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Posted Date: 9 April 2026

doi: 10.20944/preprints202604.0567.v1

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Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 April 2026 doi:10.20944/preprints202604.0567.v1

Review

Toward an Integrative Physiology of Strength: Molecular Mechanisms, Motor Intention, and AI-Driven Training Optimization

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Abstract

The scientific foundations of sport-training methodology are commonly attributed to physiological principles; however, the extent to which these principles directly inform practical training models remains unclear. This narrative review examines the historical development of training theory—from early adaptology and integrative physiology to contemporary molecular discoveries in muscle biology—and evaluates their relevance to strength development. Strength expression is shown to be highly variable, influenced by neural, mechanical, technical, and psychological factors, challenging the traditional reliance on fixed percentages of maximal strength for training prescription. Additional complexities arise from individual response variability, performance plateaus, and the interference between molecular pathways activated by strength and endurance training. Emerging artificial intelligence systems offer new opportunities for individualized training optimization, injury prediction, and motor-learning analysis, while advances in brain decoding technologies highlight the potential role of willpower and cognitive processes in strength expression. Overall, current training methodologies remain partly speculative, and substantial research is required to more clearly connect physiological mechanisms with practical training applications.

Keywords: training methodologies; origins of sport training sciences; biochemistry; muscular tension; volitive processes; brain; AI

1. Introduction

Sticking with an objective and a plan increase motivation [1] and interest in sport sciences for the methodology of training is increasing year by year (Table 1).

Table 1. Number of papers in methodology of training over the last 10 years .P = post covid peak ; E = estimate (source: author elaborations on Pudmed papers).

Annual Pubs (2015-25)

Field: Training Methodology

Year	Count	Trend
2015	1.3k	
2016	1.4k	
2017	1.5k	
2018	1.7k	
2019	1.9k	
2020	2.1k	

 doi:10.20944/preprints202604.0567.v1

2021	2.4k	(P)
2022	2.3k	
2023	2.4k	
2024	2.4k	
2025*	2.5k	(E)

The concept of organizing sports training is not new and can be traced back to Filostratus [2] and Luciano of Samosata [3] around 200 C.E., who first offered guidance on how to structure athletes' preparation. Modern approaches to sport training organization emerged during the Cold War, particularly following the success of Russian teams in international competitions. It was Lev Matveyev [4], active at the Central Sport University of Moscow in the 1970s, who first introduced the concept of periodization of sport training. After Matveyev, several scholars expanded and refined training theory by adding methodological guidelines [5–7].

A strong tradition of scientific research on sports training methods developed in Western Europe and Russia, taking the name "adaptology" [8]. Unlike upregulation, a term commonly used for biochemical, genetic, and molecular processes, adaptology is broader and integrates genetic, molecular, and organ-level adaptations into a unified framework [8]. This holistic approach seeks to explain how training induces physiological and psychological changes, creating logical connections between biological mechanisms and training outcomes. Seyulianov defines adaptology as "a science that deals with the holistic behavior of the organism of an athlete in training and competitive conditions" [8]. An example is the development of muscle mass through slow, low-load movements (20–50% 1RM) performed for long durations or to exhaustion with incomplete range of motion—an approach investigated by Popov et al. [9] following earlier work by Weider [10] and Rouet [11]. Adaptology emphasizes inter-individual variability and examines how training loads act differently among athletes.

A similar integrative approach is found in Integrative Physiology (IP) [12], which also seeks to connect different fields of biological knowledge to understand functional adaptations of physiological systems.

The aim of this narrative review is to evaluate the scientific foundations of these theories and the experimental evidence supporting them in light of recent discoveries in muscle physiology, particularly regarding strength.

