al., 2000; Revill & Fuglevand, 2017), human studies indicate similar estimates of input–output gain (i.e. the relationship between the synaptic input received by the motoneuron pool and their transformation into output firing frequency). This suggests that, despite clear receptor-level changes, altered monoaminergic drive may not be the primary mechanism underlying RT–induced increases in muscle force in humans (del Vecchio, Casolo et al., 2019; Kim et al., 2019; Nuzzo et al., 2017; Škarabot et al., 2021).

Motor unit. Indirect measures from MU recordings suggest intrinsic motoneuron adaptations. Short-termed RT (4 weeks) induces MUs to be recruited earlier, a modification typically resulting from the contribution of changes in the relative shared synaptic input and intrinsic motoneuron *subthreshold current* (del Vecchio, Casolo et al., 2019; Lecce, Conti et al., 2025). Concurrently, increases in ΔF, an established index to estimate the contribution of PICs to self-sustained motoneuron firing (see Afsharipour et al., 2020; Gorassini et al., 1998), are reported after RT interventions in different longitudinal studies in young (Lecce et al., 2025) and older humans (Orssatto, Blazevich et al., 2023), likely reflecting enhanced intrinsic motoneuron excitability. However, a recent cross-sectional comparison of chronically resistance- and endurance-trained young adults did not find between-group differences in ΔF (Škarabot et al., 2025). These discrepancies likely reflect differences in study design (*longitudinal vs. cross-sectional* design), muscle examined and contraction protocol, MU selection and decomposition criteria, contraction intensity and the specific task used to probe PICs, and the heterogeneity of participants' training histories. We therefore interpret increases in ΔF following RT as evidence compatible with augmented PIC contribution, while acknowledging that chronic training status per se does not always produce consistent cross-sectional differences in ΔF.

Changes in maximal discharge rate, or the plateau discharge rate at a given force, have been proposed to reflect an increased *rate–coding gain*, which is the sensitivity of motoneurons to synaptic input (Dideriksen & del Vecchio, 2023), fundamentally tied to PIC contribution (Heckman et al., 2008). Although several HDsEMG studies have suggested that *rate-coding gain* contributes to force and firing adaptations in young adults (del Vecchio, Casolo et al., 2019; Lecce, Conti et al., 2025; Lecce, del Vecchio et al., 2025), no study has yet quantified its precise role. This gap stems from methodological challenges in isolating the output of individual motoneurons, as opposed to the combined influence of converging inputs onto the spinal pool (del Vecchio et al., 2020). Additionally, quantifying the distinct effects of *subthreshold vs. suprathreshold* PICs, the modulatory impact of monoaminergic drive, and the balance between changes in ion–channel expression and their neuromodulator-mediated activation, remains unclear in the human cohort (Mesquita et al., 2024).

MU adaptations to RT have been demonstrated to mediate the enhancement in both maximal force production and force steadiness. Increases in maximal muscle force are accompanied by greater neural drive from spinal motoneurons and reduced MU recruitment thresholds, indicating the activation of a larger pool of MUs (del Vecchio, Casolo et al., 2019; Kim et al., 2019; Škarabot et al., 2021), with a greater extent of their changes being directly tied to a greater change in force production

(del Vecchio, Casolo et al., 2019; Lecce, Conti et al., 2025; Lecce et al., 2025). These adaptations, observed in humans, likely reflect a redistribution of synaptic inputs and an increased contribution of PICs (Dideriksen & del Vecchio, 2023; Johnson et al., 2017). Such changes manifest as a higher proportion of shared synaptic drive and increased ΔF after short-term training in both young and older recreationally active individuals (Lecce et al., 2025; Orssatto, Rodrigues et al., 2023). Furthermore, some studies reported higher muscle fibre conduction velocity and MU discharge rates in chronically strength-trained individuals relative to age-matched untrained individuals (del Vecchio et al., 2018; Škarabot et al., 2024). However, these differences are not universal and appear strongly dependent on the contraction type and contraction intensity at which MU behaviour is measured (Škarabot et al., 2025).

Enhanced force steadiness, identified as reduced variability in steady force during sustained contractions, is typically accompanied by decreased fluctuations in MU spiking activity in young individuals (Lecce, Conti et al., 2025; Vila-Chã & Falla, 2016). However, variability in individual motoneuron discharge (*independent synaptic noise*) has minimal impact on steady–state force accuracy (Castronovo et al., 2018; Dideriksen et al., 2012; Farina & Negro, 2015). Instead, shared membrane fluctuations across the active pool (*common-input variance*) are the principal determinant of force steadiness (Dideriksen et al., 2012; Enoka & Farina, 2021; Hug et al., 2023). Consistent with these statements, 4 weeks of RT markedly reduces common–input variance (see *Spinal circuitries* section), directly correlating with a more stable motoneuron neural drive and steady force production in recreationally active individuals (both males and females) (Lecce et al., 2025). The abovementioned adaptations are summarised in Fig. 1.

Cross-education. Unilateral RT intervention produces improvements in muscle strength and accuracy extending to the contralateral *untrained* limb, a phenomenon known as cross-education (Green & Gabriel, 2018; Hendy &

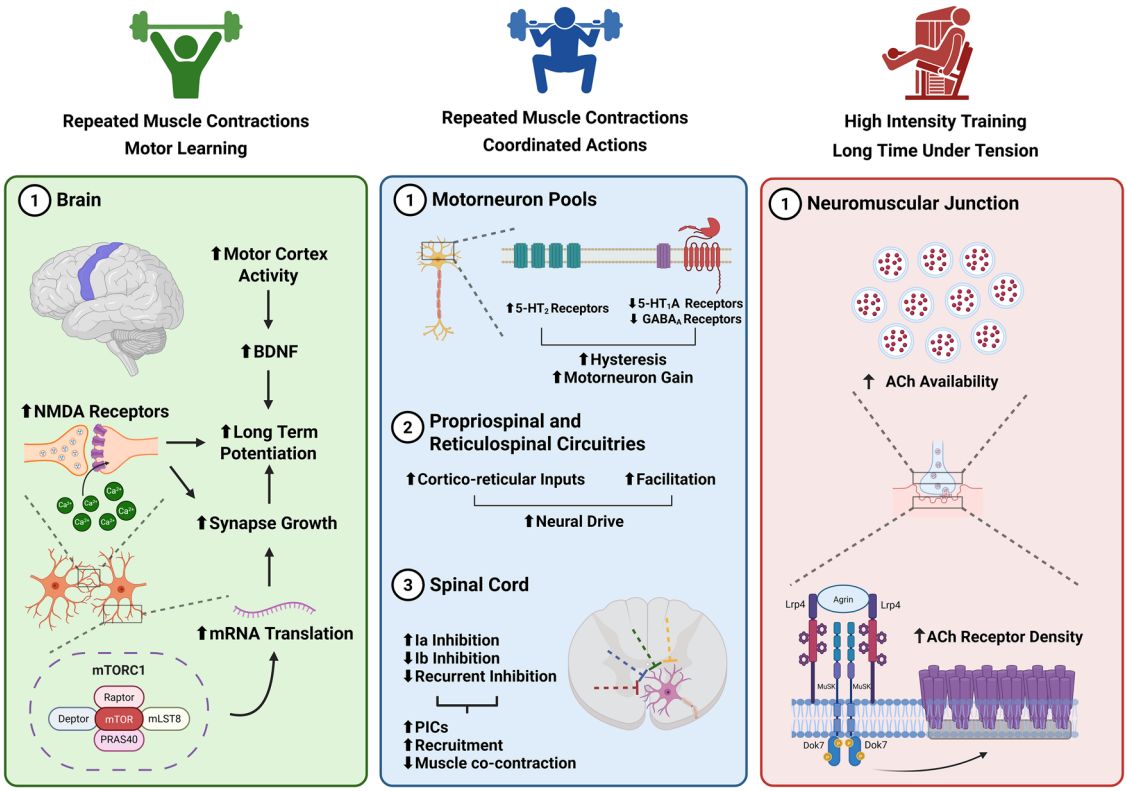


Figure 1. Adaptations in the neural system
Repeated muscle contractions promote neural adaptations by multiple pathways. In the motor cortex, repeated activity increases the level of BDNF, in turn eliciting synaptic proliferation and potentiation, a process corroborated by NMDA receptor upregulation and the mTOR cascade. Concurrently, repeated muscle contractions produce numerous modifications along the spinal cord circuitries and within spinal motoneurons, all contributing to improved excitability and a more co-ordinated muscle activity (i.e. reduced agonist–antagonist coactivation). At the level of the neuromuscular junction (NMJ), heavy mechanical overloading and metabolic stress promote a molecular cascade contributing to the increase in the neurotransmitter availability and receptor density. *The image was made using BioRender*.

Lamon, 2017; Lee & Carroll, 2007). Two complementary cortical models have been proposed to account for these adaptations. *Cross-activation* holds that unilateral exercise increases corticospinal excitability bilaterally and reduces interhemispheric inhibition of the *untrained* M1. *Bilateral access* posits that motor engrams formed in the trained hemisphere become available to the contralateral motor network via transcallosal pathways (Carson, 2020; Hendy & Lamon, 2017; Manca et al., 2018; Pearcey et al., 2022; Ruddy & Carson, 2013). Resting-state functional magnetic resonance imaging (fMRI) data from young males and females indicate strengthened functional connectivity between homologous supplementary motor areas and M1 following unilateral training, with evidence supporting the cross–activation model (Ruddy et al., 2017). Concurrently, *bilateral access* mechanisms may be central in promoting earlier and more synchronous recruitment of motoneurons in the untrained limb (Carson, 2005; Lecce et al., 2025; Lecce, Conti et al., 2025), although the characterisation of precise adaptation pathways is still unknown.

TMS data further support a multilevel model of cross–education. Inhibiting the *trained* M1 during unilateral exercise suppresses strength transfer to the contralateral untrained counterpart, whereas inhibiting the *untrained* M1 elicits no effects, indicating the trained hemisphere as the driver of adaptation transfer in young humans after a single training session (Lee et al., 2010). Supraspinal adaptations include a reduction in SICI (Carson, 2020; Latella et al., 2012; Ruddy & Carson, 2013) and increased corticospinal excitability within both M1 cortices after short-term unilateral RT intervention in humans (Frazer et al., 2017; Howatson et al., 2013; Manca et al., 2018). Collectively, these findings suggest that cross–education arises from focal disinhibition within M1 and broader interhemispheric plasticity (Goodwill et al., 2012; Muellbacher et al., 2000).

Supraspinal modifications have potential downstream effects, where gain transfer has been associated with increased EMG-signal amplitude in untrained muscles after 4 weeks of unilateral RT in young males (Pelet & Orsatti, 2021) and higher V-wave, both indicative of enhanced neural drive and overall muscle activation (Fimland, Helgerud, Solstad et al., 2009). In parallel, a greater H_{max}/M_{max} ratio has been reported in the untrained limb, suggesting greater spinal excitability (Bouguetoch et al., 2021).

As mentioned above potentiation of propriospinal interneurons and strengthening of bilateral reticulospinal projections likely underlie increased shared input to the motoneuron pool (Atkinson et al., 2022; Laliberte et al., 2019; Riddle et al., 2009). Because commissural interneurons and propriospinal pathways cross the spinal cord mid-line (Calvert & Carson, 2022; Laflamme et al., 2023; Maxwell & Soteropoulos, 2020), plasticity within these spinal circuits can increase shared input to the contralateral homologous motoneuron pool, suppress synaptic noise and lower MU recruitment thresholds, accounting for the modest (∼6%) contralateral-limb gains in maximal force output and force steadiness following a 4 week unilateral RT in humans (Lecce et al., 2025).

Unilateral RT and remote limb contractions also appear to selectively amplify diffuse monoaminergic drive, increasing intrinsic motoneuron excitability by *subthreshold* PICs while leaving *suprathreshold* PICs essentially unchanged (Lecce et al., 2025). This interpretation of human data is supported by observations of earlier MU recruitment thresholds and increased net neural drive (i.e. gain in the neural drive from the MU activation to the relative target force) with no concomitant increases in self–sustained firing or peak discharge rates, supporting a predominant *subthreshold* modulation (Green & Gabriel, 2018; Lecce, Conti et al., 2025). However, direct quantification of monoaminergic input following RT is still lacking in humans. To address these mechanistic questions, future investigations should integrate morphological assessments, channel-specific expression assays and *in vivo* electrophysiological recordings to map the temporal progression and causal role of RT–induced motoneuron modifications.

Synaptic plasticity. Across the corticospinal axis, activity–dependent synaptic plasticity unfolds through distinct yet complementary processes at multiple hierarchical levels (Fig. 2).

In the primary motor cortex, the acquisition and refinement of novel motor skills hinge on rapid, activity–triggered neurotrophin release and local protein synthesis, which together drive both structural and functional reorganisation (Adkins et al., 2006; Gómez-Palacio-Schjetnan & Escobar, 2013). It has been suggested that mature BDNF (*serum*) is released within minutes of patterned synaptic activity in humans (Arazi et al., 2021; Borges Junior et al., 2024; Walsh & Tschakovsky, 2018), initiating downstream pathways involving *extracellular signal-regulated kinase* (ERK1-2) (Impey et al., 1999; Komiyama et al., 2002; Mazzucchelli et al., 2002), *calmodulin-dependent protein kinase II* (CaMKII) (Kim & Hayashi, 2014; Martinez-Canton et al., 2021; Yasuda et al., 2022), *casein kinase* (CK2)-dependent modulation of synaptic NMDA receptor (Kimura & Matsuki, 2008; Sanz-Clemente et al., 2010; Vints et al., 2022), *insulin-like growth factor* (IGF-1) (Ding et al., 2006) and *mammalian target of rapamycin* (mTOR) pathways (Bockaert & Marin, 2015; Takei & Nawa, 2014).

Animal models suggest that enhanced BDNF expression within M1 engages synaptic potentiation via the *tyrosine kinase B* (TrkB) receptor pathway (Albini et al., 2023; Fernández-García et al., 2020) to

initiate PI3K/Akt, MAPK and PLCγ cascades, as well as Fyn-mediated phosphorylation of NMDA-receptor subunits. These convergent pathways lower the threshold for LTP induction and enhance postsynaptic excitability (Blum & Konnerth, 2005). Concurrently, mouse models have shown that BDNF enhances presynaptic release probability for both glutamate and GABA via MAPK–dependent phosphorylation of *synapsin* and amplifies evoked postsynaptic currents independently of Ca^{2+}-influx signalling (Jovanovic et al., 2000).

Because the primary extrinsic sources of synaptic noise are fluctuations in the excitation–inhibition balance (mainly driven by glutamate-GABA dynamics) and variability in neurotransmitter release probability, whereas intrinsic noise from stochastic ion-channel gating is largely attenuated by membrane capacitance, as shown *in vitro models* (Ermentrout et al., 2008; Faisal et al., 2008; Yarom & Hounsgaard, 2011), the RT-induced reduction in the estimated synaptic noise observed in humans (Lecce et al., 2025) likely reflects changes in those extrinsic factors exclusively.

NMDA receptor-mediated Ca^{2+} influx promotes both synapse formation and the stabilisation of newly potentiated connections, contributing to the expansion and reorganisation of cortical motor maps observed in *in vitro models* (Lau et al., 2009; Rosendo-Pineda et al., 2020). Calcium influx activates CaMKII, which phosphorylates *cAMP response element-binding protein* (CREB) in astrocytes (Eisner et al., 2023; Kim & Kaang, 2023), stimulating the transcription of activity-dependent genes (Lonze & Ginty, 2002; Ma et al., 2014; Yan et al., 2016). Concurrently, neuronal mTORC1 activation, via the PI3K-Akt-TSC1/2-Rheb axis, phosphorylates p70-S6K1 and *4E-binding protein-1* (4E-BP1), promoting local dendritic mRNA translation that is essential for synaptic growth and long-term potentiation (Lipton & Sahin, 2014; Panwar et al., 2023). Although the specific mechanisms by which synaptic activity couples with mTORC2 remain to be elucidated, these co-ordinated molecular events collectively support the long–term structural and functional remodelling that underpins improved motor performance.

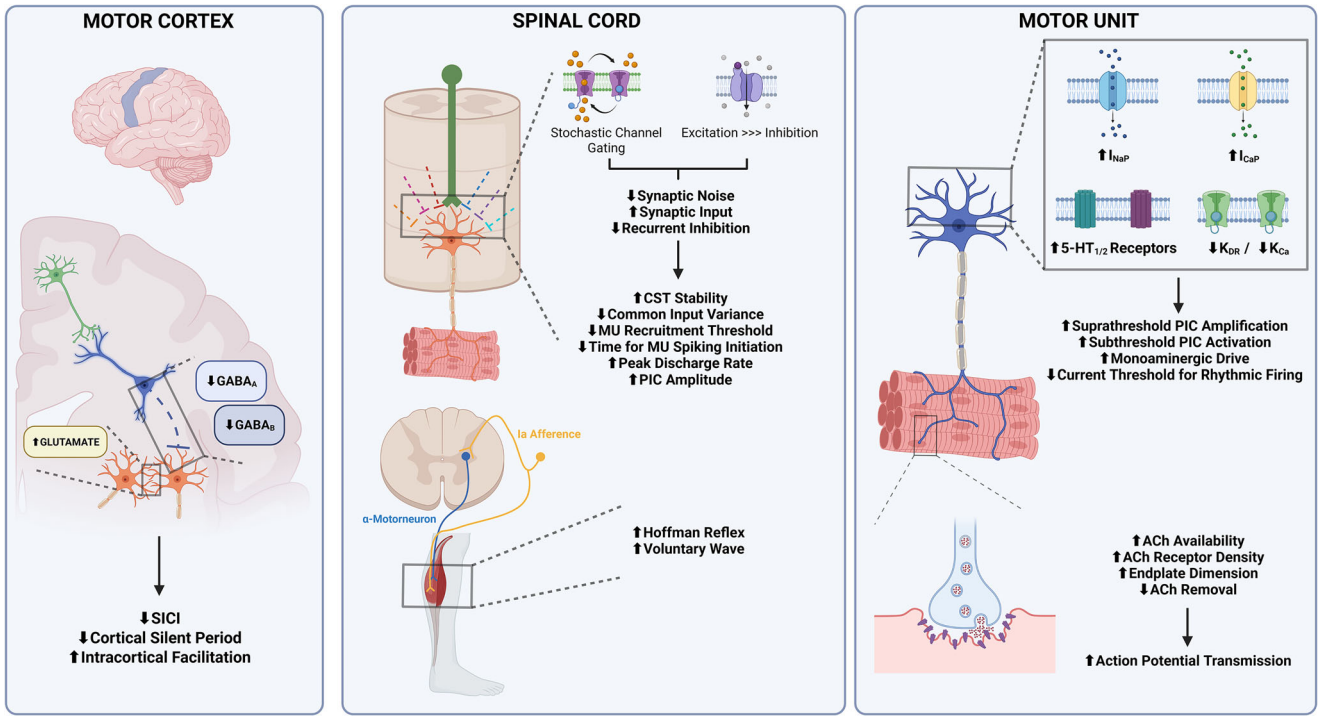


Figure 2. The potential roles of synaptic plasticity
In the motor cortex, resistance training (RT) enhances glutamate and reduces $GABA_{A/B}$ inhibition, lowering short-interval intracortical inhibition (SICI) and cortical silent period while enhancing intracortical facilitation. In the spinal cord, reduced synaptic noise and recurrent inhibition, enhanced net synaptic input, and stochastic ion-channel gating improve cumulative spike train (CST) stability, lower motor unit (MU) recruitment threshold via reduced time-to-spiking initiation, alongside increased peak firing rate, persistent inward currents (PIC) amplitude, H-reflex and voluntary wave. At the level of the MU, upregulated persistent Na^+ and Ca^{2+} currents, 5-$HT_{1/2}$ receptors and monoaminergic drive amplify sub- and suprathreshold PICs. In the neuromuscular junction (NMJ), RT elicits an increase in ACh availability, receptor density and endplate size with slower removal, all contributing to improved action-potential transmission. *The model is based on the evidence presented in the section 'synaptic plasticity'. The image was made using BioRender.*

Regular exercise drives extensive structural and functional remodelling of spinal motor circuits. In spinal motoneurons and their interneuronal partners, animal *in vitro* models suggest that exercise can expand dendritic arbours and increase synaptic spine density, reflecting dendritic outgrowth (Gardiner et al., 2006; von Bohlen Und Halbach & von Bohlen Und Halbach, 2018) alongside upregulated neurotrophic-factor synthesis and enhanced synaptic connectivity throughout the cord (Gardiner et al., 2005, 2006).

At the NMJ, 7 weeks of RT promotes the increase in presynaptic terminal branching and neurotransmitter release, endplate surface enlargement, broader evoked potential amplitudes and an increased postsynaptic receptor density in rats (Deschenes et al., 2000). It has been suggested that both acute and chronic RT can alter the gene expression of ACh receptor and *muscle-specific kinase* (MuSK) signalling proteins (Baraldo et al., 2020; Soendenbroe et al., 2020), together with the mTORC1 signalling for proper skeletal muscle innervation (Baraldo et al., 2020; Castets et al., 2020). Additionally, it seems that motoneuronal activity-induced *agrin* release promotes the aggregation of synaptic proteins on muscle fibre surface (McMahan et al., 1992; Reist et al., 1992), engaging Lrp4-MuSK-Dok7 pathways to phosphorylate and cluster AChRs (Makanae et al., 2025). Cytoskeletal remodelers (e.g. CLASP2/LL5β) capture microtubules and guide AChR–containing vesicles to the endplate (Basu et al., 2015; Rodríguez Cruz et al., 2020), whereas sub–synaptic transcription factors upregulate AChR subunit genes (Charbonnier et al., 2003). Together, these processes may explain the mechanisms underlying enlarged endplates, increased presynaptic branching and denser postsynaptic receptor fields, adaptations that occur independently of muscle fibre hypertrophy (Deschenes, 2019), although human data are lacking.

Exercise appears to selectively augment excitatory synaptic contacts on spinal motoneurons without altering inhibitory inputs, thereby shifting the balance towards greater excitatory drive (Adkins et al., 2006). In dorsal root ganglion neurons of rats, prolonged activity upregulates μ–opioid receptor subunit mRNA while reducing 5–HT_1A, TrkA, TrkB and δ–opioid receptor transcripts (Paddock et al., 2018). Training has also been associated with astrocyte proliferation, stabilisation of basal catecholamine levels, enhanced glutamate uptake and increased release of neurotrophic factors (Maugeri et al., 2021). Because these findings are primarily based on animal models, targeted investigations in humans are needed to confirm whether similar adaptations occur after RT.

Collectively, these spinal and glial changes likely account for the well-documented enhancements in corticospinal excitability and concurrent reductions in intracortical inhibition observed after exercise in humans (Christie & Kamen, 2014; Colomer-Poveda et al., 2020; Nuzzo et al., 2016; Weier et al., 2012). This framework proposes that the convergence of neurotrophic signalling, metabolic support and altered electrical activity during and after resistance exercise creates a permissive environment for motor-circuit remodelling, ultimately enhancing motor learning and performance (Ding et al., 2006; Gómez-Palacio-Schjetnan & Escobar, 2013; Perez et al., 2006; Vints et al., 2022).

Skeletal muscle adaptations

Mechanical overloading imposed by external resistance initiates numerous cascades of events in skeletal muscle, beginning with the transduction of mechanical forces into biochemical signals and culminating in myofibre hypertrophy, enhanced metabolic capacity and improved contractile properties (Fig. 3). Because previous reviews have extensively discussed the molecular and physiological pathways underlying the mechanisms of adaptations in the skeletal muscle (Ji et al., 2025; Roberts et al., 2023; Thomas et al., 2024), the following section highlights how specific training variables (i.e. % load, volume, mechanotransduction and metabolic signalling) optimally engage these adaptive pathways.

Mechanical stress. When muscle fibres are exposed to external resistive loads, particularly during eccentric contractions that stretch the active sarcomeres (Franchi et al., 2017; Ji et al., 2025), the resulting deformation of the extracellular matrix and cytoskeleton is detected by integrin complexes (Bodine, 2022; Goodman, 2019; Panwar et al., 2023; Warneke et al., 2023). In human muscles, clustering of these transmembrane receptors induces autophosphorylation of *focal adhesion kinase* (FAK) at $Y^{576/577}$ with peak activation within 4 h from the end of exercise in untrained individuals, even after a single RT session. Notably, 10 weeks of RT has been suggested to be sufficient for increasing FAK $Y^{576/577}$ phosphorylation even at rest in young male individuals (Thomas et al., 2024; Wilkinson et al., 2008).

Once activated, FAK recruits both *phospholipase D* (PLD) and *diacylglycerol kinase* ζ (DGKζ) (Ji et al., 2025; You et al., 2014), which are enzymes that produce *phosphatidic acid* (PA), a lipid second messenger. PA then binds directly to mTOR, displacing its inhibitor FKBP38 and thereby enhancing mTOR kinase activity observed in animal models (Hornberger et al., 2006). Concurrently mechanical overloading induces sustained MKK3b/6–p38MAPK–MK2 cascade that converges on mTORC1 for its activation (Zhu et al., 2025). mTORC1 phosphorylates p70S6K1 and 4E-BP1, causing its release from eIF4E to initiate cap-dependent translation (Dreyer

et al., 2006; Dunlop et al., 2009; Marabita et al., 2016; Yoon et al., 2011). By bypassing upstream growth–factor signals, this pathway increases ribosome recruitment and protein synthesis even under limited amino acid availability (Roberts et al., 2023).

Mechanical microdamage from eccentric contractions or heavy loading rapidly (within 2 h after exercise) upregulates local IGF-1 splice variants *mechano-growth factor* (MGF) and IGF-IEa in humans (Hameed et al., 2003; Matheny et al., 2010), especially within the exercised muscle (Psilander et al., 2003; Roberts et al., 2010). These peptides bind the IGF-1 receptor on adjacent fibres, inducing phosphorylation of *insulin receptor substrate 1* (IRS-1) and recruitment of PI3K to the membrane, where it converts PIP_2 to PIP_3 (Ji et al., 2025; Rommel et al., 2001; Schiaffino & Mammucari, 2011). PIP_3 has been indicated to anchor Akt/PKB (Deldicque et al., 2008; Glass, 2010; Schiaffino & Mammucari, 2011; Stitt et al., 2004), which phosphorylates TSC2, thereby lifting its inhibition on mTOR (Crossland et al., 2013; Jacobs et al., 2017) and sequesters FOXO transcription factors in the cytosol (Jaiswal et al., 2022; Léger et al., 2006; Zheng et al., 2010). This also causes the downexpression of the ubiquitin ligases MAFbx and MuRF1, observed in both animals (Baehr et al., 2014) and young humans (Mascher et al., 2008) in response to repeated RT exposure. Furthermore, Akt/mTORC2 action has been associated with enhanced glucose uptake, exerting a further anabolic effect and contributing to blood glucose management and muscle mass preservation (Laplante & Sabatini, 2012). The net effect is an enhanced protein synthesis alongside the suppression of targeted proteolysis (Ji et al., 2025; Roberts et al., 2023).

In parallel, mechanosensitive adaptor proteins concurrently activate the MAPK/ERK cascade (Ji et al., 2025). ERK1/2 phosphorylation peaks shortly after RT, with a more pronounced activation after eccentric loading compared to the concentric regime, as shown in human skeletal muscles (Boppart et al., 1999). ERK translocates to the nucleus to phosphorylate transcription factors like Elk–1, driving genes involved in cytoskeletal remodelling, cell–cycle progression and ribosomal RNA synthesis (Carlson et al., 2001; Haddad & Adams, 2004; Winter et al., 2011). Additionally, data from *in vitro* models indicate ERK can phosphorylate p70S6K1 independently of mTORC1, providing parallel anabolic signals under high mechanical tension (Arvisais et al., 2006; Roberts et al., 2023).

Myostatin (MSTN), a member of the *transforming growth factor* (TGF)-β superfamily, downregulates muscle hypertrophy by binding *activin type II receptors* (ActRsII) (Roberts et al., 2023; Schiaffino et al., 2021). MSTN action

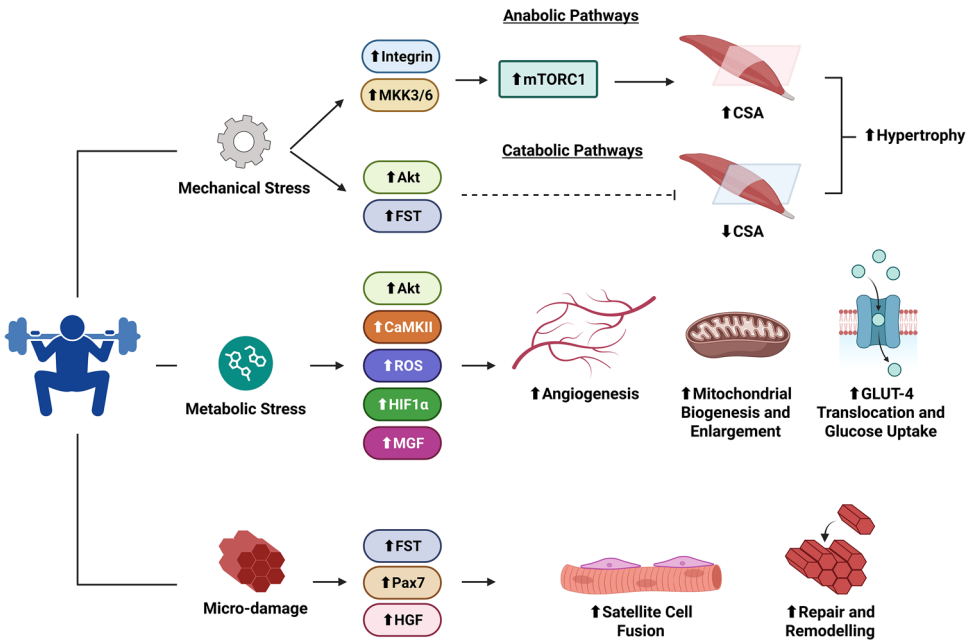


Figure 3. Adaptations in the skeletal muscle
Schematic overview of resistance training (RT)–induced mechanical stress, metabolic stress and microdamage pathways for distinct signalling cascades to promote skeletal muscle adaptations. Mechanical stress activates integrin-MKK3/6 and Akt-follistatin pathways to stimulate mTORC1–dependent protein synthesis and suppress catabolism, leading to muscle hypertrophy. Metabolic stress elevates Akt, CaMKII, reactive oxygen species (ROS), HIF–1α and mechano-growth factor (MGF) to promote angiogenesis, mitochondrial biogenesis/enlargement and GLUT–4 translocation for enhanced glucose uptake. Microdamage recruits follistatin, Pax7 and hepatocyte growth factor (HGF) to induce satellite cell fusion, repair and remodelling. *The image was made using BioRender*.

is inhibited by *follistatin* (FST), which binds and sequesters MSTN, thereby initiating pro–hypertrophic signalling (Han et al., 2019; Lee & McPherron, 2001). When MSTN engages ActRsII, Smad3 is phosphorylated and subsequently inhibits the Akt-mTOR and IGF-1 pathways (Morissette et al., 2009). In contrast, FST promotes Akt-mTOR activation and protein synthesis observed in animal skeletal muscle models (Schiaffino et al., 2021; Winbanks et al., 2012).

Mechanical overloading also induces focal damage to the sarcolemma and basement membrane, promoting the release of *hepatocyte growth factor* (HGF) and *fibroblast growth factors* (FGFs) into the satellite cell niche, as demonstrated in numerous *in vitro* and *in vivo* studies on both animal (Miller et al., 2000; Schiaffino & Bormioli, 1973; Schiaffino et al., 1972) and human skeletal muscles (Pawlikowski et al., 2017; Snijders et al., 2015; Tatsumi et al., 2002). Data from animal skeletal muscle models also indicate that within minutes of focal damage, *nitric oxide* (NO) production further contributes to satellite cell activation and adhesion decrease in the fibre-lamina complex, facilitating hypertrophy (Anderson, 2000; Buono et al., 2012). Notably, quiescent satellite cells express the transcription factor Pax7. Upon activation, these cells co-express Pax7 and MyoD and initiate proliferation. Most progeny then downregulate Pax7, upregulate myogenin and fusogenic proteins, thereby fusing with existing myofibres to expand the myonuclear domain needed to transcribe the mRNA and supporting long-term growth (Hernández-Hernández et al., 2017; Murach et al., 2021; Yin et al., 2013). A subset of daughter cells, however, reverts to quiescence by maintaining Pax7 and losing MyoD, preserving the satellite–cell pool for future repair and adaptation as shown in animal models (Zammit et al., 2004, 2006).

Beyond fusion, results from *in vitro* and *in vivo* animal models indicate that satellite cells exert nonfusion roles by releasing exosomes containing micro-RNAs and other cargo, such as *matrix metalloproteinases* (MMPs), which modulate gene expression in myofibres, fibrogenic cells and endothelial cells, thereby promoting extracellular matrix remodelling and hypertrophy (Roberts et al., 2023; Smith et al., 2020; Yamada et al., 2008).

Metabolic stress. Energetic stress from repeated or prolonged contractions, such as high-volume RT protocols with short rest or taken to failure, activates distinct adaptive pathways. As ATP is hydrolysed and AMP accumulates, the AMP:ATP ratio suddenly rises, activating *AMP-activated protein kinase* (AMPK) (Hardie, 2011; Ke et al., 2018). Consequently, AMPK phosphorylates TSC2 (T^{1227}/S^{1345}) and raptor (S^{722}/S^{792}), imposing a temporary restraint on mTOR activity to preserve cellular energy observed in both *in vitro* and *in vivo* models (Garcia & Shaw, 2017; Gwinn et al., 2008; Inoki et al., 2003). This inhibition is most pronounced during prolonged sets but is rapidly interrupted once the ATP level is restored and the Akt/mTOR signalling resumes, enabling a robust protein synthesis 1–2 h after a RT session in human skeletal muscle (Dreyer et al., 2006; Ji et al., 2025).

AMPK signalling also upregulates *peroxisome proliferator-activated receptor gamma coactivator-1 alpha* (PGC-1α), stimulating mitochondrial biogenesis and oxidative enzyme expression, as confirmed by *in vitro* and *in vivo* data (Cantó & Auwerx, 2009; Groennebaek & Vissing, 2017; Halling & Pilegaard, 2020; Wu et al., 1999; You et al., 2024). Rise in NO level also contributes to increased PGC-1α expression, further potentiating mitochondrial biogenesis in humans (Mueller et al., 2025).

Prolonged contractions or high-volume short-rest RT sessions also imply a significant rise in skeletal muscle Ca^{2+} concentration, activating CaMKII activity as a first-line calcium-buffering system. Activated CaMKII promotes mitochondrial biogenesis via PGC-1α upregulation, and it has also been suggested to influence the expression of specific muscle fibre types (Eisner et al., 2023; Martinez-Canton et al., 2021; Tavi & Westerblad, 2011; Wang et al., 2011; Wu et al., 1999). Increase in cytosolic Ca^{2+} concentration also promotes calmodulin-dependent NO formation, which is thought to enhance the maximal rate of isometric force development, unloaded shortening velocity and peak power (Kumar et al., 2022), although precise mechanisms remain to be fully elucidated. Contemporary models propose that NO at the NMJ augments excitation by promoting synaptic vesicle release, increasing ACh availability and inhibiting acetylcholinesterase, alongside sustaining higher intracellular Ca^{2+} by activating ryanodine receptors and modulating SERCA pump activity, thereby amplifying contractile output (Mueller et al., 2025).

Local hypoxia promotes HIF-1α stabilisation, inducing *vascular endothelial growth factor* (VEGF) and glycolytic enzymes to expand capillary networks and improve substrate delivery in animal (Rodriguez-Miguelez et al., 2015) and human skeletal muscles (Aragón-Vela & Casuso, 2025; Gustafsson et al., 1999; Ramakrishnan et al., 2014). Furthermore, *reactive oxygen species* (ROS), which are thought to be generated by heightened mitochondrial flux in humans (Bloomer & Goldfarb, 2004; McBride et al., 1998), act as second messengers for muscle hypertrophy (Powers et al., 2020). In moderate amounts, ROS activate NF-κB and MAPK/ERK pathways that converge on both mitochondrial (via PGC-1α) and myofibrillar protein synthesis (via p70-S6K1) (Arvisais et al., 2006; Halling & Pilegaard, 2020; Lira et al., 2010; Roberts et al., 2023; Wright et al., 2007).

Muscle contraction also promotes insulin–independent translocation of GLUT-4 to the muscle membrane, improving glucose uptake, glycaemic control and anabolic responses to RT in humans (Bellini et al., 2024; Lecce, Bellini et al., 2025). Data from *in vivo* animal models indicate that GLUT-4 mobilisation is dependent on AMPK activation in response to energy depletion (Fueger et al., 2007; Kido et al., 2021; Leprivier & Rotblat, 2020), and is further facilitated by NO signalling and CaMKII activity elicited by muscle contraction (Knudsen et al., 2020; Lecce, Bellini et al., 2025; Richter & Hargreaves, 2013).

Endocrine adaptations

RT elicits rapid hormonal changes that support both neural and muscular adaptations. Acute bouts of muscle contractions against an external load provoke transient spikes in anabolic hormones, particularly testosterone, *growth hormone* (GH) and IGF–1, alongside catabolic mediators like catecholamines and cortisol in humans (Kraemer & Ratamess, 2005; Kraemer et al., 2020). Although early work linked these brief surges (peaking within hours of exercise) to muscle hypertrophy, more recent studies demonstrate that neither the magnitude nor the duration of the acute endocrine response predicts increases in muscle protein synthesis or contributes to long-term hypertrophic gains (Morton et al., 2016; van Every et al., 2024; West & Phillips, 2012; West et al., 2009, 2010, 2012; Wilkinson et al., 2006).

Notably, research has shown that female individuals achieve comparable relative improvements in muscle mass and strength as males despite much lower baseline androgen levels (Refalo et al., 2025; Roberts et al., 2020). This is supported by evidence showing no sex-based differences between young individuals in muscle protein synthesis rate measured immediately (post-3 h) and over the following 24 h postexercise (van Every et al., 2024; West et al., 2012). Because sex-specific physiological adaptations to RT have been comprehensively reviewed elsewhere (see Handelsman et al., 2018; Hunter & Senefeld, 2024; Hyer et al., 2018; Joyner et al., 2025; Lulic-Kuryllo & Inglis, 2022; Szadvári et al., 2023), these details are not repeated in the present document.

Androgens. Heavy-load RT raises circulating androgens, which act via *androgen receptors* (ARs), promoting both neural and muscle adaptations (Brooks et al., 1998; Davey et al., 2017; Kuwahara et al., 2021; Vingren et al., 2010). Both satellite cells and myoblasts express ARs, which, upon activation by androgens, promote activation, proliferation, migration, differentiation and eventual fusion with existing muscle fibres (Braga et al., 2012; Dalbo & Roberts, 2015). Androgens also enhance Notch signalling in satellite cells, likely by lowering MSTN levels and increasing Akt activity, thereby promoting myogenesis (Dubois et al., 2012; Kovacheva et al., 2010). In addition, *in vitro* data indicate that AR activation upregulates IGF-1 expression in both satellite cells and mature muscle fibres, amplifying anabolic signalling (Sculthorpe et al., 2012). However, recent studies on animal models show that testosterone can elicit similar hypertrophy even in the absence of satellite cells (Englund et al., 2019), suggesting that additional mechanisms mediate androgen-driven muscle growth (Roberts et al., 2023).

At the molecular level, androgens can increase FST production while suppressing MSTN signalling by downregulating Acvr2b receptor expression and reducing Smad2/3 phosphorylation, inhibiting MSTN influence (Kraemer et al., 2020). Concurrently, they also promote the expression of myogenic regulators such as MyoD and myogenin, which enhance myotube formation, increase myonuclear number and ensure correct nuclear positioning within growing fibres, as demonstrated in animal models (Dubois et al., 2014; MacKrell et al., 2015; Singh et al., 2003). Androgens also appear to stimulate ribosome biogenesis, further supporting elevated rates of muscle protein synthesis (Mobley et al., 2016; Roberts et al., 2023).

Androgens also exert rapid (i.e. in a few minutes), *non–genomic* effects that complement their slower, gene-mediated activity. These swift signals occur when androgens bind directly to intracellular AR (i.e. Src kinase), to a membrane-associated AR or via altered membrane fluidity (Michels & Hoppe, 2008). Such interactions can activate G–protein–coupled receptors, stimulating PI3K and phospholipase C to raise IP_3 levels and trigger Ca^{2+} release from the sarcoplasmic reticulum (Kraemer et al., 2020). The resulting Ca^{2+} transient may modulate contractile properties in humans (Dent et al., 2012) and feed into MAPK (Ras/ERK1/2) and mTORC1/S6K1 pathways, amplifying anabolic signalling within seconds to minutes, as shown in animal skeletal muscle models (Basualto-Alarcón et al., 2013; Hamdi & Mutungi, 2010).

Chronic androgen deprivation (e.g. castration) reduces Akt/mTORC1 activity and AR expression, whereas androgen treatment restores both, and when combined with RT and *dihydrotestosterone* (DHT), further enhances AR phosphorylation, IGF–1 production, mTOR signalling and skeletal muscle hypertrophy (Kraemer et al., 2020). These non–genomic effects thus operate alongside classical AR–mediated gene transcription and even feedback via MAPK–driven AR phosphorylation to maximise muscle growth (Hamdi & Mutungi, 2010).

Androgen signalling also influences the neural system. Data obtained from *in vitro* human models indicate this pathway enhances synaptic transmission and

neurotransmitter release, increases motoneuron soma and dendritic size, and supports repair of injured peripheral nerves (Brooks et al., 1998). Moreover, evidence from animal models indicates that androgen action within central neurons is necessary to maintain fast-twitch muscle fibres, even when systemic testosterone levels rise (Davey et al., 2017). However, RT stimulus is the primary driver of muscle activation; the role of androgens in modulating neural drive warrants further investigation (Kraemer et al., 2020).

GH and IGF-1. RT induces large, pulsatile surges in GH, especially in response to high-volume, short-rest protocols (Kraemer & Ratamess, 2005; Kraemer et al., 1998; Mccall et al., 1999). GH, in turn, stimulates hepatic secretion of systemic IGF–1 and upregulates muscle–specific splice variants (e.g. mechano–growth factor) that promote metabolic, mitogenic and anabolic responses within the tissue (Florini et al., 1996). Both circulating and locally produced IGF–1 activate the PI3K-Akt-mTOR pathway (Latres et al., 2005), enhancing protein synthesis and inhibiting degradation, partly via suppression of MSTN expression (Retamales et al., 2015).

Chronic RT frequently elevates muscle IGF–1 content and receptor abundance, even when serum IGF–1 shows only modest change (Adams, 1998; Jiang et al., 2020), with moderate increases observed in middle–aged and older adults (Rodriguez-Gutierrez et al., 2023). This GH/IGF–1 axis further promotes satellite–cell proliferation and differentiation, driving fibre repair and hypertrophy. This is also supported by the observation that blocking IGF–1 signalling *in vivo* markedly blunts these growth responses (Adams, 1998; Kraemer et al., 2020; Rodriguez-Gutierrez et al., 2023).

Beyond muscle, IGF–1 crosses the blood–brain barrier to support human central nervous system plasticity and function (Frater et al., 2018). In astrocytes and the choroid plexus, it activates PI3K/Akt to recruit GLUT transporters and enhance glucose uptake in humans (Arjunan et al., 2023; Bondy & Cheng, 2004). In microglia, IGF–1 shifts cells towards a reparative phenotype via TLR4-NF-κB/NLRP3 signalling, reducing oxidative stress and inflammation (Nagaraj et al., 2018; O'Connor et al., 2008; Sun et al., 2020). Neuronal PI3K/Akt and MAPK/CREB pathways, downstream of IGF-1, inhibit cell death (via GSK–3, Bad and FOXO) and promote axon outgrowth and synaptic plasticity (Wiggin et al., 2002; Zheng & Quirion, 2006).