2. Genetic and Molecular Background

Strength production relies on two primary factors: hypertrophy and tension. Tension is influenced by neurological factors such as motor unit recruitment, action potential conduction velocity (related to axonal size), and availability of chemical mediators including acetylcholine and calcium [13]. Receptor expression and gene upregulation often occur in response to specific signals and underpin physical adaptations. Once a certain threshold of stimulation is reached, cells respond through homeostatic, adaptive, and plastic pathways. Early studies demonstrated increased expression of neurotransmitter receptors on muscle membranes following denervation [14]. Enzymatic activities—including those of citrate synthase, lactate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, phosphofructokinase, superoxide dismutase (SOD), and glutathione peroxidase—are known to increase following appropriate stimuli [15].

Transcriptional responses further regulate adaptation. For instance, hypoxic conditions stimulate transcription factors such as mTOR, MyoD, and HIF-1α to increase mRNA production [16]. Among these regulators, PGC-1α plays a key role in linking external stimuli to cellular remodeling [17].

Neurotrophic factors also influence muscle phenotype. Calcineurin has been identified as a primary determinant of fiber-type specification [18], while neurotrophins such as BDNF promote upregulation of TrkB receptors and regulate synaptogenesis [19]. Although substances mimicking neurotrophin activity (e.g., NGF analogues) have been explored [20], results have been unsatisfactory in terms of functional recovery.

PGC-1α and AMPK pathways are predominantly activated by endurance training, whereas strength training more strongly activates the mTOR pathway. These pathways appear to interfere with one another, such that stimulation of one may inhibit the other [21]. This interaction is particularly relevant for training planning, as programs that combine strength and endurance sessions in close proximity may compromise adaptations in both domains [22].

3. Adaptology in the Context of Sport Training

Supercompensation—defined as the replenishment or augmentation of system-level or organism-level capacities—remains a widely accepted framework in physical conditioning. The General Adaptation Syndrome (GAS), formulated by Hans Selye [23], was based on studies of hormonal responses to stress in the adrenal cortex of mice [24]. According to GAS, organisms respond to stressors through the phases of alarm, resistance, and either adaptation or failure. This model underlies many traditional approaches to physical training, including progressive overload.

However, GAS focuses primarily on the hypothalamic–pituitary–adrenal (HPA) axis and stress hormones such as cortisol, ACTH, and CRH, neglecting other hormonal and molecular pathways. While Selye described GAS as a non-specific response, skeletal muscle adaptation is highly specific [25]. Reevaluation of Selye's data showed that responses were in fact stimulus-specific and influenced by psychological factors [25]. This finding raises interesting hypotheses about the role of psychological states in muscle growth. Indeed, evidence shows that attentional focus on contracting muscles enhances strength gains over time [26], and positive expectations or placebo effects can improve performance and strength development [27].

4. Fitness–Fatigue Theory (Two-Factor Model)

Banister [28] introduced fatigue as a key factor limiting adaptation to increased training stimuli. In this model, positive adaptations are counteracted by fatigue, which temporarily impairs performance. Consequently, strategies to accelerate recovery from fatigue became central to training science, prompting research on overreaching and overtraining syndromes in athletes [29].

Fatigue is a psychophysical phenomenon. Physiological approaches emphasize the decline of force production over time [30], while psychological research investigates mental fatigue [31], typically assessed through declines in cognitive task performance [32]. However, how cognitive fatigue influences low-cognitive-demand physical tasks remains unclear. Moreover, distinguishing mental fatigue from related conditions such as depression is challenging, and consensus on the definition of mental fatigue is lacking [33]. Measurement tools for mental fatigue have also been questioned for their reliability [34].

A paradox in mental-fatigue research is that exercise itself improves mood—possibly through increases in testosterone [35] and reductions in neurotransmitters associated with stress—acting similarly to antidepressants [36].