IGF–1 stimulates oligodendrocyte proliferation and Schwann–cell myelination, modulating $Na^+/Ca^{2+}/K^+$ channel activity and NMDA/AMPA/kainate receptors to optimise neural excitability and neurotransmitter release (Chattopadhyay & Shubayev, 2009; Delaney et al., 2001; Ge et al., 2022; Gonzalez de La Vega et al., 2001; Sonntag et al., 2000). It also supports metabolic regulation in the brain, upregulates other neurotrophic factors, facilitates clearance of protein aggregates and stimulates angiogenesis, as observed in animal models (Carro et al., 2006; Trejo et al., 2001) and humans (Arjunan et al., 2023; Okamoto et al., 2021).

Collectively, these GH/IGF-1-mediated adaptations promise potential implications for both performance and therapeutic targets for neurodegenerative and metabolic disorders associated with sedentary lifestyles (for reviews, see Arjunan et al., 2023; Lecce et al., 2025; Pinto et al., 2023).

Catecholamines and cortisol. RT acutely elevates circulating catecholamines, which rise way above baseline levels in proportion to training intensity and duration (Guezennec et al., 1986; Kraemer et al., 1987, 1999). These hormones bind *β-adrenergic* receptors on muscle fibres to enhance Na^+/K^+-ATPase activity, augmenting ACh release at the NMJ and modulating sarcoplasmic calcium handling and contractile properties. Concurrently, catecholamines promote glycogenolysis and lipolysis to meet the rising energy demand (Barth et al., 2007; Cairns & Borrani, 2015; Roatta & Farina, 2010). NE, in particular, is implicated in the synaptic input amplification, contributing to spinal motoneuron discharge activity through its neuromodulatory action (Heckman et al., 2003, 2009; Mesquita et al., 2024).

Cortisol is considered the principal glucocorticoid in the human body (Walker & Seckl, 2001) and is likewise elevated by high-volume or short-rest RT sessions (Hakkinen & Pakarinen, 1993; Kraemer & Ratamess, 2005; Kraemer et al., 1987, 1993). Although cortisol promotes proteolysis, especially in type II fibres (Dekhuijzen et al., 1995), and antagonises insulin/IGF-1 signalling (Kraemer et al., 2020; Walker & Seckl, 2001), transient spikes are a physiological component of training stress and do not necessarily preclude muscle hypertrophy (Athanasiou et al., 2023; Oakley & Cidlowski, 2013; Ramamoorthy & Cidlowski, 2016). Furthermore, it seems that a change in the testosterone/cortisol ratio would indicate a potential change in the state of anabolism (De Luccia, 2016; Kraemer & Ratamess, 2005). This depends on the androgen counterbalance effects on cortisol catabolic actions by competing for DNA binding and downregulating glucocorticoid receptors (Kraemer et al., 2020). Eccentric contraction-RT acutely increases glucocorticoid receptor levels and myofibrillar protein breakdown, peaking 24 h after the first bout, alongside elevated serum cortisol (Willoughby et al., 2003). However, after a second identical session, both the receptor upregulation and cortisol responses are blunted, as its activity in the ubiquitin–proteasome pathway. This suggests that repeated eccentric training induces a

protective adaptation, limiting muscle catabolism and damage (Kraemer & Ratamess, 2005).

Although chronic overtraining-induced cortisol elevations (i.e. high resting cortisol concentration) can impair muscle gains, the acute hormonal fluctuations elicited by well–designed resistance exercise have only a temporary catabolic effect in humans (Armstrong et al., 2022; Kraemer et al., 2020; Kreher & Schwartz, 2012; Kuipers & Keizer, 1988; Lee et al., 2015).

Reconciling the time-course of neural and muscular adaptations to RT

A long-standing and operationally helpful rule of thumb holds that early strength gains are predominantly neural, whereas muscular (metabolic and structural) adaptations emerge later. The empirical data presented above support rapid, use-dependent plasticity within supraspinal and spinal networks that reduces intracortical inhibition and increases descending and motoneuronal drive to muscle within weeks of training; these neural changes account for much of the initial rise in voluntary force. However, portraying adaptation as strictly sequential '*neural first, muscle later*' is misleading, as no study has precisely partitioned the temporal contributions of neural and muscular mechanisms to increases in force output.

A single bout of RT elicits robust increases in intramuscular anabolic signalling and muscle-protein synthesis (mTOR-pathway activation within 1–2 h), although these acute molecular responses require repeated, cumulative stimuli to produce measurable hypertrophy. Acute endocrine responses also occur but do not reliably predict longer-term hypertrophic gains. Recent work emphasises overlap and reciprocity: neural plasticity can persist beyond the earliest weeks and continue to contribute to strength improvements alongside progressive intramuscular remodelling, whereas muscle adaptations (e.g. satellite-cell activation, ribosome biogenesis and increases in fibre cross-sectional area) begin soon after exercise but require time to accumulate into macroscopic growth.

Taken together, the evidence favours an integrated, stimulus-dependent model in which neural and muscular mechanisms are both engaged early after exposure to resistive loading but follow different temporal courses and dose dependencies. Practically, an absolute sequential narrative (*neural – then muscle*) could be reconsidered in favour of wording that (1) acknowledges rapid neural plasticity as a major driver of very early strength gains; (2) recognises that molecular and metabolic muscle responses occur acutely after single bouts but need repeated overload to yield cumulative hypertrophy; and (3) emphasises that the relative contribution of each mechanism depends on training variables (load, volume, velocity) and participant status, with neural and muscular contributions tightly coupled across the continuum of RT adaptations.

Specificity of neuromuscular adaptations

Activity-dependent plasticity within the human neuromuscular system is well documented (Ajay & Bhalla, 2006; Chin, 2005; Gómez-Palacio-Schjetnan & Escobar, 2013; Snijders et al., 2015), yet the precise integration of the underlying molecular pathways and the associated plastic responses is not fully defined. Existing data indicate that both the nature and magnitude of neuromuscular adaptations are critically determined by training parameters. In particular, these neuromuscular adaptations depend on the training intensity, duration, rest and specific training modality (i.e. contraction regimens and lengthening/shortening speed), as extensively detailed above. A summary of the reported evidence, detailing the underlying molecular mechanisms and the functional modifications associated with the neuromuscular system, is presented in Table 1.

Implications for human performance

RT elicits marked changes in maximal force production (MVF or 1RM), maximal power output (MP), rate of force development (RFD) and muscle endurance (ME) in healthy individuals (Aagaard et al., 2002b; Folland & Williams, 2007; Kraemer et al., 2002; Lecce, Romagnoli, Frinolli et al., 2024; Makaruk et al., 2024). The classical *repetition continuum* model posits that heavy loads (>80%1RM) optimise strength, moderate loads (60%–80%1RM) preferentially promote hypertrophy when sufficient volume is performed, and lighter loads (<60%1RM) and prolonged contractions/sets most effectively improve endurance (Kraemer & Ratamess, 2004; Schoenfeld et al., 2021). Contemporary investigations largely corroborate this concept, with heavy-load RT consistently producing the greatest improvements in 1RM, whereas moderate- and light-load protocols, when matched in volumes, enhance both strength and hypertrophy, with light loads yielding the largest gains in ME (Baz-Valle et al., 2022; Schoenfeld et al., 2017). Adaptations in MP and RFD, however, are primarily induced by the velocity and intent of movement in RT rather than load per se, underscoring the specificity of the stimuli for developing the capacity of rapid force production (Behm & Sale, 1993a, 1993b; Haff & Nimphius, 2012).

Below, the quantitative outcomes (% change) for each variable by load and contraction regime are discussed by distinguishing short-term (between 4 and 8 weeks)

Table 1. Physiological adaptive pathways

Stimulus	Underlying mechanisms	Adaptations
Mechanical stress	Muscle fibres:	↑ Ribosome biogenesis
Heavy resistance	↑ Integrin – FAK – PLD/DGKζ – PA – mTORC1	↑ Mitochondrial biogenesis
Eccentric loading	↑ MKK3/6 – p38 MAPK – MK2 – mTORC1	↑ GLUT1-4 translocation
	↑ mTORC1 – p70S6K1 + 4E-BP1	↑ Protein synthesis
	↑ ERK1/2 – p70S6K1	↓ Proteolysis
	↑ IGF-1/MGF – IRS-1 – PI3K – PIP3 – Akt/PKB	↑ Angiogenesis
	↑ Akt – ↓ FOXO + ↓ MAFbx/MuRF1	↑ CSA
	↑ FST – ↓ MSTN	
Metabolic stress	Muscle fibres and capillary:	
Prolonged contractions	↑ IGF-1/MGF – IRS-1 – PI3K – PIP3 – Akt/PKB	
Short-rest sessions	↑ Akt/PKB – ↓ TSC2 – ↑ mTORC1	
	↑ CaMKII – PGC-1α	
	↑ ROS – NF-κB – MAPK/ERK – PGC-1α + p70S6K1	
	↑ HIF1α – VEGF	
Microdamage	Satellite cells:	↑ Fusion to myofibres
Heavy resistance	↑ HGF/FGF – NO – SC activation	↑ Myonuclei
Eccentric loading	↑ Pax7 + ↑ MyoD – myogenin + fusogenic molecules	↑ Repair activity
	↑ FST – ↓ Smad3	↑ Remodelling activity
	↑ Exosomal micro-RNA/MMP	
Activity dependent	NMJ:	↑ ACh availability
High resistance	↑ Catecholamines – ↑ β-AR	↑ Vesicle release
Prolonged contractions	↑ NO	↓ Acetylcholinerase
	↑ Lrp4-MuSK-Dok7	↑ Terminal branching
	↑ CLASP2/LL5β	↑ Ach receptor density
Voluntary activity	Spinal circuitries and motoneurons:	↑ Common synaptic input
Muscle contractions	↑ 5-HT_2/α_1 – AR	↓ Synaptic noise
Co-ordinated actions	↓ 5-HT_1A/$GABA_A$	↑ Motoneuron excitability
Repeated activity	↑ Propriospinal/reticulospinal	↑ Input–output slope
	↑ NMDA, AMPA (?)	↓ MU-RT
	↓ Ia inhibition	↓ MU-ISIv
	↓ Recurrent inhibition	↑ MU-DR
	↑ Sub-suprathreshold PICs	
Voluntary activity	Supraspinal regions and cortex:	↑ Corticospinal drive
Motor learning	↑ BDNF – TrkB – PI3K/Akt	↓ SICI
Repeated contractions	↑ MAPK/ERK – PLCγ Fyn – NMDAR	↑ LTP
	↑ mTORC1 (neuronal)	↑ Cross-education

Abbreviations: BDNF, brain-derived neurotrophic factor; FGF, fibroblast growth factor; HGF, hepatocyte growth factor; PIC, persistent inward current; ROS, reactive oxygen species; SICI, short-interval intracortical inhibition; VEDF, vascular endothelial growth factor.

vs. long-term (>12 weeks) training, balancing different arbitrary perspectives on acute and more prolonged exposure to RT intervention (Ashton et al., 2020; Hughes et al., 2018; Pearcey et al., 2021). Because the present review summarises the specificity of RT effects on performance metrics, detailed hypertrophy protocols and muscle–size outcomes are not included here but summarised in many relevant reviews (see Baz-Valle et al., 2022; Bernárdez-Vázquez et al., 2022; Currier et al., 2023; Grgic et al., 2022; Schoenfeld, 2010; Schoenfeld et al., 2017, 2021; Warneke et al., 2023).

Derived from this synthesis, specific loading recommendations to maximise each performance variable are summarised in Table 2.

Maximal strength. RT elicits the largest short-term improvements in maximal force production when heavy loads are used. Meta-analytic data indicate that protocols employing loads > 80% 1RM increase 1RM by an average of ∼35% compared to ∼28% following lighter-load (<60% 1RM) protocols in interventions of similar duration (Schoenfeld et al., 2017). When comparing moderate- and light-load interventions across a 12-week intervention in active young male and female individuals, RT produces comparable strength gains (Kapsis et al., 2022). Across studies, heavy-load RT typically elicits 20%–40% increases in 1RM, moderate-load protocols 15%–30% and light-load regimens 10%–20%, with the magnitude of adaptation influenced by participants'

Table 2. Loading recommendations for performance.

RT MODALITY	LOAD	1RM	MP	RFD	ME
CONTROLLED CONTRACTIONS	Heavy (≥85%1RM)	***	**	**	**
	Moderate (60%–80%1RM)	**	**	*	***
	Light (<60%1RM)	*	*	*	***
BALLISTIC CONTRACTIONS	Heavy (≥85% 1RM)	***	***	***	*
	Moderate (60%–80%1RM)	*	***	***	**
	Light (<60%1RM)	*	**	***	***

Note: Magnitude of change is defined as small*, moderate** and large*** based on del Vecchio et al. (2024); Frost et al. (2016); Haff and Nimphius (2012); Kapsis et al. (2022); Lecce et al. (2024); Mangine et al. (2008); Schoenfeld et al. (2017, 2021).
Abbreviations: 1RM, one-repetition maximum; ME, muscle endurance; MP, maximal power output; RFD, rate of force development.

training level, total volume and contraction velocity (Mangine et al., 2008; Munn et al., 2005; Schoenfeld et al., 2016, 2021; Weakley et al., 2023).

The canonical stimulus for maximal strength development is represented by dynamic contractions performed under heavy resistive loading. Nonetheless, eccentric-contraction RT, often employing supramaximal loads, can evoke even greater strength and hypertrophic adaptations, owing to elevated mechanical tension and unique neural activation patterns during muscle lengthening overloading (Enoka, 1996; Roig et al., 2009; Schoenfeld et al., 2021). Contraction velocity further modulates these adaptations. In chronically strength-trained male and female athletes, both slow-controlled and ballistic regimens produce equivalent improvements in 1RM (Lecce, Romagnoli, Frinolli et al., 2024; Lecce, Romagnoli, Maffiuletti et al., 2025; Mangine et al., 2008), whereas untrained individuals take larger benefits from higher-velocity efforts, suggesting that movement intent and contraction speed may outweigh time under tension in promoting early strength gains in this population (Munn et al., 2005).

Ballistic contractions performed without substantial external resistance provided by heavy loads produce mechanical stimuli that are insufficient to elicit maximal strength gains (i.e. 1RM). However, it is well accepted that combining rapid contractions with heavy-load RT (≥80% 1RM), the contribution of elevated mechanical overload and enhanced neural activation produces greater long-term gains in maximal strength than either modality alone (Behm, 1995; Behm & Sale, 1993a, 1993b; Boccia et al., 2025; del Vecchio et al., 2024; Haff & Nimphius, 2012; Lecce, Romagnoli, Frinolli et al., 2024; Pearcey et al., 2021; Tøien et al., 2022).

Both young and older adults gain significant strength benefits from RT, although absolute improvements tend to be minor in the elderly population. In a meta–analysis of healthy older adults (mean age ≥ 60 years) undergoing 4–16 weeks of RT, mean increases in maximal strength were approximately 18% (Guizelini et al., 2018). By contrast, younger cohorts typically achieve larger relative improvements in the range of 20%–40% over comparable intervention durations (Roberts et al., 2020).

When accounting for baseline differences, males and females attain equivalent relative gains in 1RM, with similar increases in muscle cross–sectional area and lower-limb strength (Roberts et al., 2020). Notably, untrained females may experience greater percentage improvements in upper-body strength than their male counterparts, despite males' higher absolute gains driven by greater initial force-producing capacity. Although absolute 1RM enhancements are greater in males (Joyner et al., 2025), sex does not appear to influence the *relative* magnitude of maximal strength or maximal neural drive adaptations to RT (Hunter & Senefeld, 2024; Lecce, Conti et al., 2024; Roberts et al., 2020).

Maximal power. RT elicits robust adaptations in MP, yet the nature of the stimulus dictates the magnitude and specificity of the response. Consistent with the principle of specificity, low-load ballistic or plyometric protocols maximise both movement velocity and RFD, whereas heavy–load RT primarily enhances maximal strength, thereby potentiating MP under high-load conditions (Haff & Nimphius, 2012; Lecce, Romagnoli, Frinolli et al., 2024; Lecce, Romagnoli, Maffiuletti et al., 2025; Maffiuletti et al., 2016; Nishioka & Okada, 2023). Indeed, ballistic contractions produce greater enhancements in MP across diverse modalities (free weights, pneumatic devices,

isotonic machines) than do slow or non–ballistic regimens in both male and female individuals at any training level (Balshaw et al., 2016; Frost et al., 2016; Lecce, Romagnoli, Maffiuletti et al., 2025; Mc Dermott et al., 2022).

When ballistic exercises are performed with light-to-moderate loads, increases in MP are most pronounced at those specific loads, whereas heavy–load training improves MP predominantly at higher %1RM (Haff & Nimphius, 2012). By systematically incorporating ballistic movements across the entire overloading spectrum, it is expected that a shift in the force-velocity-power relationship will be observed, reflecting concurrent gains in maximal strength and maximal shortening speed. This load-velocity-power adaptation occurs in both untrained and trained individuals (González-Badillo et al., 2014; Lecce, Romagnoli, Frinolli et al., 2024; Morin & Samozino, 2016; Pareja-Blanco et al., 2014) and is underpinned by distinct neural and contractile modifications evoked by ballistic loading (Boccia et al., 2025; del Vecchio, Negro et al., 2019, 2022, 2024; Maffiuletti et al., 2016).

By contrast, RT performed exclusively with slow, controlled contractions increases MP predominantly through gains in maximal force, often resulting in the absence of a net change, or even a relative decline, when MP is normalised to 1RM or MVF (Folland et al., 2014; Haff & Nimphius, 2012; Lecce, Romagnoli, Maffiuletti et al., 2025). Such adaptations suggest that prolonged emphasis on slow-velocity loading may attenuate the expression of MP relative to underlying force-producing capacity, a critical determinant of athletic performance in younger populations and of quality of life in older adults (D'Antona, 2003; Ferretti et al., 1994; Folland et al., 2014; Losa-Reyna et al., 2020; Reid & Fielding, 2012).

Rate of force development. RFD is mathematically expressed as the slope of the force-time curve (Δforce/Δtime) and represents the principal index of the rapid force production (Kozinc et al., 2022; Maffiuletti et al., 2016). Both ballistic and slow-heavy RT interventions can increase RFD. However, greater improvements in early-phase RFD (0–100 ms) predominantly require ballistic contractions that prioritise rapid muscle activation, as it implies both higher MU recruitment speed and maximal discharge rates (del Vecchio, Negro et al., 2019, 2024; Maffiuletti et al., 2016). Although non–ballistic RT also enhances MU discharge rates (Aagaard, 2003; del Vecchio, Casolo et al., 2019; Lecce et al., 2025; Lecce, Conti et al., 2025), the lack of rapid recruitment observed with slow-type contractions limits gains in the initial RFD window (del Vecchio et al., 2022). Notably, even chronically strength–trained individuals, despite exhibiting higher MU discharge rates than untrained counterparts (Casolo et al., 2021), demonstrate comparable relative RFD when normalised to %1RM, a finding partly attributed to training-induced slowing of intrinsic contractile properties (Škarabot et al., 2024).

Expected RFD improvements vary by training modality and population. In young individuals, short-term ballistic RT interventions typically induce 10%–40% improvements in RFD (Aagaard et al., 2002b; Balshaw et al., 2016; de Oliveira et al., 2013; Häkkukinen et al., 1985; Maffiuletti et al., 2016; Tillin & Folland, 2014; van Cutsem et al., 1998). Older adults can also achieve approximately 20%–30% gains in RFD across both acute and chronic RT interventions (Häkkinen et al., 2001). Notably, no changes in RFD, especially when normalised to MVF or 1RM, are expected when training with slow isometric-contraction RT (Balshaw et al., 2016; Del Vecchio et al., 2022; Lecce, Romagnoli, Maffiuletti et al., 2025; Tillin & Folland, 2014).

Muscle endurance. Local ME, which is the capacity to sustain the maximal number of repetitions to failure at a specific submaximal load, is most effectively enhanced by high-repetition, low-load RT ($\geq$15 repetitions at <60%1RM) compared to heavy-load RT (Schoenfeld et al., 2021). Across a 9 week intervention prescribing very light (>100 repetitions per set) and moderate ($\sim$30 repetitions per set) loads produced markedly greater increases in both absolute (same load) and relative (same %1RM) ME than the heavy-load group (absolute ME: $\sim$40% *vs.* $\sim$28%; relative ME: $\sim$25% *vs.* $\sim$7%) (Anderson & Kearney, 1982).

Older individuals demonstrate similar relative endurance enhancements using 10–15 RM regimens (Chodzko-Zajko et al., 2009; Wang et al., 2023), with no significant advantage for heavier loads (Schoenfeld et al., 2021). Despite greater fatigue resistance for females compared to males, their endurance adaptations to light-load, high-volume training closely mirror those of male individuals (Hunter & Senefeld, 2024), indicating minimal sex–based disparity in ME modifications with RT (Hunter, 2014; Schoenfeld et al., 2021). These findings underscore that, regardless of age or sex, low-load, high–repetition training is the optimal strategy for enhancing ME.

Conclusions

RT elicits integrated neuromuscular remodelling, whereby mechanosensitive signalling and hormonal cascades drive both neural adaptations and muscle-tissue plasticity. These modifications culminate in enhanced strength, power, rapid force production and endurance. Although considerable progress has been made in mapping individual molecular pathways and functional

outcomes, the precise translation of intracellular events into performance gains remains to be fully elucidated. Moreover, the modulation of these adaptations by age, sex and pathological status is poorly defined. Addressing these points through studies that couple detailed molecular profiling with rigorous, population-specific performance measures will deepen our understanding of RT physiology and improve clinical and athletic prescriptions to optimise health, function and independence across the lifespan.

References

Aagaard, P. (2003). Training-induced changes in neural function. *Exercise and Sport Sciences Reviews*, **31**(2), 61–67.

Aagaard, P. (2018). Spinal and supraspinal control of motor function during maximal eccentric muscle contraction: Effects of resistance training. *Journal of Sport and Health Science*, **7**(3), 282–293.

Aagaard, P., Bojsen-Møller, J., & Lundbye-Jensen, J. (2020). Assessment of neuroplasticity with strength training. *Exercise and Sport Sciences Reviews*, **48**(4), 151–162.

Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002a). Neural adaptation to resistance training: Changes in evoked V-wave and H-reflex responses. *Journal of Applied Physiology*, **92**(6), 2309–2318.

Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002b). Increased rate of force development and neural drive of human skeletal muscle following resistance training. *Journal of Applied Physiology*, **93**(4), 1318–1326.

Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, S. P., Halkjær-Kristensen, J., & Dyhre-Poulsen, P. (2000). Neural inhibition during maximal eccentric and concentric quadriceps contraction: Effects of resistance training. *Journal of Applied Physiology*, **89**(6), 2249–2257.

Aagaard, P., Suetta, C., Caserotti, P., Magnusson, S. P., & Kjær, M. (2010). Role of the nervous system in sarcopenia and muscle atrophy with aging: Strength training as a countermeasure. *Scandinavian Journal of Medicine & Science in Sports*, **20**(1), 49–64.

Abbasi, L., Rojhani Shirazi, Z., Roshdi, G., Razeghi, M., & Motealleh, A. (2022). Spinal adaptation following exercise training: Narrative review. *Journal of Rehabilitation Sciences & Research*, **9**(2), 55–59.

Adams, G. R. (1998). 2 role of insulin-like growth factor-I in the regulation of skeletal muscle adaptation to increased loading. *Exercise and Sport Sciences Reviews*, **26**, 31–60.

Adkins, D. L., Boychuk, J., Remple, M. S., & Kleim, J. A. (2006). Motor training induces experience-specific patterns of plasticity across motor cortex and spinal cord. *Journal of Applied Physiology*, **101**(6), 1776–1782.

Afsharipour, B., Manzur, N., Duchcherer, J., Fenrich, K. F., Thompson, C. K., Negro, F., Quinlan, K. A., Bennett, D. J., & Gorassini, M. A. (2020). Estimation of self-sustained activity produced by persistent inward currents using firing rate profiles of multiple motor units in humans. *Journal of Neurophysiology*, **124**(1), 63–85.

Ajay, S. M., & Bhalla, U. S. (2006). Synaptic plasticity in vitro and in silico: Insights into an intracellular signaling maze. *Physiology*, **21**(4), 289–296.

Albini, M., Krawczun-Rygmaczewska, A., & Cesca, F. (2023). Astrocytes and brain-derived neurotrophic factor (BDNF). *Neuroscience Research*, **197**, 42–51.

Alvarez, F. J., Benito-Gonzalez, A., & Siembab, V. C. (2013). Principles of interneuron development learned from Renshaw cells and the motoneuron recurrent inhibitory circuit. *Annals of the New York Academy of Sciences*, **1279**(1), 22–31.

Andersen, H., Nielsen, S., Mogensen, C. E., & Jakobsen, J. (2004). Muscle strength in type 2 diabetes. *Diabetes*, **53**(6), 1543–1548.

Anderson, J. E. (2000). A role for nitric oxide in muscle repair: Nitric oxide–mediated activation of muscle satellite cells ed. Pollard TD. *Molecular Biology of the Cell*, **11**(5), 1859–1874.

Anderson, T., & Kearney, J. T. (1982). Effects of three resistance training programs on muscular strength and absolute and relative endurance. *Research Quarterly for Exercise and Sport*, **53**(1), 1–7.

Ansdell, P., Brownstein, C. G., Škarabot, J., Angius, L., Kidgell, D., Frazer, A., Hicks, K. M., Durbaba, R., Howatson, G., Goodall, S., & Thomas, K. (2020). Task-specific strength increases after lower-limb compound resistance training occurred in the absence of corticospinal changes in vastus lateralis. *Experimental Physiology*, **105**(7), 1132–1150.

Aragón-Vela, J., & Casuso, R. A. (2025). Effect of hypoxia-inducible factor 1 on vascular endothelial growth factor expression in exercised human skeletal muscle: A systematic review and meta-analysis. *American Journal of Physiology-Cell Physiology*, **329**(1), C272–C282.

Arazi, H., Babaei, P., Moghimi, M., & Asadi, A. (2021). Acute effects of strength and endurance exercise on serum BDNF and IGF-1 levels in older men. *BioMed Central Geriatrics*, **21**(1), 50.

Arjunan, A., Sah, D. K., Woo, M., & Song, J. (2023). Identification of the molecular mechanism of insulin-like growth factor-1 (IGF-1): A promising therapeutic target for neurodegenerative diseases associated with metabolic syndrome. *Cell & Bioscience*, **13**(1), 16.

Armstrong, L. E., Bergeron, M. F., Lee, E. C., Mershon, J. E., & Armstrong, E. M. (2022). Overtraining syndrome as a complex systems phenomenon. *Frontiers in Network Physiology*, **1**, 794392.

Arvisais, E. W., Romanelli, A., Hou, X., & Davis, J. S. (2006). AKT-independent phosphorylation of TSC2 and activation of mTOR and ribosomal protein S6 kinase signaling by prostaglandin F2α. *Journal of Biological Chemistry*, **281**(37), 26904–26913.

Ashton, R. E., Tew, G. A., Aning, J. J., Gilbert, S. E., Lewis, L., & Saxton, J. M. (2020). Effects of short-term, medium-term and long-term resistance exercise training on cardiometabolic health outcomes in adults: Systematic review with meta-analysis. *British Journal of Sports Medicine*, **54**(6), 341–348.

Athanasiou, N., Bogdanis, G. C., & Mastorakos, G. (2023). Endocrine responses of the stress system to different types of exercise. *Reviews in Endocrine & Metabolic Disorders*, **24**(2), 251–266.

Atkinson, E., Škarabot, J., Ansdell, P., Goodall, S., Howatson, G., & Thomas, K. (2022). Does the reticulospinal tract mediate adaptation to resistance training in humans?. *Journal of Applied Physiology*, **133**(3), 689–696.

Baehr, L. M., Tunzi, M., & Bodine, S. C. (2014). Muscle hypertrophy is associated with increases in proteasome activity that is independent of MuRF1 and MAFbx expression. *Frontiers in Physiology*, **5**, 69.

Balshaw, T. G., Massey, G. J., Maden-Wilkinson, T. M., Lanza, M. B., & Folland, J. P. (2019). Neural adaptations after 4 years vs 12 weeks of resistance training vs untrained. *Scandinavian Journal of Medicine & Science in Sports*, **29**(3), 348–359.

Balshaw, T. G., Massey, G. J., Maden-Wilkinson, T. M., Tillin, N. A., & Folland, J. P. (2016). Training-specific functional, neural, and hypertrophic adaptations to explosive- vs. sustained-contraction strength training. *Journal of Applied Physiology*, **120**(11), 1364–1373.

Baraldo, M., Geremia, A., Pirazzini, M., Nogara, L., Solagna, F., Türk, C., Nolte, H., Romanello, V., Megighian, A., Boncompagni, S., Kruger, M., Sandri, M., & Blaauw, B. (2020). Skeletal muscle mTORC1 regulates neuromuscular junction stability. *Journal of Cachexia, Sarcopenia and Muscle*, **11**(1), 208–225.

Barrué-Belou, S., Marque, P., & Duclay, J. (2018). Recurrent inhibition is higher in eccentric compared to isometric and concentric maximal voluntary contractions. *Acta Physiologica*, **223**(4), e13064.

Barth, E., Albuszies, G., Baumgart, K., Matejovic, M., Wachter, U., Vogt, J., Radermacher, P., & Calzia, E. (2007). Glucose metabolism and catecholamines: *Critical Care Medicine*, **35**(Suppl), S508–S518.

Basu, S., Sladecek, S., Martinez de La Peña, Y., Valenzuela, I., Akaaboune, M., Smal, I., Martin, K., Galjart, N., & Brenner, H. R. (2015). CLASP2-dependent microtubule capture at the neuromuscular junction membrane requires LL5β and actin for focal delivery of acetylcholine receptor vesicles ed. Martin TFJ. *Molecular Biology of the Cell*, **26**(5), 938–951.

Basualto-Alarcón, C., Jorquera, G., Altamirano, F., Jaimovich, E., & Estrada, M. (2013). Testosterone signals through mTOR and androgen receptor to induce muscle hypertrophy. *Medicine and Science in Sports and Exercise*, **45**(9), 1712–1720.

Baz-Valle, E., Balsalobre-Fernández, C., Alix-Fages, C., & Santos-Concejero, J. (2022). A systematic review of the effects of different resistance training volumes on muscle hypertrophy. *Journal of Human Kinetics*, **81**, 199–210.

Bazzucchi, I., Riccio, M. E., & Felici, F. (2008). Tennis players show a lower coactivation of the elbow antagonist muscles during isokinetic exercises. *Journal of Electromyography and Kinesiology*, **18**(5), 752–759.

Beaumont, E., & Gardiner, P. (2002). Effects of daily spontaneous running on the electrophysiological properties of hindlimb motoneurones in rats. *The Journal of Physiology*, **540**(1), 129–138.

Behm, D. G. (1995). Neuromuscular implications and applications of resistance training. *Journal of Strength and Conditioning Research*, **9**, 264–274.

Behm, D. G., & Sale, D. G. (1993*a*). Intended rather than actual movement velocity determines velocity-specific training response. *Journal of Applied Physiology*, **74**(1), 359–368.

Behm, D. G., & Sale, D. G. (1993*b*). Velocity specificity of resistance training. *Sports Medicine (Auckland, NZ)*, **15**(6), 374–388.

Bellini, A., Scotto di Palumbo, A., Nicolò, A., Bazzucchi, I., & Sacchetti, M. (2024). Exercise prescription for postprandial glycemic management. *Nutrients*, **16**(8), 1170.

Bernárdez-Vázquez, R., Raya-González, J., Castillo, D., & Beato, M. (2022). Resistance training variables for optimization of muscle hypertrophy: An umbrella review. *Frontiers in Sports and Active Living*, **4**, 949021.

Binder, M. D., Powers, R. K., & Heckman, C. J. (2020). Nonlinear input-output functions of motoneurons. *Physiology*, **35**(1), 31–39.

Bloomer, R. J., & Goldfarb, A. H. (2004). Anaerobic exercise and oxidative stress: A review. *Canadian Journal of Applied Physiology*, **29**(3), 245–263.

Blum, R., & Konnerth, A. (2005). Neurotrophin-mediated rapid signaling in the central nervous system: Mechanisms and functions. *Physiology*, **20**(1), 70–78.

Boccia, G., Brustio, P. R., Salvaggio, F., Grossio, L., Calcagno, E., Pintore, A., Rainoldi, A., & Samozino, P. (2025). The rate of torque development as a determinant of the torque–velocity relationship. *Scandinavian Journal of Medicine & Science in Sports*, **35**(3), e70035.

Bockaert, J., & Marin, P. (2015). mTOR in brain physiology and pathologies. *Physiological Reviews*, **95**(4), 1157–1187.

Bodine, S. C. (2022). The role of mTORC1 in the regulation of skeletal muscle mass. *Faculty Reviews*, **11**, 32.

Bondy, C. A., & Cheng, C. M. (2004). Signaling by insulin-like growth factor 1 in brain. *European Journal of Pharmacology*, **490**(1–3), 25–31.

Boppart, M. D., Aronson, D., Gibson, L., Roubenoff, R., Abad, L. W., Bean, J., Goodyear, L. J., & Fielding, R. A. (1999). Eccentric exercise markedly increases c-Jun NH2 -terminal kinase activity in human skeletal muscle. *Journal of Applied Physiology*, **87**(5), 1668–1673.

Borges Junior, M., Tavares, L. F. J., Nagata, G. Y., Barroso, L. S. S., Fernandes, H. B., Souza-Gomes, A. F., Miranda, A. S., & Nunes-Silva, A. (2024). Impact of strength training intensity on brain-derived neurotrophic factor. *International Journal of Sports Medicine*, **45**, 155–161.

Bouguetoch, A., Martin, A., & Grosprêtre, S. (2021). Does partial activation of the neuromuscular system induce cross-education training effect? Case of a pilot study on motor imagery and neuromuscular electrical stimulation. *European Journal of Applied Physiology*, **121**(8), 2337–2348.

Braga, M., Bhasin, S., Jasuja, R., Pervin, S., & Singh, R. (2012). Testosterone inhibits transforming growth factor-β signaling during myogenic differentiation and proliferation of mouse satellite cells: Potential role of follistatin in mediating testosterone action. *Molecular and Cellular Endocrinology*, **350**(1), 39–52.

Braith, R. W., & Stewart, K. J. (2006). Resistance exercise training: Its role in the prevention of cardiovascular disease. *Circulation*, **113**(22), 2642–2650.

Brooks, B. P., Merry, D. E., Paulson, H. L., Lieberman, A. P., Kolson, D. L., & Fischbeck, K. H. (1998). A cell culture model for androgen effects in motor neurons. *Journal of Neurochemistry*, **70**(3), 1054–1060.

Buono, R., Vantaggiato, C., Pisa, V., Azzoni, E., Bassi, M. T., Brunelli, S., Sciorati, C., & Clementi, E. (2012). Nitric oxide sustains long-term skeletal muscle regeneration by regulating fate of satellite cells via signaling pathways requiring Vangl2 and cyclic GMP. *Stem Cells*, **30**(2), 197–209.

Burke, D., Gandevia, S. C., & McKeon, B. (1984). Monosynaptic and oligosynaptic contributions to human ankle jerk and H-reflex. *Journal of Neurophysiology*, **52**(3), 435–448.

Cairns, S. P., & Borrani, F. (2015). β-adrenergic modulation of skeletal muscle contraction: Key role of excitation–contraction coupling. *The Journal of Physiology*, **593**(21), 4713–4727.

Calvert, G. H. M., & Carson, R. G. (2022). Neural mechanisms mediating cross education: With additional considerations for the ageing brain. *Neuroscience and Biobehavioral Reviews*, **132**, 260–288.

Calvin, W. H., & Stevens, C. F. (1968). Synaptic noise and other sources of randomness in motoneuron interspike intervals. *Journal of Neurophysiology*, **31**(4), 574–587.

Cantó, C., & Auwerx, J. (2009). PGC-1α, SIRT1 and AMPK, an energy sensing network that controls energy expenditure. *Current Opinion in Lipidology*, **20**, 98–105.

Cantrell, A. R., & Catterall, W. A. (2001). Neuromodulation of Na+ channels: An unexpected form of cellular platicity. *Nature Reviews Neuroscience*, **2**(6), 397–407.

Carlson, C. J., Fan, Z., Gordon, S. E., & Booth, F. W. (2001). Time course of the MAPK and PI3-kinase response within 24 h of skeletal muscle overload. *Journal of Applied Physiology*, **91**(5), 2079–2087.

Carro, E., Trejo, J. L., Gerber, A., Loetscher, H., Torrado, J., Metzger, F., & Torres-Aleman, I. (2006). Therapeutic actions of insulin-like growth factor I on APP/PS2 mice with severe brain amyloidosis. *Neurobiology of Aging*, **27**(9), 1250–1257.

Carroll, T. J., Barton, J., Hsu, M., & Lee, M. (2009). The effect of strength training on the force of twitches evoked by corticospinal stimulation in humans. *Acta Physiologica*, **197**(2), 161–173.

Carroll, T. J., Riek, S., & Carson, R. G. (2002). The sites of neural adaptation induced by resistance training in humans. *The Journal of Physiology*, **544**(2), 641–652.

Carson, R. G. (2005). Neural pathways mediating bilateral interactions between the upper limbs. *Brain Research Reviews*, **49**(3), 641–662.

Carson, R. G. (2020). Inter-hemispheric inhibition sculpts the output of neural circuits by co-opting the two cerebral hemispheres. *The Journal of Physiology*, **598**(21), 4781–4802.

Casolo, A., del Vecchio, A., Balshaw, T. G., Maeo, S., Lanza, M. B., Felici, F., Folland, J. P., & Farina, D. (2021). Behavior of motor units during submaximal isometric contractions in chronically strength-trained individuals. *Journal of Applied Physiology*, **131**(5), 1584–1598.

Castets, P., Ham, D. J., & Rüegg, M. A. (2020). The TOR pathway at the neuromuscular junction: More than a metabolic player? *Frontiers in Molecular Neuroscience*, **13**, 162.

Castronovo, A. M., Mrachacz-Kersting, N., Stevenson, A. J. T., Holobar, A., Enoka, R. M., & Farina, D. (2018). Decrease in force steadiness with aging is associated with increased power of the common but not independent input to motor neurons. *Journal of Neurophysiology*, **120**(4), 1616–1624.

Charbonnier, F., Gaspera, B. D., Armand, A.-S., Lécolle, S., Launay, T., Gallien, C.-L., & Chanoine, C. (2003). Specific activation of the acetylcholine receptor subunit genes by MyoD family proteins. *Journal of Biological Chemistry*, **278**(35), 33169–33174.

Chattopadhyay, S., & Shubayev, V. I. (2009). MMP-9 controls Schwann cell proliferation and phenotypic remodeling via IGF-1 and ErbB receptor-mediated activation of MEK/ERK pathway. *Glia*, **57**(12), 1316–1325.

Chen, K., & Dai, Y. (2022). Chronic exercise increases excitability of lamina X neurons through enhancement of persistent inward currents and dendritic development in mice. *The Journal of Physiology*, **600**(16), 3775–3793.

Cheng, F., Li, N., Yang, J., Yang, J., Yang, W., Ran, J., Sun, P., & Liao, Y. (2024). The effect of resistance training on patients with secondary sarcopenia: A systematic review and meta-analysis. *Scientific Reports*, **14**(1), 28784.

Chin, E. R. (2005). Role of Ca2+/calmodulin-dependent kinases in skeletal muscle plasticity. *Journal of Applied Physiology*, **99**(2), 414–423.

Chodzko-Zajko, W. J., Proctor, D. N., Fiatarone Singh, M. A., Minson, C. T., Nigg, C. R., Salem, G. J., & Skinner, J. S. (2009). Exercise and physical activity for older adults. *Medicine and Science in Sports and Exercise*, **41**(7), 1510–1530.

Christie, A., & Kamen, G. (2010). Short-term training adaptations in maximal motor unit firing rates and after-hyperpolarization duration. *Muscle & Nerve*, **41**(5), 651–660.

Christie, A., & Kamen, G. (2014). Cortical inhibition is reduced following short-term training in young and older adults. *AGE*, **36**(2), 749–758.

Colomer-Poveda, D., Hortobágyi, T., Keller, M., Romero-Arenas, S., & Márquez, G. (2020). Training intensity-dependent increases in corticospinal but not intracortical excitability after acute strength training. *Scandinavian Journal of Medicine & Science in Sports*, **30**(4), 652–661.

Cormery, B., Beaumont, E., Csukly, K., & Gardiner, P. (2005). Hindlimb unweighting for 2 weeks alters physiological properties of rat hindlimb motoneurones. *The Journal of Physiology*, **568**(3), 841–850.

Coxon, J. P., Cash, R. F. H., Hendrikse, J. J., Rogasch, N. C., Stavrinos, E., Suo, C., & Yücel, M. (2018). GABA concentration in sensorimotor cortex following high-intensity exercise and relationship to lactate levels. *The Journal of Physiology*, **596**(4), 691–702.

Crossland, H., Kazi, A. A., Lang, C. H., Timmons, J. A., Pierre, P., Wilkinson, D. J., Smith, K., Szewczyk, N. J., & Atherton, P. J. (2013). Focal adhesion kinase is required for IGF-I-mediated growth of skeletal muscle cells via a TSC2/mTOR/S6K1-associated pathway. *American Journal of Physiology-Endocrinology and Metabolism*, **305**(2), E183–E193.

Currier, B. S., Mcleod, J. C., Banfield, L., Beyene, J., Welton, N. J., D'Souza, A. C., Keogh, J. A. J., Lin, L., Coletta, G., Yang, A., Colenso-Semple, L., Lau, K. J., Verboom, A., & Phillips, S. M. (2023). Resistance training prescription for muscle strength and hypertrophy in healthy adults: A systematic review and bayesian network meta-analysis. *British Journal of Sports Medicine*, **57**(18), 1211–1220.

Dai, Y., Cheng, Y., Ge, R., Chen, K., & Yang, L. (2024). Exercise-induced adaptation of neurons in the vertebrate locomotor system. *Journal of Sport and Health Science*, **13**(2), 160–171.

Dai, Y., Jones, K. E., Fedirchuk, B., McCrea, D. A., & Jordan, L. M. (2002). A modelling study of locomotion-induced hyperpolarization of voltage threshold in cat lumbar motoneurones. *The Journal of Physiology*, **544**(2), 521–536.

Dalbo, V. J., & Roberts, M. D. (2015). The activity of satellite cells and myonuclei during 8 weeks of strength training in young men with suppressed testosterone. *Acta Physiologica*, **213**(3), 556–558.

Damas, F., Phillips, S. M., Lixandrão, M. E., Vechin, F. C., Libardi, C. A., Roschel, H., Tricoli, V., & Ugrinowitsch, C. (2016). Early resistance training-induced increases in muscle cross-sectional area are concomitant with edema-induced muscle swelling. *European Journal of Applied Physiology*, **116**(1), 49–56.

D'Antona, G. (2003). The effect of ageing and immobilization on structure and function of human skeletal muscle fibres. *The Journal of Physiology*, **552**, 499–511.

Davey, R. A., Clarke, M. V., Russell, P. K., Rana, K., Seto, J., Roeszler, K. N., How, J. M. Y., Chia, L. Y., North, K., & Zajac, J. D. (2017). Androgen action via the Androgen receptor in neurons within the brain positively regulates muscle mass in male mice. *Endocrinology*, **158**(10), 3684–3695.

de Luccia, T. P. B. (2016). Use of the testosterone/cortisol ratio variable in sports. *Open Sports Sciences Journal*, **9**(1), 104–113.

de Oliveira, F. B. D., Rizatto, G. F., & Denadai, B. S. (2013). Are early and late rate of force development differently influenced by fast-velocity resistance training? *Clinical Physiology and Functional Imaging*, **33**(4), 282–287.