5. Hormesis

Hormesis describes the phenomenon in which low doses of a stressor produce beneficial biological effects [37]. The concept became widespread in the 1950s when low doses of gamma radiation were found to enhance plant growth, reduce pain, and produce other health-related effects [38]. At that time, the long-term effects of chronic radiation exposure were poorly understood, and numerous commercial products containing radioactive compounds were marketed, resulting in radiation poisoning and even deaths [39]. This historical example illustrates how beneficial effects of a method may be overestimated without considering harmful side effects in other physiological systems.

 doi:10.20944/preprints202604.0567.v1

Recent rat studies have reported reparative effects of low-dose gamma radiation on damaged muscle tissue [40]. In exercise science, hormesis suggests that low-load exercise performed consistently may induce positive adaptations in skeletal muscle [39]. Proposed mechanisms include redox-mediated pathways involving hydrogen peroxide, nitric oxide, and PGC-1α activation within mitochondria [39].

6. Mechanotransduction

Mechanotransduction investigates how physical forces—such as osmotic pressure, hemodynamic pressure, shear stress, compressive forces, and particularly tensile forces—trigger biochemical responses in cells [41,42]. Several mechanistic links between mechanical tension and muscle remodeling have been identified, yet the precise pathways remain incompletely understood [43]. Strength training increases mechanical tension primarily in type II (fast-twitch) fibers, while type I fibers exhibit smaller and less well-understood responses [43]. Currently, mTOR is considered a key mediator between tension and protein synthesis [44].

Historically, antioxidant supplementation, cryotherapy, and NSAID (non-steroideal anti-inflammation drugs) use have been recommended to reduce exercise-induced oxidative stress and inflammation. However, ROS (reactive oxygen species) and inflammatory reactions are essential signaling mediators, and reducing them may attenuate training adaptations. Similar concerns apply to dietary strategies such as carbohydrate restriction or blood flow restriction, which may enhance certain adaptations but compromise others. Although many of these interventions affect transcription factors, kinases, and protein synthesis, it remains unclear how they interact, whether their effects are complementary or antagonistic, and whether they meaningfully influence long-term adaptation to exercise [45].

7. Grounded on Physiological Facts?

Training methodologies often prescribe percentages of maximal strength to structure programs aimed at increasing force production. Strength is commonly stated to depend on muscular tension. However, the term maximal strength is frequently used ambiguously—sometimes referring to the execution of a task (e.g., lifting a weight), which depends not only on muscular tension but also on factors such as balance, technical skill, and psychological states (e.g., fear of injury). In other contexts, maximal strength refers to the capacity to generate high tension, as measured by isometric or isokinetic devices.

Several factors challenge the concept of a stable, measurable "maximal strength." First, human strength exhibits substantial daily variability. Strength can fluctuate by up to 22% within the same day [46], with typical variations ranging from 20–40% and an average of about 10%, largely due to circadian hormonal influences. The late afternoon (4–6 p.m.) is generally the optimal time for strength performance.

Secondly, technical mastery of lifting or exercise execution significantly affects maximal strength assessment [47,48]. Even lifting speed is an important determinant of measured strength [49]. To standardize contraction speed and reduce variability, isokinetic devices were introduced [50]. However, device-based assessments introduce new complications: each dynamometer has unique mechanical characteristics—even between units from the same manufacturer—making between-day comparisons difficult due to system instability [50]. Additional issues include torque overshoot, the artificial constraints of mono-axial movements (whereas joints normally move along multi-axial paths), joint alignment challenges, participant stabilization, and the high cost of instrumentation—all of which limit the practicality of dynamometry in field contexts [51].

A further complexity in understanding training adaptations is the presence of non-responders—individuals who fail to improve performance or exhibit structural adaptations such as hypertrophy [52]. Although some argue that true "global" non-responders may not exist—suggesting instead

 doi:10.20944/preprints202604.0567.v1

inadequate stimulus, insensitivity of measurement tools, or unrecognized small improvements—physiological variability likely results in genuine low-responders [53].