Dekhuijzen, P. N., Gayan-Ramirez, G., Bisschop, A., De Bock, V., Dom, R., & Decramer, M. (1995). Corticosteroid treatment and nutritional deprivation cause a different pattern of atrophy in rat diaphragm. *Journal of Applied Physiology*, **78**(2), 629–637.

del Vecchio, A., Casolo, A., Dideriksen, J. L., Aagaard, P., Felici, F., Falla, D., & Farina, D. (2022). Lack of increased rate of force development after strength training is explained by specific neural, not muscular, motor unit adaptations. *Journal of Applied Physiology*, **132**(1), 84–94.

del Vecchio, A., Casolo, A., Negro, F., Scorcelletti, M., Bazzucchi, I., Enoka, R., Felici, F., & Farina, D. (2019). The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding. *The Journal of Physiology*, **597**, 1873–1887.

del Vecchio, A., Enoka, R. M., & Farina, D. (2024). Specificity of early motor unit adaptations with resistive exercise training. *The Journal of Physiology*, **602**, 2679–2688.

del Vecchio, A., Holobar, A., Falla, D., Felici, F., Enoka, R. M., & Farina, D. (2020). Tutorial: Analysis of motor unit discharge characteristics from high-density surface EMG signals. *Journal of Electromyography and Kinesiology*, **53**, 102426.

del Vecchio, A., Negro, F., Falla, D., Bazzucchi, I., Farina, D., & Felici, F. (2018). Higher muscle fiber conduction velocity and early rate of torque development in chronically strength-trained individuals. *Journal of Applied Physiology*, **125**, 1218–1226.

del Vecchio, A., Negro, F., Holobar, A., Casolo, A., Folland, J. P., Felici, F., & Farina, D. (2019). You are as fast as your motor neurons: Speed of recruitment and maximal discharge of motor neurons determine the maximal rate of force development in humans. *The Journal of Physiology*, **597**, 2445–2456.

Delaney, C. L., Russell, J. W., Cheng, H.-L., & Feldman, E. L. (2001). Insulin-like growth factor-I and over-expression of bcl-xL prevent glucose-mediated apoptosis in Schwann cells. *Journal of Neuropathology and Experimental Neurology*, **60**(2), 147–160.

Deldicque, L., Atherton, P., Patel, R., Theisen, D., Nielens, H., Rennie, M. J., & Francaux, M. (2008). Decrease in akt/PKB signalling in human skeletal muscle by resistance exercise. *European Journal of Applied Physiology*, **104**(1), 57–65.

Dent, J. R., Fletcher, D. K., & McGuigan, M. R. (2012). Evidence for a non-genomic action of testosterone in skeletal muscle which may improve athletic performance: Implications for the female athlete. *Journal of Sports Science and Medicine*, **11**, 363–370.

Deschenes, M. R. (2019). Adaptations of the neuromuscular junction to exercise training. *Current Opinion in Physiology*, **10**, 10–16.

Deschenes, M. R., Judelson, D. A., Kraemer, W. J., Meskaitis, V. J., Volek, J. S., Nindl, B. C., Harman, F. S., & Deaver, D. R. (2000). Effects of resistance training on neuromuscular junction morphology. *Muscle & Nerve*, **23**(10), 1576–1581.

Di Lazzaro, V., Oliviero, A., Profice, P., Saturno, E., Pilato, F., Insola, A., Mazzone, P., Tonali, P., & Rothwell, J. C. (1998). Comparison of descending volleys evoked bytranscranial magnetic and electric stimulation in conscious humans. *Electroencephalography and Clinical Neurophysiology Motor Control*, **109**, 397–401.

Dideriksen, J., & del Vecchio, A. (2023). Adaptations in motor unit properties underlying changes in recruitment, rate coding, and maximum force. *Journal of Neurophysiology*, **129**(1), 235–246.

Dideriksen, J. L., Negro, F., Enoka, R. M., & Farina, D. (2012). Motor unit recruitment strategies and muscle properties determine the influence of synaptic noise on force steadiness. *Journal of Neurophysiology*, **107**(12), 3357–3369.

Ding, Q., Vaynman, S., Akhavan, M., Ying, Z., & Gomez-Pinilla, F. (2006). Insulin-like growth factor I interfaces with brain-derived neurotrophic factor-mediated synaptic plasticity to modulate aspects of exercise-induced cognitive function. *Neuroscience*, **140**(3), 823–833.

Dreyer, H. C., Fujita, S., Cadenas, J. G., Chinkes, D. L., Volpi, E., & Rasmussen, B. B. (2006). Resistance exercise increases AMPK activity and reduces 4E-BP1 phosphorylation and protein synthesis in human skeletal muscle. *The Journal of Physiology*, **576**(2), 613–624.

Dubois, V., Laurent, M., Boonen, S., Vanderschueren, D., & Claessens, F. (2012). Androgens and skeletal muscle: Cellular and molecular action mechanisms underlying the anabolic actions. *Cellular and Molecular Life Sciences*, **69**(10), 1651–1667.

Dubois, V., Laurent, M. R., Sinnesael, M., Cielen, N., Helsen, C., Clinckemalie, L., Spans, L., Gayan-Ramirez, G., Deldicque, L., Hespel, P., Carmeliet, G., Vanderschueren, D., & Claessens, F. (2014). A satellite cell-specific knockout of the androgen receptor reveals myostatin as a direct androgen target in skeletal muscle. *Federation of American Societies for Experimental Biology Journal*, **28**(7), 2979–2994.

Duclay, J., Martin, A., Robbe, A., & Pousson, M. (2008). Spinal reflex plasticity during maximal dynamic contractions after eccentric training. *Medicine and Science in Sports and Exercise*, **40**(4), 722–734.

Duclay, J., Pasquet, B., Martin, A., & Duchateau, J. (2011). Specific modulation of corticospinal and spinal excitabilities during maximal voluntary isometric, shortening and lengthening contractions in synergist muscles. *The Journal of Physiology*, **589**(11), 2901–2916.

Dunlop, E. A., Dodd, K. M., Seymour, L. A., & Tee, A. R. (2009). Mammalian target of rapamycin complex 1-mediated phosphorylation of eukaryotic initiation factor 4E-binding protein 1 requires multiple protein–protein interactions for substrate recognition. *Cellular Signalling*, **21**(7), 1073–1084.

Eisner, D., Neher, E., Taschenberger, H., & Smith, G. (2023). Physiology of intracellular calcium buffering. *Physiological Reviews*, **103**(4), 2767–2845.

Englund, D. A., Peck, B. D., Murach, K. A., Neal, A. C., Caldwell, H. A., McCarthy, J. J., Peterson, C. A., & Dupont-Versteegden, E. E. (2019). Resident muscle stem cells are not required for testosterone-induced skeletal muscle hypertrophy. *American Journal of Physiology-Cell Physiology*, **317**(4), C719–C724.

Enoka, R. M. (1996). Eccentric contractions require unique activation strategies by the nervous system. *Journal of Applied Physiology*, **81**(6), 2339–2346.

Enoka, R. M., & Farina, D. (2021). Force steadiness: From motor units to voluntary actions. *Physiology*, **36**(2), 114–130.

Ermentrout, G. B., Galán, R. F., & Urban, N. N. (2008). Reliability, synchrony and noise. *Trends in Neuroscience (Tins)*, **31**(8), 428–434.

Evans, W., Willey, Q., Hanson, E. D., & Stoner, L. (2018). Effects of resistance training on arterial stiffness in persons at risk for cardiovascular disease: A meta-analysis. *Sports Medicine (Auckland, NZ)*, **48**(12), 2785–2795.

Faisal, A. A., Selen, L. P. J., & Wolpert, D. M. (2008). Noise in the nervous system. *Nature Reviews Neuroscience*, **9**(4), 292–303.

Falvo, M. J., Sirevaag, E. J., Rohrbaugh, J. W., & Earhart, G. M. (2010). Resistance training induces supraspinal adaptations: Evidence from movement-related cortical potentials. *European Journal of Applied Physiology*, **109**(5), 923–933.

Farina, D., & Negro, F. (2015). Common synaptic input to motor neurons, motor unit synchronization, and force control. *Exercise and Sport Sciences Reviews*, **43**(1), 23–33.

Farmer, J., Zhao, X., Van Praag, H., Wodtke, K., Gage, F. H., & Christie, B. R. (2004). Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult male sprague–dawley rats in vivo. *Neuroscience*, **124**(1), 71–79.

Fernández-García, S., Sancho-Balsells, A., Longueville, S., Hervé, D., Gruart, A., Delgado-García, J. M., Alberch, J., & Giralt, A. (2020). Astrocytic BDNF and TrkB regulate severity and neuronal activity in mouse models of temporal lobe epilepsy. *Cell Death & Disease*, **11**(6), 411.

Ferretti, G., Narici, M. V., Binzoni, T., Gariod, L., Le Bas, J. F., Reutenauer, H., & Cerretelli, P. (1994). Determinants of peak muscle power: Effects of age and physical conditioning. *European Journal of Applied Physiology*, **68**(2), 111–115.

Fimland, M. S., Helgerud, J., Gruber, M., Leivseth, G., & Hoff, J. (2009). Functional maximal strength training induces neural transfer to single-joint tasks. *European Journal of Applied Physiology*, **107**(1), 21–29.

Fimland, M. S., Helgerud, J., Solstad, G. M., Iversen, V. M., Leivseth, G., & Hoff, J. (2009). Neural adaptations underlying cross-education after unilateral strength training. *European Journal of Applied Physiology*, **107**(6), 723–730.

Florini, J. R., Ewton, D. Z., & Coolican, S. A. (1996). Growth hormone and the insulin-like Growth factor system in myogenesis. *Endocrine Reviews*, **17**, 481–517.

Folland, J. P., Buckthorpe, M. W., & Hannah, R. (2014). Human capacity for explosive force production: Neural and contractile determinants. *Scandinavian Journal of Medicine & Science in Sports*, **24**(6), 894–906.

Folland, J. P., & Williams, A. G. (2007). The adaptations to strength training: Morphological and neurological contributions to increased strength. *Sports Medicine (Auckland, NZ)*, **37**(2), 145–168.

Franchi, M. V., Reeves, N. D., & Narici, M. V. (2017). Skeletal muscle remodeling in response to eccentric vs. Concentric loading: Morphological, molecular, and metabolic adaptations. *Frontiers in Physiology*, **8**, 447.

Frater, J., Lie, D., Bartlett, P., & McGrath, J. J. (2018). Insulin-like growth factor 1 (IGF-1) as a marker of cognitive decline in normal ageing: A review. *Ageing Research Reviews*, **42**, 14–27.

Frazer, A. K., Williams, J., Spittle, M., & Kidgell, D. J. (2017). Cross-education of muscular strength is facilitated by homeostatic plasticity. *European Journal of Applied Physiology*, **117**(4), 665–677.

Frost, D. M., Bronson, S., Cronin, J. B., & Newton, R. U. (2016). Changes in maximal strength, velocity, and power after 8 weeks of training with pneumatic or free weight resistance. *Journal of Strength and Conditioning Research*, **30**(4), 934–944.

Fueger, P. T., Li, C. Y., Ayala, J. E., Shearer, J., Bracy, D. P., Charron, M. J., Rottman, J. N., & Wasserman, D. H. (2007). Glucose kinetics and exercise tolerance in mice lacking the GLUT4 glucose transporter. *The Journal of Physiology*, **582**(2), 801–812.

Gabriel, D. A., Kamen, G., & Frost, G. (2006). Neural adaptations to resistive exercise: Mechanisms and recommendations for training practices. *Sports Medicine (Auckland, NZ)*, **36**(2), 133–149.

Garcia, D., & Shaw, R. J. (2017). AMPK: Mechanisms of cellular energy sensing and restoration of metabolic balance. *Molecular Cell*, **66**(6), 789–800.

Gardiner, P., Beaumont, E., & Cormery, B. (2005). Motoneurones "learn" and "forget" physical activity. *Canadian Journal of Applied Physiology*, **30**(3), 352–370.

Gardiner, P., Dai, Y., & Heckman, C. J. (2006). Effects of exercise training on α-motoneurons. *Journal of Applied Physiology*, **101**(4), 1228–1236.

Ge, L., Liu, S., Rubin, L., Lazarovici, P., & Zheng, W. (2022). Research progress on neuroprotection of insulin-like growth factor-1 towards glutamate-induced neurotoxicity. *Cells*, **11**(4), 666.

Ge, R., & Dai, Y. (2020). Three-week treadmill exercise enhances persistent inward currents, facilitates dendritic plasticity, and upregulates the excitability of dorsal raphe serotonin neurons in ePet-EYFP mice. *Frontiers in Cellular Neuroscience*, **14**, 575626.

Geertsen, S. S., Lundbye-Jensen, J., & Nielsen, J. B. (2008). Increased central facilitation of antagonist reciprocal inhibition at the onset of dorsiflexion following explosive strength training. *Journal of Applied Physiology*, **105**(3), 915–922.

Glass, D. J. (2010). PI3 Kinase regulation of skeletal muscle hypertrophy and atrophy. In C. Rommel, B. Vanhaesebroeck, & P. K. Vogt (Eds), *Phosphoinositide 3-kinase in Health and Disease*, Current Topics in Microbiology and Immunology (pp. 267–278). Springer Berlin Heidelberg, Berlin, Heidelberg. Available at: http://link.springer.com/10.1007/82_2010_78 (Accessed June 25, 2025).

Glover, I. S., & Baker, S. N. (2020). Cortical, corticospinal, and reticulospinal contributions to strength training. *Journal of Neuroscience*, **40**(30), 5820–5832.

Gómez-Feria, J., Martín-Rodríguez, J. F., & Mir, P. (2023). Corticospinal adaptations following resistance training and its relationship with strength: A systematic review and multivariate meta-analysis. *Neuroscience and Biobehavioral Reviews*, **152**, 105289.

Gómez-Palacio-Schjetnan, A., & Escobar, M. L. (2013). Neurotrophins and synaptic plasticity. In C. Belzung, P. Wigmore, & Current Topics in Behavioral Neurosciences (Eds), *Neurogenesis and Neural Plasticity* (pp. 117–136). Springer Berlin Heidelberg, Berlin, Heidelberg. Available at: http://link.springer.com/10.1007/7854_2012_231 (Accessed June 10, 2025).

Gonzalez de La Vega, A., Buño, W., Pons, S., Garcia-Calderat, M. S., Garcia-Galloway, E., & Torres-Aleman, I. (2001). Insulin-like growth factor I potentiates kainate receptors through a phosphatidylinositol 3-kinase dependent pathway. *Neuroreport*, **12**(6), 1293–1296.

González-Badillo, J. J., Rodríguez-Rosell, D., Sánchez-Medina, L., Gorostiaga, E. M., & Pareja-Blanco, F. (2014). Maximal intended velocity training induces greater gains in bench press performance than deliberately slower half-velocity training. *European Journal of Sport Science*, **14**(8), 772–781.

Goodman, C. A. (2019). Role of mTORC1 in mechanically induced increases in translation and skeletal muscle mass. *Journal of Applied Physiology*, **127**(2), 581–590.

Goodwill, A. M., Pearce, A. J., & Kidgell, D. J. (2012). Cortico-motor plasticity following unilateral strength training. *Muscle & Nerve*, **46**(3), 384–393.

Gorassini, M. A., Bennett, D. J., & Yang, J. F. (1998). Self-sustained firing of human motor units. *Neuroscience Letters*, **247**(1), 13–16.

Grau, J. W., Hudson, K. E., Johnston, D. T., & Partipilo, S. R. (2024). Updating perspectives on spinal cord function: Motor coordination, timing, relational processing, and memory below the brain. *Frontiers in Systems Neuroscience*, **18**, 1184597.

Green, L. A., & Gabriel, D. A. (2018). The cross education of strength and skill following unilateral strength training in the upper and lower limbs. *Journal of Neurophysiology*, **120**(2), 468–479.

Grgic, J., Schoenfeld, B. J., Orazem, J., & Sabol, F. (2022). Effects of resistance training performed to repetition failure or non-failure on muscular strength and hypertrophy: A systematic review and meta-analysis. *Journal of Sport and Health Science*, **11**(2), 202–211.

Griffin, L., & Cafarelli, E. (2007). Transcranial magnetic stimulation during resistance training of the tibialis anterior muscle. *Journal of Electromyography and Kinesiology*, **17**(4), 446–452.

Groennebaek, T., & Vissing, K. (2017). Impact of resistance training on skeletal muscle mitochondrial biogenesis, content, and function. *Frontiers in Physiology*, **8**, 713.

Guezennec, Y., Leger, L., Lhoste, F., Aymonod, M., & Pesquies, P. (1986). Hormone and metabolite response to weight-lifting training sessions. *International Journal of Sports Medicine*, **07**(02), 100–105.

Guizelini, P. C., De Aguiar, R. A., Denadai, B. S., Caputo, F., & Greco, C. C. (2018). Effect of resistance training on muscle strength and rate of force development in healthy older adults: A systematic review and meta-analysis. *Experimental Gerontology*, **102**, 51–58.

Gustafsson, T., Puntschart, A., Kaijser, L., Jansson, E., & Sundberg, C. J. (1999). Exercise-induced expression of angiogenesis-related transcription and growth factors in human skeletal muscle. *American Journal of Physiology-Heart and Circulatory Physiology*, **276**(2), H679–H685.

Gwinn, D. M., Shackelford, D. B., Egan, D. F., Mihaylova, M. M., Mery, A., Vasquez, D. S., Turk, B. E., & Shaw, R. J. (2008). AMPK phosphorylation of Raptor mediates a metabolic checkpoint. *Molecular Cell*, **30**(2), 214–226.

Haddad, F., & Adams, G. R. (2004). Inhibition of MAP/ERK kinase prevents IGF-I-induced hypertrophy in rat muscles. *Journal of Applied Physiology*, **96**(1), 203–210.

Haff, G. G., & Nimphius, S. (2012). Training principles for power. *Strength & Conditioning Journal*, **34**(6), 2–12.

Häkkinen, K., Kraemer, W. J., Newton, R. U., & Alen, M. (2001). Changes in electromyographic activity, muscle fibre and force production characteristics during heavy resistance/power strength training in middle-aged and older men and women. *Acta Physiologica Scandinavica*, **171**, 51–62.

Hakkinen, K., & Pakarinen, A. (1993). Acute hormonal responses to two different fatiguing heavy-resistance protocols in male athletes. *Journal of Applied Physiology*, **74**(2), 882–887.

Häkkukinen, K., Komi, P. V., & Alén, M. (1985). Effect of explosive type strength training on isometric force- and relaxation-time, electromyographic and muscle fibre characteristics of leg extensor muscles. *Acta Physiologica Scandinavica*, **125**(4), 587–600.

Halling, J. F., & Pilegaard, H. (2020). PGC-1α-mediated regulation of mitochondrial function and physiological implications. *Applied Physiology, Nutrition and Metabolism*, **45**(9), 927–936.

Hamdi, M. M., & Mutungi, G. (2010). Dihydrotestosterone activates the MAPK pathway and modulates maximum isometric force through the EGF receptor in isolated intact mouse skeletal muscle fibres. *The Journal of Physiology*, **588**(3), 511–525.

Hameed, M., Orrell, R. W., Cobbold, M., Goldspink, G., & Harridge, S. D. R. (2003). Expression of IGF-I splice variants in young and old human skeletal muscle after high resistance exercise. *The Journal of Physiology*, **547**(1), 247–254.

Han, X., Møller, L. L. V., De Groote, E., Bojsen-Møller, K. N., Davey, J., Henríquez-Olguin, C., Li, Z., Knudsen, J. R., Jensen, T. E., Madsbad, S., Gregorevic, P., Richter, E. A., & Sylow, L. (2019). Mechanisms involved in follistatin-induced hypertrophy and increased insulin action in skeletal muscle. *Journal of Cachexia, Sarcopenia and Muscle*, **10**(6), 1241–1257.

Handelsman, D. J., Hirschberg, A. L., & Bermon, S. (2018). Circulating testosterone as the hormonal basis of sex differences in athletic performance. *Endocrine Reviews*, **39**(5), 803–829.

Hardie, D. G. (2011). AMP-activated protein kinase—An Energy sensor that regulates all aspects of cell function. *Genes & Development*, **25**(18), 1895–1908.

Heckman, C. J. (1994). Computer simulations of the effects of different synaptic input systems on the steady-state input-output structure of the motoneuron pool. *Journal of Neurophysiology*, **71**(5), 1727–1739.

Heckman, C. J., Johnson, M., Mottram, C., & Schuster, J. (2008). Persistent inward currents in spinal motoneurons and their influence on Human motoneuron firing patterns. *The Neuroscientist*, **14**(3), 264–275.

Heckman, C. J., Lee, R. H., & Brownstone, R. M. (2003). Hyperexcitable dendrites in motoneurons and their neuromodulatory control during motor behavior. *Trends in Neuroscience (Tins)*, **26**(12), 688–695.

Heckman, C. J., Mottram, C., Quinlan, K., Theiss, R., & Schuster, J. (2009). Motoneuron excitability: The importance of neuromodulatory inputs. *Clinical Neurophysiology*, **120**(12), 2040–2054.

Hendy, A. M., & Lamon, S. (2017). The cross-education phenomenon: Brain and beyond. *Frontiers in Physiology*, **8**, 297.

Hernández-Hernández, J. M., García-González, E. G., Brun, C. E., & Rudnicki, M. A. (2017). The myogenic regulatory factors, determinants of muscle development, cell identity and regeneration. *Seminars in Cell & Developmental Biology*, **72**, 10–18.

Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, **117**(4), 500–544.

Hornberger, T. A., Chu, W. K., Mak, Y. W., Hsiung, J. W., Huang, S. A., & Chien, S. (2006). The role of phospholipase D and phosphatidic acid in the mechanical activation of mTOR signaling in skeletal muscle. *Proceedings of the National Academy of Sciences of the United States of America*, **103**(12), 4741–4746.

Howatson, G., Zult, T., Farthing, J. P., Zijdewind, I., & Hortobágyi, T. (2013). Mirror training to augment cross-education during resistance training: A hypothesis. *Frontiers in Human Neuroscience*, **7**, 396.

Hubbard, J. I., Stenhouse, D., & Eccles, R. M. (1967). Origin of synaptic noise. *Science*, **157**(3786), 330–331.

Hug, F., Avrillon, S., Ibáñez, J., & Farina, D. (2023). Common synaptic input, synergies and size principle: Control of spinal motor neurons for movement generation. *The Journal of Physiology*, **601**(1), 11–20.

Hughes, D. C., Ellefsen, S., & Baar, K. (2018). Adaptations to endurance and strength training. *Cold Spring Harbor Perspectives in Medicine*, **8**(6), a029769.

Hultborn, H., & Pierrot-Deseilligny, E. (1979). Changes in recurrent inhibition during voluntary soleus contractions in man studied by an H-reflex technique. *The Journal of Physiology*, **297**(0), 229–251.