A plateau in performance or the achievement of genetic limits further complicates adaptation models. When athletes approach maximal performance levels, increasingly large training volumes are required to maintain or further improve results, with progressively smaller gains [54]. Evidence from "minimal dose" research suggests that higher-level athletes require training intensities >85% of 1RM to produce even modest improvements, particularly in strength–power sports [55].

8. Algorithms for the Optimization of Sport Training

The advent of large-scale artificial intelligence (AI) introduces powerful new tools for optimizing sport training. Physiological data from wearable devices can be fed into reinforcement-learning algorithms such as Proximal Policy Optimization (PPO) to regulate training intensity in real time [56]. Other systems use Deterministic Policy Gradient (DDPG) methods to generate individualized training plans incorporating environmental conditions and athlete history [57]. Additional algorithms optimize concurrent training programs by minimizing interference between competing physiological pathways—such as endurance- and strength-related molecular signaling [58,59]. Recursive neural networks can predict decrements in jumping performance over time [60].

AI has also transformed injury-prevention strategies. Random forest models predict injury probability in soccer players based on behavioral and historical data [61]. Clustering methods can categorize athletes into "response groups," distinguishing those who respond more favorably to pyramid-style progressive intensification from those who benefit from polarized training programs [62,63]. Automated biomechanical systems have also been developed to monitor and refine technique in competitive weightlifting [64,65].

However, integrating AI into daily training raises questions about reliability and the psychological dynamics of human–machine interaction. The effectiveness of these systems depends partly on coach–athlete and athlete–AI communication. Current "affective AI" technologies remain limited in interpreting emotions, though some systems can infer mood from linguistic content or facial features [66]. Studies have attempted to classify emotional responses to dance based on movement smoothness [67,68]. In tennis, motion analysis and pose estimation can identify player fatigue: lowered head and shoulder posture correlates with reduced energy levels and deteriorating mood [69]. Likewise, vocal parameters such as reduced fundamental frequency (pitch) have been linked to discouragement and low energy during competition [70].

9. Psychological Factors: The Strength of the Will

Recent research has revived interest in willpower as a determinant of muscular strength. Psychological investigation of strength dates back to the 1800s; for instance, Sigmund Freud conducted strength measurements on himself during experiments with psychoactive substances [71]. A conceptual link between muscular strength and willpower—and the idea that will can be trained—has been explored in contemporary psychology [72,73]. Overcoming small, progressive challenges in everyday life is proposed as a practical method for training willpower.

Physiologically, willpower is associated with strong activation of motor pathways, including dopamine activity in motor cortical regions such as the striatum [74]. Ernst Mach described will as a summation of stored sensations of effort and success transmitted through neural structures to generate movement [75], concluding that "will is nothing more than a particular case of nervous excitation... the psychical and the physical processes are identical in their content" [76].

Despite these theories, the scientific study of will remains nascent. Only a few investigations have directly linked cognitive processes to motor activation [77]. One promising approach integrates high-resolution fMRI with EEG to identify the temporal coupling between neural activity in the primary motor cortex and the emergence of motor commands [78].

 doi:10.20944/preprints202604.0567.v1

Recent advances in "mind-captioning" AI allow for the translation of thoughts into verbal statements or images. Semantic decoding algorithms can translate fMRI voxel patterns into human language [79]. Unlike methods relying on intact motor cortical structures to decode intended actions [80], mind captioning can infer motion intentions even when motor areas are damaged.

10. Conclusions

Training theory and methodology are grounded in physiological principles. However, the connection between these principles and practical training prescriptions is often based more on logical inference than on direct empirical validation. The scientific literature presents mixed and sometimes contradictory results. Thus, training methodology remains in its developmental stages and relies heavily on speculative reasoning rather than robust science.

Significant work is needed to bridge the gap between physiological mechanisms and practical training applications. Recent advances in AI and brain sciences offer promising avenues for understanding motor learning, including the possibility of identifying and correcting faulty motor patterns directly at the cognitive level, as motor plans are generated in the brain.

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doi:10.20944/preprints202604.0567.v1

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