Hunter, S. K. (2014). Sex differences in human fatigability: Mechanisms and insight to physiological responses. *Acta Physiologica*, **210**(4), 768–789.

Hunter, S. K., & Senefeld, J. W. (2024). Sex differences in human performance. *The Journal of Physiology*, **602**(17), 4129–4156.

Hyer, M. M., Phillips, L. L., & Neigh, G. N. (2018). Sex differences in synaptic plasticity: Hormones and beyond. *Frontiers in Molecular Neuroscience*, **11**, 266.

Hyngstrom, A. S., Johnson, M. D., Miller, J. F., & Heckman, C. J. (2007). Intrinsic electrical properties of spinal motoneurons vary with joint angle. *Nature Neuroscience*, **10**(3), 363–369.

Impey, S., Obrietan, K., & Storm, D. R. (1999). Making new connections. *Neuron*, **23**, 11–14.

Inoki, K., Zhu, T., & Guan, K.-L. (2003). TSC2 mediates cellular energy response to control cell growth and survival. *Cell*, **115**(5), 577–590.

Jacobs, B. L., McNally, R. M., Kim, K.-J., Blanco, R., Privett, R. E., You, J.-S., & Hornberger, T. A. (2017). Identification of mechanically regulated phosphorylation sites on tuberin (TSC2) that control mechanistic target of rapamycin (mTOR) signaling. *Journal of Biological Chemistry*, **292**(17), 6987–6997.

Jaiswal, N., Gavin, M., Loro, E., Sostre-Colón, J., Roberson, P. A., Uehara, K., Rivera-Fuentes, N., Neinast, M., Arany, Z., Kimball, S. R., Khurana, T. S., & Titchenell, P. M. (2022). AKT controls protein synthesis and oxidative metabolism via combined mTORC1 and FOXO1 signalling to govern muscle physiology. *Journal of Cachexia, Sarcopenia and Muscle*, **13**(1), 495–514.

Jami, L. (1992). Golgi tendon organs in mammalian skeletal muscle: Functional properties and central actions. *Physiological Reviews*, **72**(3), 623–666.

Ji, F., Lee, H. S., & Kim, J.-H. (2025). Resistance exercise and skeletal muscle: Protein synthesis, degradation, and controversies. *European Journal of Applied Physiology*, **125**(9), 2353–2382.

Jiang, Q., Lou, K., Hou, L., Lu, Y., Sun, L., Tan, S. C., Low, T. Y., Kord-Varkaneh, H., & Pang, S. (2020). The effect of resistance training on serum insulin-like growth factor 1(IGF-1): A systematic review and meta-analysis. *Complementary Therapies in Medicine*, **50**, 102360.

Johnson, M. D., Thompson, C. K., Tysseling, V. M., Powers, R. K., & Heckman, C. J. (2017). The potential for understanding the synaptic organization of human motor commands via the firing patterns of motoneurons. *Journal of Neurophysiology*, **118**(1), 520–531.

Jones, E. J., Chiou, S., Atherton, P. J., Phillips, B. E., & Piasecki, M. (2022). Ageing and exercise-induced motor unit remodelling. *The Journal of Physiology*, **600**(8), 1839–1849.

Jovanovic, J. N., Czernik, A. J., Fienberg, A. A., Greengard, P., & Sihra, T. S. (2000). Synapsins as mediators of BDNF-enhanced neurotransmitter release. *Nature Neuroscience*, **3**(4), 323–329.

Joyner, M. J., Hunter, S. K., & Senefeld, J. W. (2025). Evidence on sex differences in sports performance. *Journal of Applied Physiology*, **138**, 274–281.

Kapsis, D. P., Tsoukos, A., Psarraki, M. P., Douda, H. T., Smilios, I., & Bogdanis, G. C. (2022). Changes in body composition and strength after 12 weeks of high-intensity functional training with two different loads in physically active men and women: A randomized controlled study. *Sports*, **10**, 7.

Katz, R., & Pierrot-Deseilligny, E. (1999). Recurrent inhibition in humans. *Progress in Neurobiology*, **57**, 325–355.

Ke, R., Xu, Q., Li, C., Luo, L., & Huang, D. (2018). Mechanisms of AMPK in the maintenance of ATP balance during energy metabolism. *Cell Biology International*, **42**(4), 384–392.

Kida, H., Kawakami, R., Sakai, K., Otaku, H., Imamura, K., Han, T., Sakimoto, Y., & Mitsushima, D. (2023). Motor training promotes both synaptic and intrinsic plasticity of layer V pyramidal neurons in the primary motor cortex. *The Journal of Physiology*, **601**(2), 335–353.

Kidgell, D. J., Bonanno, D. R., Frazer, A. K., Howatson, G., & Pearce, A. J. (2017). Corticospinal responses following strength training: A systematic review and meta-analysis. *European Journal of Neuroscience*, **46**(11), 2648–2661.

Kidgell, D. J., & Pearce, A. J. (2010). Corticospinal properties following short-term strength training of an intrinsic hand muscle. *Human Movement Science*, **29**(5), 631–641.

Kidgell, D. J., Stokes, M. A., Castricum, T. J., & Pearce, A. J. (2010). Neurophysiological responses after short-term strength training of the biceps brachii muscle. *Journal of Strength and Conditioning Research*, **24**(11), 3123–3132.

Kido, K., Egawa, T., Fujiyoshi, H., Suzuki, H., Kawanaka, K., & Hayashi, T. (2021). AMPK is indispensable for overload-induced muscle glucose uptake and glycogenesis but dispensable for inducing hypertrophy in mice. *Federation of American Societies for Experimental Biology Journal*, **35**(4), e21459.

Kiehn, O. (2016). Decoding the organization of spinal circuits that control locomotion. *Nature Reviews Neuroscience*, **17**(4), 224–238.

Kim, E. H., Hassan, A. S., & Heckman, C. J. (2019). Changes in motor unit discharge patterns following strength training. *The Journal of Physiology*, **597**(14), 3509–3510.

Kim, J., & Kaang, B.-K. (2023). Cyclic AMP response element-binding protein (CREB) transcription factor in astrocytic synaptic communication. *Frontiers in Synaptic Neuroscience*, **14**, 1059918.

Kim, K., & Hayashi, Y. (2014). CaMKII: The Swiss army knife of synaptic plasticity. *The Journal of Physiology*, **592**(22), 4807–4808.

Kimura, R., & Matsuki, N. (2008). Protein kinase CK2 modulates synaptic plasticity by modification of synaptic NMDA receptors in the hippocampus. *The Journal of Physiology*, **586**(13), 3195–3206.

Knudsen, J. R., Steenberg, D. E., Hingst, J. R., Hodgson, L. R., Henriquez-Olguin, C., Li, Z., Kiens, B., Richter, E. A., Wojtaszewski, J. F. P., Verkade, P., & Jensen, T. E. (2020). Prior exercise in humans redistributes intramuscular GLUT4 and enhances insulin-stimulated sarcolemmal and endosomal GLUT4 translocation. *Molecular Metabolism*, **39**, 100998.

Koceja, D. M., Davison, E., & Robertson, C. T. (2004). Neuromuscular characteristics of endurance- and power-trained athletes. *Research Quarterly for Exercise and Sport*, **75**(1), 23–30.

Komiyama, N. H., Watabe, A. M., Carlisle, H. J., Porter, K., Charlesworth, P., Monti, J., Strathdee, D. J. C., O'Carroll, C. M., Martin, S. J., Morris, R. G. M., O'Dell, T. J., & Grant, S. G. N. (2002). SynGAP regulates ERK/MAPK signaling, synaptic plasticity, and learning in the complex with postsynaptic density 95 and NMDA receptor. *Journal of Neuroscience*, **22**(22), 9721–9732.

Kovacheva, E. L., Sinha Hikim, A. P., Shen, R., Sinha, I., & Sinha-Hikim, I. (2010). Testosterone supplementation reverses sarcopenia in aging through regulation of myostatin, c-Jun NH2-terminal kinase, notch, and akt signaling pathways. *Endocrinology*, **151**(2), 628–638.

Kozinc, Ž., Smajla, D., & Šarabon, N. (2022). The rate of force development scaling factor: A review of underlying factors, assessment methods and potential for practical applications. *European Journal of Applied Physiology*, **122**(4), 861–873.

Kraemer, W., Noble, B., Clark, M., & Culver, B. (1987). Physiologic responses to heavy-resistance exercise with very short rest periods. *International Journal of Sports Medicine*, **08**(04), 247–252.

Kraemer, W. J., Fleck, S. J., Dziados, J. E., Harman, E. A., Marchitelli, L. J., Gordon, S. E., Mello, R., Frykman, P. N., Koziris, L. P., & Triplett, N. T. (1993). Changes in hormonal concentrations after different heavy-resistance exercise protocols in women. *Journal of Applied Physiology*, **75**(2), 594–604.

Kraemer, W. J., Fleck, S. J., Maresh, C. M., Ratamess, N. A., Gordon, S. E., Goetz, K. L., Harman, E. A., Frykman, P. N., Volek, J. S., Mazzetti, S. A., Fry, A. C., Marchitelli, L. J., & Patton, J. F. (1999). Acute hormonal responses to a single bout of heavy resistance exercise in trained power lifters and untrained men. *Canadian Journal of Applied Physiology*, **24**(6), 524–537.

Kraemer, W. J., & Ratamess, N. A. (2004). Fundamentals of resistance training: Progression and exercise prescription: *Medicine and Science in Sports and Exercise*, **36**(4), 674–688.

Kraemer, W. J., & Ratamess, N. A. (2005). Hormonal responses and adaptations to resistance exercise and training. *Sports Medicine (Auckland, NZ)*, **35**(4), 339–361.

Kraemer, W. J., Ratamess, N. A., & French, D. N. (2002). Resistance training for health and performance. *Current Sports Medicine Reports*, **1**(3), 165–171.

Kraemer, W. J., Ratamess, N. A., Hymer, W. C., Nindl, B. C., & Fragala, M. S. (2020). Growth hormone(s), testosterone, insulin-like growth factors, and cortisol: Roles and integration for cellular development and growth with exercise. *Frontiers in Endocrinology*, **11**, 33.

Kraemer, W. J., Staron, R. S., Hagerman, F. C., Hikida, R. S., Fry, A. C., Gordon, S. E., Nindl, B. C., Gothshalk, L. A., Volek, J. S., Marx, J. O., Newton, R. U., & Häkkinen, K. (1998). The effects of short-term resistance training on endocrine function in men and women. *European Journal of Applied Physiology*, **78**(1), 69–76.

Kreher, J. B., & Schwartz, J. B. (2012). Overtraining syndrome: A practical guide. *Sports Health Multidiscip Approach*, **4**(2), 128–138.

Krutki, P., Hałuszka, A., Mrówczyński, W., Gardiner, P. F., & Celichowski, J. (2015). Adaptations of motoneuron properties to chronic compensatory muscle overload. *Journal of Neurophysiology*, **113**(7), 2769–2777.

Krutki, P., Mrówczyński, W., Bączyk, M., Łochyński, D., & Celichowski, J. (2017). Adaptations of motoneuron properties after weight-lifting training in rats. *Journal of Applied Physiology*, **123**(3), 664–673.

Kuipers, H., & Keizer, H. A. (1988). Overtraining in elite athletes: Review and directions for the future. *Sports Medicine (Auckland, NZ)*, **6**(2), 79–92.

Kumar, R., Coggan, A. R., & Ferreira, L. F. (2022). Nitric oxide and skeletal muscle contractile function. *Nitric Oxide*, **122–123**, 54–61.

Kuo, J. J., Lee, R. H., Johnson, M. D., Heckman, H. M., & Heckman, C. J. (2003). Active dendritic integration of inhibitory synaptic inputs in vivo. *Journal of Neurophysiology*, **90**(6), 3617–3624.

Kuwahara, N., Nicholson, K., Isaacs, L., & MacLusky, N. J. (2021). Androgen effects on neural plasticity. *Androgens: Clinical Research and Therapeutics*, **2**, 216–230.

Laflamme, O. D., Markin, S. N., Deska-Gauthier, D., Banks, R., Zhang, Y., Danner, S. M., & Akay, T. (2023). Distinct roles of spinal commissural interneurons in transmission of contralateral sensory information. *Current Biology*, **33**(16), 3452–3464.e4.

Laliberte, A. M., Goltash, S., Lalonde, N. R., & Bui, T. V. (2019). Propriospinal neurons: Essential elements of locomotor control in the intact and possibly the injured spinal cord. *Frontiers in Cellular Neuroscience*, **13**, 512.

Laplante, M., & Sabatini, D. M. (2012). mTOR signaling in growth control and disease. *Cell*, **149**(2), 274–293.

Latella, C., Kidgell, D. J., & Pearce, A. J. (2012). Reduction in corticospinal inhibition in the trained and untrained limb following unilateral leg strength training. *European Journal of Applied Physiology*, **112**(8), 3097–3107.

Latres, E., Amini, A. R., Amini, A. A., Griffiths, J., Martin, F. J., Wei, Y., Lin, H. C., Yancopoulos, G. D., & Glass, D. J. (2005). Insulin-like Growth Factor-1 (IGF-1) inversely regulates atrophy-induced genes via the phosphatidylinositol 3-Kinase/Akt/mammalian target of rapamycin (PI3K/Akt/mTOR) pathway. *Journal of Biological Chemistry*, **280**(4), 2737–2744.

Lau, C. G., Takeuchi, K., Rodenas-Ruano, A., Takayasu, Y., Murphy, J., Bennett, M. V. L., & Zukin, R. S. (2009). Regulation of NMDA receptor Ca2+ signalling and synaptic plasticity. *Biochemical Society Transactions*, **37**(6), 1369–1374.

Lecce, E., Amoruso, P., Del Vecchio, A., Casolo, A., Felici, F., Farina, D., & Bazzucchi, I. (2025). Neural determinants of the increase in muscle strength and force steadiness of the untrained limb following a 4 week unilateral training. *The Journal of Physiology*, **603**(12), 3605–3630.

Lecce, E., Bellini, A., Greco, G., Martire, F., Scotto di Palumbo, A., Sacchetti, M., & Bazzucchi, I. (2025). Physiological mechanisms of neuromuscular impairment in diabetes-related complications: Can physical exercise help prevent it? *The Journal of Physiology*. Advance Online Publication. https://doi.org/10.1113/JP287589

Lecce, E., Conti, A., del Vecchio, A., Felici, F., Scotto di Palumbo, A., Sacchetti, M., & Bazzucchi, I. (2025). Cross-education: Motor unit adaptations mediate the strength increase in non-trained muscles following 8 weeks of unilateral resistance training. *Frontiers in Physiology*, **15**, 1512309.

Lecce, E., Conti, A., Nuccio, S., Felici, F., & Bazzucchi, I. (2024). Characterising sex-related differences in lower- and higher-threshold motor unit behaviour through high-density surface electromyography. *Experimental Physiology*, **109**(8), 1317–1329.

Lecce, E., del Vecchio, A., Nuccio, S., Felici, F., & Bazzucchi, I. (2025). Higher dominant muscle strength is mediated by motor unit discharge rates and proportion of common synaptic inputs. *Scientific Reports*, **15**(1), 8269.

Lecce, E., Romagnoli, R., Frinolli, G., Felici, F., Piacentini, M. F., & Bazzucchi, I. (2024). Exerting force at the maximal speed drives the increase in power output in elite athletes after 4 weeks of resistance training. *European Journal of Applied Physiology*, **125**(2), 327–338.

Lecce, E., Romagnoli, R., Maffiuletti, N. A., Frinolli, G., Felici, F., Piacentini, M. F., & Bazzucchi, I. (2025). In the reign of velocity: Ballistic training enhances rapid force production in chronically strength-trained athletes. *International Journal of Sports Physiology and Performance*, **20**(11), 1481–1492.

Lee, D. Y., Kim, E., & Choi, M. H. (2015). Technical and clinical aspects of cortisol as a biochemical marker of chronic stress. *Biochemistry and Molecular Biology Report*, **48**(4), 209–216.

Lee, M., & Carroll, T. J. (2007). Cross education: Possible mechanisms for the contralateral effects of unilateral resistance training. *Sports Medicine (Auckland, NZ)*, **37**(1), 1–14.

Lee, M., Gandevia, S. C., & Carroll, T. J. (2009). Short-term strength training does not change cortical voluntary activation. *Medicine and Science in Sports and Exercise*, **41**(7), 1452–1460.

Lee, M., Hinder, M. R., Gandevia, S. C., & Carroll, T. J. (2010). The ipsilateral motor cortex contributes to cross-limb transfer of performance gains after ballistic motor practice. *The Journal of Physiology*, **588**(1), 201–212.

Lee, R. H., & Heckman, C. J. (1998). Bistability in spinal motoneurons in vivo: Systematic variations in persistent inward currents. *Journal of Neurophysiology*, **80**(2), 583–593.

Lee, S.-J., & McPherron, A. C. (2001). Regulation of myostatin activity and muscle growth. *Proceedings of the National Academy of Sciences of the United States of America*, **98**(16), 9306–9311.

Léger, B., Cartoni, R., Praz, M., Lamon, S., Dériaz, O., Crettenand, A., Gobelet, C., Rohmer, P., Konzelmann, M., Luthi, F., & Russell, A. P. (2006). Akt signalling through GSK-3β, mTOR and Foxo1 is involved in human skeletal muscle hypertrophy and atrophy. *The Journal of Physiology*, **576**, 923–933.

Leprivier, G., & Rotblat, B. (2020). How does mTOR sense glucose starvation? AMPK is the usual suspect. *Cell Death Discovery*, **6**(1), 27.

Lipton, J. O., & Sahin, M. (2014). The neurology of mTOR. *Neuron*, **84**(2), 275–291.

Lira, V. A., Benton, C. R., Yan, Z., & Bonen, A. (2010). PGC-1α regulation by exercise training and its influences on muscle function and insulin sensitivity. *American Journal of Physiology-Endocrinology and Metabolism*, **299**(2), E145–E161.

Lombardo, J., & Harrington, M. A. (2016). Nonreciprocal mechanisms in up- and downregulation of spinal motoneuron excitability by modulators of KCNQ/K_v 7 channels. *Journal of Neurophysiology*, **116**(5), 2114–2124.

Lonze, B. E., & Ginty, D. D. (2002). Function and regulation of CREB family transcription factors in the nervous system. *Neuron*, **35**(4), 605–623.

Losa-Reyna, J., Alcazar, J., Rodríguez-Gómez, I., Alfaro-Acha, A., Alegre, L. M., Rodríguez-Mañas, L., Ara, I., & García-García, F. J. (2020). Low relative mechanical power in older adults: An operational definition and algorithm for its application in the clinical setting. *Experimental Gerontology*, **142**, 111141.

Lulic-Kuryllo, T., & Inglis, J. G. (2022). Sex differences in motor unit behaviour: A review. *Journal of Electromyography and Kinesiology*, **66**, 102689.

Ma, H., Groth, R. D., Cohen, S. M., Emery, J. F., Li, B., Hoedt, E., Zhang, G., Neubert, T. A., & Tsien, R. W. (2014). γCaMKII shuttles Ca^{2+}/CaM to the nucleus to trigger CREB phosphorylation and gene expression. *Cell*, **159**(2), 281–294.

MacDonell, C. W., Power, K. E., Chopek, J. W., Gardiner, K. R., & Gardiner, P. F. (2015). Extensor motoneurone properties are altered immediately before and during fictive locomotion in the adult decerebrate rat. *The Journal of Physiology*, **593**(10), 2327–2342.

MacKrell, J. G., Yaden, B. C., Bullock, H., Chen, K., Shetler, P., Bryant, H. U., & Krishnan, V. (2015). Molecular targets of androgen signaling that characterize skeletal muscle recovery and regeneration. *Nuclear Recept Signal*, **13**(1), nrs.13005.

Maddock, R. J., Casazza, G. A., Buonocore, M. H., & Tanase, C. (2011). Vigorous exercise increases brain lactate and glx (glutamate+glutamine): A dynamic 1H-MRS study. *Neuroimage*, **57**(4), 1324–1330.

Maddock, R. J., Casazza, G. A., Fernandez, D. H., & Maddock, M. I. (2016). Acute modulation of cortical glutamate and GABA content by physical activity. *Journal of Neuroscience*, **36**(8), 2449–2457.

Maffiuletti, N. A., Aagaard, P., Blazevich, A. J., Folland, J., Tillin, N., & Duchateau, J. (2016). Rate of force development: Physiological and methodological considerations. *European Journal of Applied Physiology*, **116**(6), 1091–1116.

Makanae, Y., Ato, S., Kouzaki, K., Tamura, Y., & Nakazato, K. (2025). Acute high-intensity muscle contraction moderates AChR gene expression independent of rapamycin-sensitive mTORC1 pathway in rat skeletal muscle. *Experimental Physiology*, **110**(1), 127–146.

Makaruk, H., Starzak, M., Tarkowski, P., Sadowski, J., & Winchester, J. (2024). The effects of resistance training on sport-specific performance of elite athletes: A systematic review with meta-analysis. *Journal of Human Kinetics*, **91**, 135–155.

Manca, A., Hortobágyi, T., Rothwell, J., & Deriu, F. (2018). Neurophysiological adaptations in the untrained side in conjunction with cross-education of muscle strength: A systematic review and meta-analysis. *Journal of Applied Physiology*, **124**(6), 1502–1518.

Mangine, G. T., Ratamess, N. A., Hoffman, J. R., Faigenbaum, A. D., Kang, J., & Chilakos, A. (2008). The effects of combined ballistic and heavy resistance training on maximal lower- and upper-body strength in recreationally trained men. *Journal of Strength and Conditioning Research*, **22**(1), 132–139.

Marabita, M., Baraldo, M., Solagna, F., Ceelen, J. J. M., Sartori, R., Nolte, H., Nemazanyy, I., Pyronnet, S., Kruger, M., Pende, M., & Blaauw, B. (2016). S6K1 is required for increasing skeletal muscle force during hypertrophy. *Cell Reports*, **17**(2), 501–513.

Martin, S. J., & Morris, R. G. M. (2002). New life in an old idea: The synaptic plasticity and memory hypothesis revisited. *Hippocampus*, **12**(5), 609–636.

Martinez-Canton, M., Gallego-Selles, A., Gelabert-Rebato, M., Martin-Rincon, M., Pareja-Blanco, F., Rodriguez-Rosell, D., Morales-Alamo, D., Sanchis-Moysi, J., Dorado, C., Jose Gonzalez-Badillo, J., & Calbet, J. A. L. (2021). Role of CaMKII and sarcolipin in muscle adaptations to strength training with different levels of fatigue in the set. *Scandinavian Journal of Medicine & Science in Sports*, **31**(1), 91–103.

Martino, G., Valli, G., Sarto, F., Franchi, M. V., Narici, M. V., & de Vito, G. (2024). Neuromodulatory contribution to muscle force production after short-term unloading and active recovery. *Medicine and Science in Sports and Exercise*, **56**(9), 1830–1839.

Mascher, H., Tannerstedt, J., Brink-Elfegoun, T., Ekblom, B., Gustafsson, T., & Blomstrand, E. (2008). Repeated resistance exercise training induces different changes in mRNA expression of MAFbx and MuRF-1 in human skeletal muscle. *American Journal of Physiology-Endocrinology and Metabolism*, **294**(1), E43–E51.

Matheny, R. W., Nindl, B. C., & Adamo, M. L. (2010). Minireview: Mechano-growth factor: A putative product of IGF-I gene expression involved in tissue repair and regeneration. *Endocrinology*, **151**(3), 865–875.

Maugeri, G., D'Agata, V., Magrì, B., Roggio, F., Castorina, A., Ravalli, S., di Rosa, M., & Musumeci, G. (2021). Neuroprotective effects of physical activity via the adaptation of astrocytes. *Cells*, **10**(6), 1542.

Maxwell, D. J., & Soteropoulos, D. S. (2020). The mammalian spinal commissural system: Properties and functions. *Journal of Neurophysiology*, **123**(1), 4–21.

Mazzucchelli, C., Vantaggiato, C., Ciamei, A., Fasano, S., Pakhotin, P., Krezel, W., Welzl, H., Wolfer, D. P., Pagès, G., Valverde, O., Marowsky, A., Porrazzo, A., Orban, P. C., Maldonado, R., Ehrengruber, M. U., Cestari, V., Lipp, H. P., Chapman, P. F., Pouysségur, J., & Brambilla, R. (2002). Knockout of ERK1 MAP kinase enhances synaptic plasticity in the striatum and facilitates striatal-mediated learning and memory. *Neuron*, **34**(5), 807–820.

Mc Dermott, E. J., Balshaw, T. G., Brooke-Wavell, K., Maden-Wilkinson, T. M., & Folland, J. P. (2022). Fast and ballistic contractions involve greater neuromuscular power production in older adults during resistance exercise. *European Journal of Applied Physiology*, **122**(7), 1639–1655.

McBride, J. M., Kraemer, W. J., Triplett-McBride, T., & Sebastianelli, W. (1998). Effect of resistance exercise on free radical production. *Medicine and Science in Sports and Exercise*, **30**(1), 67–72.

Mccall, G. E., Byrnes, W. C., Fleck, S. J., Dickinson, A., & Kraemer, W. J. (1999). Acute and chronic hormonal responses to resistance training designed to promote muscle hypertrophy. *Canadian Journal of Applied Physiology*, **24**(1), 96–107.

McMahan, U. J., Horton, S. E., Werle, M. J., Honig, L. S., Kröger, S., Ruegg, M. A., & Escher, G. (1992). Agrin isoforms and their role in synaptogenesis. *Current Opinion in Cell Biology*, **4**(5), 869–874.

McNeil, C. J., Butler, J. E., Taylor, J. L., & Gandevia, S. C. (2013). Testing the excitability of human motoneurons. *Frontiers in Human Neuroscience*, **7**, 152.

Mesquita, R. N. O., Taylor, J. L., Heckman, C. J., Trajano, G. S., & Blazevich, A. J. (2024). Persistent inward currents in human motoneurons: Emerging evidence and future directions. *Journal of Neurophysiology*, **132**(4), 1278–1301.

Mesquita, R. N. O., Taylor, J. L., Trajano, G. S., Škarabot, J., Holobar, A., Gonçalves, B. A. M., & Blazevich, A. J. (2022). Effects of reciprocal inhibition and whole-body relaxation on persistent inward currents estimated by two different methods. *The Journal of Physiology*, **600**(11), 2765–2787.

Michels, G., & Hoppe, U. C. (2008). Rapid actions of androgens. *Frontiers in Neuroendocrinology*, **29**(2), 182–198.

Miller, K. J., Thaloor, D., Matteson, S., & Pavlath, G. K. (2000). Hepatocyte growth factor affects satellite cell activation and differentiation in regenerating skeletal muscle. *American Journal of Physiology-Cell Physiology*, **278**(1), C174–C181.

Mobley, C. B., Mumford, P. W., Kephart, W. C., Conover, C. F., Beggs, L. A., Balaez, A., Yarrow, J. F., Borst, S. E., Beck, D. T., & Roberts, M. D. (2016). Effects of testosterone treatment on markers of skeletal muscle ribosome biogenesis. *Andrologia*, **48**(9), 1055–1065.

Morin, J.-B., & Samozino, P. (2016). Interpreting power-force-velocity profiles for individualized and specific training. *International Journal of Sports Physiology and Performance*, **11**(2), 267–272.

Morissette, M. R., Cook, S. A., Buranasombati, C., Rosenberg, M. A., & Rosenzweig, A. (2009). Myostatin inhibits IGF-I-induced myotube hypertrophy through Akt. *American Journal of Physiology-Cell Physiology*, **297**(5), 1124–1132.

Moritani, T., & deVries, H. (1979). Neural factors versus hypertrophy in the time course of muscle strength gain. *American Journal of Physical Medicine*, **58**, 115–130.

Morton, R. W., Oikawa, S. Y., Wavell, C. G., Mazara, N., McGlory, C., Quadrilatero, J., Baechler, B. L., Baker, S. K., & Phillips, S. M. (2016). Neither load nor systemic hormones determine resistance training-mediated hypertrophy or strength gains in resistance-trained young men. *Journal of Applied Physiology*, **121**(1), 129–138.

Muellbacher, W., Facchini, S., Boroojerdi, B., & Hallett, M. (2000). Changes in motor cortex excitability during ipsilateral hand muscle activation in humans. *Clinical Neurophysiology*, **111**(2), 344–349.

Mueller, B. J., Roberts, M. D., Mobley, C. B., Judd, R. L., & Kavazis, A. N. (2025). Nitric oxide in exercise physiology: Past and present perspectives. *Frontiers in Physiology*, **15**, 1504978.

Munn, J., Herbert, R. D., Hancock, M. J., & Gandevia, S. C. (2005). Resistance training for strength: Effect of number of sets and contraction speed. *Medicine and Science in Sports and Exercise*, **37**(9), 1622–1626.

Murach, K. A., Fry, C. S., Dupont-Versteegden, E. E., McCarthy, J. J., & Peterson, C. A. (2021). Fusion and beyond: Satellite cell contributions to loading-induced skeletal muscle adaptation. *Federation of American Societies for Experimental Biology Journal: Official Publication of the Federation of American Societies for Experimental Biology*, **35**(10), e21893.

Nagaraj, K., Lapkina-Gendler, L., Sarfstein, R., Gurwitz, D., Pasmanik-Chor, M., Laron, Z., Yakar, S., & Werner, H. (2018). Identification of thioredoxin-interacting protein (TXNIP) as a downstream target for IGF1 action. *Proceedings of the National Academy of Sciences of the United States of America*, **115**(5), 1045–1050.

Neeper, S. A., Góauctemez-Pinilla, F., Choi, J., & Cotman, C. (1995). Exercise and brain neurotrophins. *Nature*, **373**(6510), 109–109.

Nishioka, T., & Okada, J. (2023). Ballistic exercise versus heavy resistance exercise protocols: Which resistance priming is more effective for improving neuromuscular performance on the following day?. *Journal of Strength and Conditioning Research*, **37**(10), 1939–1946.

Nuzzo, J. L., Barry, B. K., Gandevia, S. C., & Taylor, J. L. (2016). Acute strength training increases responses to stimulation of corticospinal axons. *Medicine and Science in Sports and Exercise*, **48**, 139–150.

Nuzzo, J. L., Barry, B. K., Jones, M. D., Gandevia, S. C., & Taylor, J. L. (2017). Effects of four weeks of strength training on the corticomotoneuronal pathway. *Medicine and Science in Sports and Exercise*, **49**(11), 2286–2296.

Oakley, R. H., & Cidlowski, J. A. (2013). The biology of the glucocorticoid receptor: New signaling mechanisms in health and disease. *Journal of Allergy and Clinical Immunology*, **132**(5), 1033–1044.

O'Connor, J. C., McCusker, R. H., Strle, K., Johnson, R. W., Dantzer, R., & Kelley, K. W. (2008). Regulation of IGF-I function by proinflammatory cytokines: At the interface of immunology and endocrinology. *Cellular Immunology*, **252**, 91–110.

Okamoto, N., Yoshino, K., Kitagawa, S., Fujii, R., Hamada, S., Ikenouchi, A., Konishi, Y., Ueda, N., Eto, Y., Tsutsumi, Y., & Yoshimura, R. (2021). Association between serum insulin-like growth factor 1 levels and the clinical symptoms of chronic schizophrenia: Preliminary findings. *Front Psychiatry*, **12**, 653802.

Orssatto, L. B. R., Blazevich, A. J., & Trajano, G. S. (2023). Ageing reduces persistent inward current contribution to motor neurone firing: Potential mechanisms and the role of exercise. *The Journal of Physiology*, **601**(17), 3705–3716.

Orssatto, L. B. R., Rodrigues, P., Mackay, K., Blazevich, A. J., Borg, D. N., Souza, T. R. D., Sakugawa, R. L., Shield, A. J., & Trajano, G. S. (2023). Intrinsic motor neuron excitability is increased after resistance training in older adults. *Journal of Neurophysiology*, **129**(3), 635–650.

Paddock, N., Sheppard, P., & Gardiner, P. (2018). Chronic increases in daily neuromuscular activity promote changes in gene expression in small and large dorsal root ganglion neurons in rat. *Neuroscience*, **388**, 171–180.

Panwar, V., Singh, A., Bhatt, M., Tonk, R. K., Azizov, S., Raza, A. S., Sengupta, S., Kumar, D., & Garg, M. (2023). Multifaceted role of mTOR (mammalian target of rapamycin) signaling pathway in human health and disease. *Signal Transduct Target Ther*, **8**(1), 375.

Pareja-Blanco, F., Rodríguez-Rosell, D., Sánchez-Medina, L., Gorostiaga, E., & González-Badillo, J. (2014). Effect of movement velocity during resistance training on neuromuscular performance. *International Journal of Sports Medicine*, **35**, 916–924.

Pawlikowski, B., Vogler, T. O., Gadek, K., & Olwin, B. B. (2017). Regulation of skeletal muscle stem cells by fibroblast growth factors. *Developmental Dynamics*, **246**(5), 359–367.

Pearcey, G. E. P., Alizedah, S., Power, K. E., & Button, D. C. (2021). Chronic resistance training: Is it time to rethink the time course of neural contributions to strength gain?. *European Journal of Applied Physiology*, **121**(9), 2413–2422.

Pearcey, G. E. P., Power, K. E., & Button, D. C. (2014). Differences in supraspinal and spinal excitability during various force outputs of the biceps brachii in chronic- and non-resistance trained individuals ed. Avenanti A. *PLoS ONE*, **9**(5), e98468.

Pearcey, G. E. P., Smith, L. A., Sun, Y., & Zehr, E. P. (2022). 1894 revisited: Cross-education of skilled muscular control in women and the importance of representation ed. Masani K. *PLoS ONE*, **17**(3), e0264686.

Pelet, D. C. S., & Orsatti, F. L. (2021). Effects of resistance training at different intensities of load on cross-education of muscle strength. *Applied Physiology, Nutrition and Metabolism*, **46**(10), 1279–1289.

Perez, M. A., & Cohen, L. G. (2008). Mechanisms underlying functional changes in the primary motor cortex ipsilateral to an active hand. *Journal of Neuroscience*, **28**(22), 5631–5640.

Perez, M. A., Lundbye-Jensen, J., & Nielsen, J. B. (2006). Changes in corticospinal drive to spinal motoneurones following visuo-motor skill learning in humans. *The Journal of Physiology*, **573**(3), 843–855.

Piasecki, M. (2024). Motor unit adaptation to disuse: Crossing the threshold from firing rate suppression to neuromuscular junction transmission. *The Journal of Physiology*, **603**(13), 3701–3709.

Pinto, A. J., Bergouignan, A., Dempsey, P. C., Roschel, H., Owen, N., Gualano, B., & Dunstan, D. W. (2023). Physiology of sedentary behavior. *Physiological Reviews*, **103**(4), 2561–2622.

Power, K. E., Carlin, K. P., & Fedirchuk, B. (2012). Modulation of voltage-gated sodium channels hyperpolarizes the voltage threshold for activation in spinal motoneurones. *Experimental Brain Research*, **217**(2), 311–322.

Powers, S. K., Deminice, R., Ozdemir, M., Yoshihara, T., Bomkamp, M. P., & Hyatt, H. (2020). Exercise-induced oxidative stress: Friend or foe? *Journal of Sport and Health Science*, **9**(5), 415–425.

Prescott, S. A., & De Koninck, Y. (2005). Integration time in a subset of spinal Lamina I neurons is lengthened by sodium and calcium currents acting synergistically to prolong subthreshold depolarization. *Journal of Neuroscience*, **25**(19), 4743–4754.

Proske, U. (1979). The golgi tendon organ. *Trends in Neuroscience (Tins)*, **2**, 7–8.

Proske, U., & Gandevia, S. C. (2012). The proprioceptive senses: Their roles in signaling body shape, body position and movement, and muscle force. *Physiological Reviews*, **92**(4), 1651–1697.

Psilander, N., Damsgaard, R., & Pilegaard, H. (2003). Resistance exercise alters MRF and IGF-I mRNA content in human skeletal muscle. *Journal of Applied Physiology*, **95**(3), 1038–1044.

Ramakrishnan, S., Anand, V., & Roy, S. (2014). Vascular endothelial growth factor signaling in hypoxia and inflammation. *Journal of Neuroimmune Pharmacology*, **9**(2), 142–160.

Ramamoorthy, S., & Cidlowski, J. A. (2016). Corticosteroids: Mechanisms of action in health and disease. *Rheumatic Disease Clinics of North America*, **42**(1), 15–31.

Ramírez-Jarquín, U. N., & Tapia, R. (2018). Excitatory and inhibitory neuronal circuits in the spinal cord and their role in the control of motor neuron function and degeneration. *Acs Chemical Neuroscience*, **9**(2), 211–216.

Refalo, M. C., Nuckols, G., Galpin, A. J., Gallagher, I. J., Hamilton, D. L., & Fyfe, J. J. (2025). Sex differences in absolute and relative changes in muscle size following resistance training in healthy adults: A systematic review with bayesian meta-analysis. *PeerJ*, **13**, e19042.

Reid, K. F., & Fielding, R. A. (2012). Skeletal muscle power: A critical determinant of physical functioning in older adults. *Exercise and Sport Sciences Reviews*, **40**(1), 4–12.

Reist, N. E., Werle, M. J., & McMahan, U. J. (1992). Agrin released by motor neurons induces the aggregation of acetylcholine receptors at neuromuscular junctions. *Neuron*, **8**(5), 865–868.

Rekling, J. C., Funk, G. D., Bayliss, D. A., Dong, X.-W., & Feldman, J. L. (2000). Synaptic control of motoneuronal excitability. *Physiological Reviews*, **80**(2), 767–852.

Retamales, A., Zuloaga, R., Valenzuela, C. A., Gallardo-Escarate, C., Molina, A., & Valdés, J. A. (2015). Insulin-like growth factor-1 suppresses the myostatin signaling pathway during myogenic differentiation. *Biochemical and Biophysical Research Communications*, **464**(2), 596–602.

Revill, A. L., & Fuglevand, A. J. (2017). Inhibition linearizes firing rate responses in human motor units: Implications for the role of persistent inward currents. *The Journal of Physiology*, **595**(1), 179–191.

Richter, E. A., & Hargreaves, M. (2013). Exercise, GLUT4, and skeletal muscle glucose uptake. *Physiological Reviews*, **93**(3), 993–1017.

Riddle, C. N., Edgley, S. A., & Baker, S. N. (2009). Direct and indirect connections with upper limb motoneurons from the primate reticulospinal tract. *Journal of Neuroscience*, **29**(15), 4993–4999.

Roatta, S., & Farina, D. (2010). Sympathetic actions on the skeletal muscle. *Exercise and Sport Sciences Reviews*, **38**(1), 31–35.

Roberts, B. M., Nuckols, G., & Krieger, J. W. (2020). Sex differences in resistance training: A systematic review and meta-analysis. *Journal of Strength and Conditioning Research*, **34**(5), 1448–1460.

Roberts, M. D., Dalbo, V. J., Sunderland, K. L., Poole, C. N., Hassell, S. E., Bemben, D., Cramer, J., Stout, J., & Kerksick, C. M. (2010). IGF-1 splice variant and IGF-1 peptide expression patterns in young and old human skeletal muscle prior to and following sequential exercise bouts. *European Journal of Applied Physiology*, **110**(5), 961–969.

Roberts, M. D., McCarthy, J. J., Hornberger, T. A., Phillips, S. M., Mackey, A. L., Nader, G. A., Boppart, M. D., Kavazis, A. N., Reidy, P. T., Ogasawara, R., Libardi, C. A., Ugrinowitsch, C., Booth, F. W., & Esser, K. A. (2023). Mechanisms of mechanical overload-induced skeletal muscle hypertrophy: Current understanding and future directions. *Physiological Reviews*, **103**(4), 2679–2757.

Rodríguez Cruz, P. M., Cossins, J., Beeson, D., & Vincent, A. (2020). The neuromuscular junction in health and disease: Molecular mechanisms governing synaptic formation and homeostasis. *Frontiers in Molecular Neuroscience*, **13**, 610964.

Rodriguez-Gutierrez, E., Torres-Costoso, A., Pascual-Morena, C., Pozuelo-Carrascosa, D. P., Garrido-Miguel, M., & Martinez-Vizcaino, V. (2023). Effects of resistance exercise on neuroprotective factors in middle and late life: A systematic review and meta-analysis. *Aging and Disease*, **14**(4), 1264–1275.

Rodriguez-Miguelez, P., Lima-Cabello, E., Martínez-Flórez, S., Almar, M., Cuevas, M. J., & González-Gallego, J. (2015). Hypoxia-inducible factor-1 modulates the expression of vascular endothelial growth factor and endothelial nitric oxide synthase induced by eccentric exercise. *Journal of Applied Physiology*, **118**(8), 1075–1083.

Roig, M., O'Brien, K., Kirk, G., Murray, R., McKinnon, P., Shadgan, B., & Reid, W. D. (2009). The effects of eccentric versus concentric resistance training on muscle strength and mass in healthy adults: A systematic review with meta-analysis. *British Journal of Sports Medicine*, **43**(8), 556–568.

Rommel, C., Bodine, S. C., Clarke, B. A., Rossman, R., Nunez, L., Stitt, T. N., Yancopoulos, G. D., & Glass, D. J. (2001). Mediation of IGF-1-induced skeletal myotube hypertrophy by PI(3)K/akt/mTOR and PI(3)K/akt/GSK3 pathways. *Nature Cell Biology*, **3**(11), 1009–1013.

Rosendo-Pineda, M. J., Vicente, J. J., Vivas, O., Pacheco, J., Loza-Huerta, A., Sampieri, A., Wordeman, L., Moreno, C., & Vaca, L. (2020). Phosphorylation of NMDA receptors by cyclin B/CDK1 modulates calcium dynamics and mitosis. *Communications Biology*, **3**(1), 665.

Ruddy, K. L., & Carson, R. G. (2013). Neural pathways mediating cross education of motor function. *Frontiers in Human Neuroscience*, **7**, 397.

Ruddy, K. L., Leemans, A., Woolley, D. G., Wenderoth, N., & Carson, R. G. (2017). Structural and functional cortical connectivity mediating cross education of motor function. *Journal of Neuroscience*, **37**(10), 2555–2564.

Rusakov, D. A., Savtchenko, L. P., & Latham, P. E. (2020). Noisy synaptic conductance: Bug or a feature? *Trends in Neuroscience (Tins)*, **43**(6), 363–372.

Sanz-Clemente, A., Matta, J. A., Isaac, J. T. R., & Roche, K. W. (2010). Casein Kinase 2 regulates the NR2 subunit composition of synaptic NMDA receptors. *Neuron*, **67**(6), 984–996.

Scaglioni, G., Ferri, A., Minetti, A. E., Martin, A., Van Hoecke, J., Capodaglio, P., Sartorio, A., & Narici, M. V. (2002). Plantar flexor activation capacity and H reflex in older adults: Adaptations to strength training. *Journal of Applied Physiology*, **92**(6), 2292–2302.

Schiaffino, S., & Bormioli, S. P. (1973). Adaptive changes in developing rat skeletal muscle in response to functional overload. *Experimental Neurology*, **40**(1), 126–137.

Schiaffino, S., & Mammucari, C. (2011). Regulation of skeletal muscle growth by the IGF1-akt/PKB pathway: Insights from genetic models. *Skelet Muscle*, **1**(1), 4.

Schiaffino, S., Pierobon Bormioli, S., & Aloisi, M. (1972). Cell proliferation in rat skeletal muscle during early stages of compensatory hypertrophy. *Virchows Archiv B: Cell Pathology*, **11**(1), 268–273.

Schiaffino, S., Reggiani, C., Akimoto, T., & Blaauw, B. (2021). Molecular mechanisms of skeletal muscle hypertrophy. *Journal of Clinical Neuromuscular Disease*, **8**(2), 169–183.

Schoenfeld, B. J. (2010). The mechanisms of muscle hypertrophy and their application to resistance training. *Journal of Strength and Conditioning Research*, **24**(10), 2857–2872.

Schoenfeld, B. J., Contreras, B., Vigotsky, A. D., & Peterson, M. (2016). Differential effects of heavy versus moderate loads on measures of strength and hypertrophy in resistance-trained men. *Journal of Sports Science and Medicine*, **15**, 715–722.

Schoenfeld, B. J., Grgic, J., Ogborn, D., & Krieger, J. W. (2017). Strength and hypertrophy adaptations between low- vs. high-load resistance training: A systematic review and meta-analysis. *Journal of Strength and Conditioning Research*, **31**(12), 3508–3523.

Schoenfeld, B. J., Grgic, J., Van Every, D. W., & Plotkin, D. L. (2021). Loading recommendations for muscle strength, hypertrophy, and local endurance: A re-examination of the repetition continuum. *Sports*, **9**(2), 32.

Schwindt, P. C., & Crill, W. E. (1980). Properties of a persistent inward current in normal and TEA-injected motoneurons. *Journal of Neurophysiology*, **43**(6), 1700–1724.

Sculthorpe, N., Solomon, A. M., Sinanan, A. C. M., Bouloux, P.-M. G., Grace, F., & Lewis, M. P. (2012). Androgens affect myogenesis In vitro and increase local IGF-1 expression. *Medicine and Science in Sports and Exercise*, **44**(4), 610–615.

Shapiro, N. P., & Lee, R. H. (2007). Synaptic amplification versus bistability in motoneuron dendritic processing: A top-down modeling approach. *Journal of Neurophysiology*, **97**(6), 3948–3960.

Siddique, U., Rahman, S., Frazer, A. K., Pearce, A. J., Howatson, G., & Kidgell, D. J. (2020). Determining the sites of neural adaptations to resistance training: A systematic review and meta-analysis. *Sports Medicine (Auckland, NZ)*, **50**(6), 1107–1128.

Singh, R., Artaza, J. N., Taylor, W. E., Gonzalez-Cadavid, N. F., & Bhasin, S. (2003). Androgens stimulate myogenic differentiation and inhibit adipogenesis in C3H 10T1/2 pluripotent cells through an androgen receptor-mediated pathway. *Endocrinology*, **144**(11), 5081–5088.

Škarabot, J., Brownstein, C. G., Casolo, A., del Vecchio, A., & Ansdell, P. (2021). The knowns and unknowns of neural adaptations to resistance training. *European Journal of Applied Physiology*, **121**, 675–685.

Škarabot, J., Casolo, A., Balshaw, T. G., Maeo, S., Lanza, M. B., Holobar, A., Farina, D., Folland, J. P., & Del Vecchio, A. (2024). Greater motor unit discharge rate during rapid contractions in chronically strength-trained individuals. *Journal of Neurophysiology*, **132**, 1896–1906.

Škarabot, J., Folland, J. P., Holobar, A., Baker, S. N., & Del Vecchio, A. (2022). Startlingstimuli increase maximal motor unit discharge rate and rate of forcedevelopment in humans. *Journal of Neurophysiology*, **128**, 455–469.

Škarabot, J., Thomason, H. W., Nazaroff, B. M., Connelly, C. D., Valenčič, T., Ho, M. L., Tyagi, K., Beauchamp, J. A., & Pearcey, G. E. (2025). Training-induced alterations in the modulation of human motoneuron discharge patterns with contraction force. Available at: http://biorxiv.org/lookup/doi/10.1101/2025.06.02.657380 (Accessed November 3, 2025).

Smith, L. R., Kok, H. J., Zhang, B., Chung, D., Spradlin, R. A., Rakoczy, K. D., Boesze-Battaglia, K., & Barton, E. R. (2020). Matrix metalloproteinase 13 from satellite cells is required for efficient muscle growth and regeneration. *Cellular Physiology and Biochemistry*, **54**, 333–353.

Snijders, T., Nederveen, J. P., McKay, B. R., Joanisse, S., Verdijk, L. B., van Loon, L. J. C., & Parise, G. (2015). Satellite cells in human skeletal muscle plasticity. *Frontiers in Physiology*, **6**, 283.

Soendenbroe, C., Bechshøft, C. J. L., Heisterberg, M. F., Jensen, S. M., Bomme, E., Schjerling, P., Karlsen, A., Kjaer, M., Andersen, J. L., & Mackey, A. L. (2020). Key components of human myofibre denervation and neuromuscular junction stability are modulated by age and exercise. *Cells*, **9**(4), 893.

Sonntag, W. E., Bennett, S. A., Khan, A. S., Thornton, P. L., Xu, X., Ingram, R. L., & Brunso-Bechtold, J. K. (2000). Age and insulin-like growth factor-1 modulate N-methyl-D-aspartate receptor subtype expression in rats. *Brain Research Bulletin*, **51**(4), 331–338.

Stagg, C. J., Bestmann, S., Constantinescu, A. O., Moreno Moreno, L., Allman, C., Mekle, R., Woolrich, M., Near, J., Johansen-Berg, H., & Rothwell, J. C. (2011). Relationship between physiological measures of excitability and levels of glutamate and GABA in the human motor cortex. *The Journal of Physiology*, **589**(23), 5845–5855.

Stitt, T. N., Drujan, D., Clarke, B. A., Panaro, F., Timofeyva, Y., Kline, W. O., Gonzalez, M., Yancopoulos, G. D., & Glass, D. J. (2004). The IGF-1/PI3K/Akt pathway prevents expression of muscle atrophy-induced ubiquitin ligases by inhibiting FOXO transcription factors. *Molecular Cell*, **14**(3), 395–403.

Sturm, H., Schmied, A., Vedel, J., & Pagni, S. (1997). Firing pattern of type-identified wrist extensor motor units during wrist extension and hand clenching in humans. *The Journal of Physiology*, **504**(3), 735–745.

Sun, Z., Wu, K., Gu, L., Huang, L., Zhuge, Q., Yang, S., & Wang, Z. (2020). IGF-1R stimulation alters microglial polarization via TLR4/NF-κb pathway after cerebral hemorrhage in mice. *Brain Research Bulletin*, **164**, 221–234.

Szadvári, I., Ostatníková, D., & Babková Durdiaková, J. (2023). Sex differences matter: Males and females are equal but not the same. *Physiology & Behavior*, **259**, 114038.

Takei, N., & Nawa, H. (2014). mTOR signaling and its roles in normal and abnormal brain development. *Frontiers in Molecular Neuroscience*, **7**, 28.

Tallent, J., Woodhead, A., Frazer, A. K., Hill, J., Kidgell, D. J., & Howatson, G. (2021). Corticospinal and spinal adaptations to motor skill and resistance training: Potential mechanisms and implications for motor rehabilitation and athletic development. *European Journal of Applied Physiology*, **121**(3), 707–719.

Tatsumi, R., Hattori, A., Ikeuchi, Y., Anderson, J. E., & Allen, R. E. (2002). Release of hepatocyte growth factor from mechanically stretched skeletal muscle satellite cells and role of pH and nitric oxide ed. Guidotti G. *Molecular Biology of the Cell*, **13**(8), 2909–2918.

Tavi, P., & Westerblad, H. (2011). The role of in vivo Ca2+ signals acting on Ca2+-calmodulin-dependent proteins for skeletal muscle plasticity. *The Journal of Physiology*, **589**(21), 5021–5031.

Theodosiadou, A., Henry, M., Duchateau, J., & Baudry, S. (2023). Revisiting the use of Hoffmann reflex in motor control research on humans. *European Journal of Applied Physiology*, **123**(4), 695–710.

Thomas, A. C. Q., Stead, C. A., Burniston, J. G., & Phillips, S. M. (2024). Exercise-specific adaptations in human skeletal muscle: Molecular mechanisms of making muscles fit and mighty. *Free Radical Biology and Medicine*, **223**, 341–356.

Thorstensen, J. R., Henderson, T. T., & Kavanagh, J. J. (2024). Serotonergic and noradrenergic contributions to motor cortical and spinal motoneuronal excitability in humans. *Neuropharmacology*, **242**, 109761.

Tian, J., Fan, J., & Zhang, T. (2023). Mitochondria as a target for exercise-mitigated type 2 diabetes. *Journal of Molecular Histology*, **54**(6), 543–557.

Tillin, N. A., & Folland, J. P. (2014). Maximal and explosive strength training elicit distinct neuromuscular adaptations, specific to the training stimulus. *European Journal of Applied Physiology*, **114**(2), 365–374.

Tøien, T., Malmo, T., Espedal, L., & Wang, E. (2022). Maximal intended velocity enhances strength training-induced neuromuscular stimulation in older adults. *European Journal of Applied Physiology*, **122**, 2627–2636.

Trejo, J. L., Carro, E., & Torres-Alemán, I. (2001). Circulating insulin-like growth factor I mediates exercise-induced increases in the number of new neurons in the adult hippocampus. *Journal of Neuroscience*, **21**(5), 1628–1634.

Valli, G., Sarto, F., Casolo, A., Del Vecchio, A., Franchi, M. V., Narici, M. V., & De Vito, G. (2024). Lower limb suspension induces threshold-specific alterations of motor units properties that are reversed by active recovery. *Journal of Sport and Health Science*, **13**(2), 264–276.

van Cutsem, M., Duchateau, J., & Hainaut, K. (1998). Changes in single motor unit behaviour contribute to the increase in contraction speed after dynamic training in humans. *The Journal of Physiology*, **513**(1), 295–305.

van Every, D. W., D'Souza, A. C., & Phillips, S. M. (2024). Hormones, hypertrophy, and hype: An evidence-guided primer on endogenous endocrine influences on exercise-induced muscle hypertrophy. *Exercise and Sport Sciences Reviews*, **52**(4), 117–125.

Vangsgaard, S., Taylor, J. L., Hansen, E. A., & Madeleine, P. (2014). Changes in H reflex and neuromechanical properties of the trapezius muscle after 5 weeks of eccentric training: A randomized controlled trial. *Journal of Applied Physiology*, **116**(12), 1623–1631.

Vila-Chã, C., & Falla, D. (2016). Strength training, but not endurance training, reduces motor unit discharge rate variability. *Journal of Electromyography and Kinesiology*, **26**, 88–93.

Vincent, K. R., & Vincent, H. K. (2006). Resistance training for individuals with cardiovascular disease. *Journal of Cardiopulmonary Rehabilitation*, **26**(4), 207–216.

Vingren, J. L., Kraemer, W. J., Ratamess, N. A., Anderson, J. M., Volek, J. S., & Maresh, C. M. (2010). Testosterone physiology in resistance exercise and training: The up-stream regulatory elements. *Sports Medicine (Auckland, NZ)*, **40**(12), 1037–1053.

Vints, W. A. J., Levin, O., Fujiyama, H., Verbunt, J., & Masiulis, N. (2022). Exerkines and long-term synaptic potentiation: Mechanisms of exercise-induced neuroplasticity. *Frontiers in Neuroendocrinology*, **66**, 100993.

von Bohlen Und Halbach, O., & von Bohlen Und Halbach, V. (2018). BDNF effects on dendritic spine morphology and hippocampal function. *Cell and Tissue Research*, **373**(3), 729–741.

Walker, B. R., & Seckl, J. R. (2001). Cortisol metabolism. In *International Textbook of Obesity*, 1st edn. ed. P. Björntorp, pp. 241–268. Wiley. Available at: https://onlinelibrary.wiley.com/doi/10.1002/0470846739.ch18 (Accessed June 30, 2025).

Walsh, J. J., & Tschakovsky, M. E. (2018). Exercise and circulating BDNF: Mechanisms of release and implications for the design of exercise interventions. *Applied Physiology, Nutrition and Metabolism*, **43**(11), 1095–1104.

Wang, B., Davies, T. B., Way, K. L., Tran, D. L., Davis, G. M., Singh, M. F., & Hackett, D. A. (2023). Effect of resistance training on local muscle endurance in middle-aged and older adults: A systematic review with meta-analysis and meta-regression. *Archives of Gerontology and Geriatrics*, **109**, 104954.

Wang, L., Mascher, H., Psilander, N., Blomstrand, E., & Sahlin, K. (2011). Resistance exercise enhances the molecular signaling of mitochondrial biogenesis induced by endurance exercise in human skeletal muscle. *Journal of Applied Physiology*, **111**(5), 1335–1344.

Warneke, K., Lohmann, L. H., Lima, C. D., Hollander, K., Konrad, A., Zech, A., Nakamura, M., Wirth, K., Keiner, M., & Behm, D. G. (2023). Physiology of stretch-mediated hypertrophy and strength increases: A narrative review. *Sports Medicine (Auckland, NZ)*, **53**(11), 2055–2075.

Weakley, J., Schoenfeld, B. J., Ljungberg, J., Halson, S. L., & Phillips, S. M. (2023). Physiological responses and adaptations to lower load resistance training: Implications for health and performance. *Sports Med - Open*, **9**(1), 28.

Weier, A. T., Pearce, A. J., & Kidgell, D. J. (2012). Strength training reduces intracortical inhibition. *Acta Physiologica*, **206**(2), 109–119.

West, D. W. D., Burd, N. A., Churchward-Venne, T. A., Camera, D. M., Mitchell, C. J., Baker, S. K., Hawley, J. A., Coffey, V. G., & Phillips, S. M. (2012). Sex-based comparisons of myofibrillar protein synthesis after resistance exercise in the fed state. *Journal of Applied Physiology*, **112**(11), 1805–1813.

West, D. W. D., Burd, N. A., Tang, J. E., Moore, D. R., Staples, A. W., Holwerda, A. M., Baker, S. K., & Phillips, S. M. (2010). Elevations in ostensibly anabolic hormones with resistance exercise enhance neither training-induced muscle hypertrophy nor strength of the elbow flexors. *Journal of Applied Physiology*, **108**(1), 60–67.

West, D. W. D., Kujbida, G. W., Moore, D. R., Atherton, P., Burd, N. A., Padzik, J. P., De Lisio, M., Tang, J. E., Parise, G., Rennie, M. J., Baker, S. K., & Phillips, S. M. (2009). Resistance exercise-induced increases in putative anabolic hormones do not enhance muscle protein synthesis or intracellular signalling in young men. *The Journal of Physiology*, **587**(21), 5239–5247.

West, D. W. D., & Phillips, S. M. (2012). Associations of exercise-induced hormone profiles and gains in strength and hypertrophy in a large cohort after weight training. *European Journal of Applied Physiology*, **112**(7), 2693–2702.

Westcott, W. L. (2012). Resistance training is medicine: Effects of strength training on health. *Current Sports Medicine Reports*, **11**(4), 209–216.

Wiggin, G. R., Soloaga, A., Foster, J. M., Murray-Tait, V., Cohen, P., & Arthur, J. S. C. (2002). MSK1 and MSK2 are required for the mitogen- and stress-induced phosphorylation of CREB and ATF1 in fibroblasts. *Molecular and Cellular Biology*, **22**(8), 2871–2881.

Wilkinson, S. B., Phillips, S. M., Atherton, P. J., Patel, R., Yarasheski, K. E., Tarnopolsky, M. A., & Rennie, M. J. (2008). Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle. *The Journal of Physiology*, **586**(15), 3701–3717.

Wilkinson, S. B., Tarnopolsky, M. A., Grant, E. J., Correia, C. E., & Phillips, S. M. (2006). Hypertrophy with unilateral resistance exercise occurs without increases in endogenous anabolic hormone concentration. *European Journal of Applied Physiology*, **98**(6), 546–555.

Willoughby, D. S., Taylor, M., & Taylor, L. (2003). Glucocorticoid receptor and ubiquitin expression after repeated eccentric exercise. *Medicine and Science in Sports and Exercise*, **35**(12), 2023–2031.

Winbanks, C. E., Weeks, K. L., Thomson, R. E., Sepulveda, P. V., Beyer, C., Qian, H., Chen, J. L., Allen, J. M., Lancaster, G. I., Febbraio, M. A., Harrison, C. A., McMullen, J. R., Chamberlain, J. S., & Gregorevic, P. (2012). Follistatin-mediated skeletal muscle hypertrophy is regulated by Smad3 and mTOR independently of myostatin. *Journal of Cell Biology*, **197**(7), 997–1008.

Winter, J. N., Jefferson, L. S., & Kimball, S. R. (2011). ERK and akt signaling pathways function through parallel mechanisms to promote mTORC1 signaling. *American Journal of Physiology-Cell Physiology*, **300**(5), C1172–C1180.

Woodrow, L., Sheppard, P., & Gardiner, P. F. (2013). Transcriptional changes in rat α-motoneurons resulting from increased physical activity. *Neuroscience*, **255**, 45–54.

Wright, D. C., Han, D.-H., Garcia-Roves, P. M., Geiger, P. C., Jones, T. E., & Holloszy, J. O. (2007). Exercise-induced mitochondrial biogenesis begins before the increase in muscle PGC-1α expression. *Journal of Biological Chemistry*, **282**(1), 194–199.

Wu, Z., Puigserver, P., Andersson, U., Zhang, C., Adelmant, G., Mootha, V., Troy, A., Cinti, S., Lowell, B., Scarpulla, R. C., & Spiegelman, B. M. (1999). Mechanisms controlling mitochondrial biogenesis and respiration through the thermogenic coactivator PGC-1. *Cell*, **98**(1), 115–124.

Yacyshyn, A. F., Woo, E. J., Price, M. C., & McNeil, C. J. (2016). Motoneuron responsiveness to corticospinal tract stimulation during the silent period induced by transcranial magnetic stimulation. *Experimental Brain Research*, **234**(12), 3457–3463.

Yamada, M., Sankoda, Y., Tatsumi, R., Mizunoya, W., Ikeuchi, Y., Sunagawa, K., & Allen, R. E. (2008). Matrix metalloproteinase-2 mediates stretch-induced activation of skeletal muscle satellite cells in a nitric oxide-dependent manner. *International Journal of Biochemistry & Cell Biology*, **40**(10), 2183–2191.

Yan, X., Liu, J., Ye, Z., Huang, J., He, F., Xiao, W., Hu, X., & Luo, Z. (2016). CaMKII-mediated CREB phosphorylation is involved in Ca2+-induced BDNF mRNA transcription and neurite outgrowth promoted by electrical stimulation ed. Hetman M. *PLoS ONE*, **11**(9), e0162784.

Yarom, Y., & Hounsgaard, J. (2011). Voltage fluctuations in neurons: Signal or noise?. *Physiological Reviews*, **91**(3), 917–929.

Yasuda, R., Hayashi, Y., & Hell, J. W. (2022). CaMKII: A central molecular organizer of synaptic plasticity, learning and memory. *Nature Reviews Neuroscience*, **23**(11), 666–682.

Yin, H., Price, F., & Rudnicki, M. A. (2013). Satellite cells and the muscle stem cell niche. *Physiological Reviews*, **93**(1), 23–67.

Yoon, M.-S., Sun, Y., Arauz, E., Jiang, Y., & Chen, J. (2011). Phosphatidic acid activates Mammalian Target of Rapamycin Complex 1 (mTORC1) kinase by displacing FK506 Binding Protein 38 (FKBP38) and exerting an allosteric effect. *Journal of Biological Chemistry*, **286**(34), 29568–29574.

You, J.-S., Lincoln, H. C., Kim, C.-R., Frey, J. W., Goodman, C. A., Zhong, X.-P., & Hornberger, T. A. (2014). The role of diacylglycerol kinase ζ and phosphatidic acid in the mechanical activation of mammalian target of Rapamycin (mTOR) signaling and skeletal muscle hypertrophy. *Journal of Biological Chemistry*, **289**(3), 1551–1563.

You, W., Knoops, K., Berendschot, T. T. J. M., Benedikter, B. J., Webers, C. A. B., Reutelingsperger, C. P. M., & Gorgels, T. G. M. F. (2024). PGC-1a mediated mitochondrial biogenesis promotes recovery and survival of neuronal cells from cellular degeneration. *Cell Death Discovory*, **10**(1), 180.

Zammit, P. S., Golding, J. P., Nagata, Y., Hudon, V., Partridge, T. A., & Beauchamp, J. R. (2004). Muscle satellite cells adopt divergent fates. *Journal of Cell Biology*, **166**(3), 347–357.

Zammit, P. S., Relaix, F., Nagata, Y., Ruiz, A. P., Collins, C. A., Partridge, T. A., & Beauchamp, J. R. (2006). Pax7 and myogenic progression in skeletal muscle satellite cells. *Journal of Cell Science*, **119**(9), 1824–1832.

Zhang, Q., & Dai, Y. (2020). A modeling study of spinal motoneuron recruitment regulated by ionic channels during fictive locomotion. *Journal of Computational Neuroscience*, **48**(4), 409–428.

Zheng, B., Ohkawa, S., Li, H., Roberts-Wilson, T. K., & Price, S. R. (2010). FOXO3a mediates signaling crosstalk that coordinates ubiquitin and atrogin-1/MAFbx expression during glucocorticoid-induced skeletal muscle atrophy. *Faseb Journal*, **24**(8), 2660–2669.

Zheng, W.-H., & Quirion, R. (2006). Insulin-like growth factor-1 (IGF-1) induces the activation/phosphorylation of Akt kinase and cAMP response element-binding protein (CREB) by activating different signaling pathways in PC12 cells. *BioMed Central Neuroscience (Electronic Resource)*, **7**(1), 51.

Zhu, W. G., Thomas, A. C. Q., Wilson, G. M., McGlory, C., Hibbert, J. E., Flynn, C. G. K., Sayed, R. K. A., Paez, H. G., Meinhold, M., Jorgenson, K. W., You, J.-S., Steinert, N. D., Lin, K.-H., MacInnis, M. J., Coon, J. J., Phillips, S. M., & Hornberger, T. A. (2025). Identification of a resistance-exercise-specific signalling pathway that drives skeletal muscle growth. *Nature Metabolism*, **7**(7), 1404–1423.

Zuo, C., Yin, Y., Zheng, Z., Mu, R., Liang, Y., Wang, S., & Ye, C. (2025). Unlocking the full potential of resistance training: A comparative analysis of low- and high-intensity effects on neurotrophic growth factors and homocysteine. *Discover Applied Sciences*, **7**(2), 108.

Additional information

Competing interests

The authors declare that they have no competing interests.

Author contributions

E.L. designed and conceived this review. All authors drafted and critically revised the article. All authors have approved the final version of the manuscript submitted for publication and agreed to be accountable for all aspects of the work. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

Funding

The Laboratory of Exercise Physiology needed no additional funding for this article.

Keywords

motor cortex, motor unit, muscle strength, neuromuscular system, resistance training, strength training

Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the HTML view of the article. Supporting information files available:

Peer Review History