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Exercise-Associated Muscle Cramps: Pathophysiology and Evidence-Based Prevention Strategies - a narrative review

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Abstract

Background. Exercise-associated muscle cramps (EAMC) are among the most common acute conditions affecting athletes across endurance, team, and individual sports, yet their pathophysiology remains contested. Two principal theories dominate: the historical dehydration-electrolyte depletion hypothesis and the neuromuscular control theory, with emerging evidence implicating fatigue-related spinal disinhibition, persistent inward currents, and impaired termination of contraction.

Aim. To critically synthesise current evidence on the pathophysiology, risk factors, and prevention and treatment strategies for EAMC, situating this condition within exercise physiology, electrolyte and magnesium homeostasis, and heat-related illness.

Materials and Methods. This narrative review draws on peer-reviewed epidemiological studies, prospective and case-control cohorts, randomised controlled trials, neurophysiological studies, genetic analyses, consensus statements, and mechanistic reviews addressing muscle cramping, electrolyte disorders, magnesium physiology, and heat illness.

Results. Cohort studies consistently identify prior cramping history, longer race distance, higher relative exercise intensity, chronic disease, allergy history, and previous injury as independent predictors of EAMC, whereas dehydration and serum electrolyte concentrations show

inconsistent associations. Neurophysiological studies demonstrate muscle-specific, rather than generalised, alterations in motoneuron discharge behaviour among cramp-susceptible individuals.

Conclusions. EAMC pathophysiology is multifactorial, and no single mechanism explains all presentations. Evidence-based prevention should prioritise correction of identifiable individual risk factors and targeted neuromuscular strategies over generalised hydration or electrolyte protocols.

Keywords: muscle cramp; exercise physiology; neuromuscular control; electrolyte disorders; magnesium deficiency; heat-related illness; sports medicine

1. Introduction

Exercise-associated muscle cramps (EAMC) are defined as sudden, painful, involuntary contractions of skeletal muscle occurring during or shortly after physical exercise, typically resolving within seconds to minutes but occasionally persisting for longer periods with residual soreness [1]. The condition has been documented in athletic populations for well over a century, yet despite its ubiquity, EAMC remains one of the least mechanistically understood complaints in sports medicine. Cramping affects a remarkably heterogeneous range of individuals, from elite ultra-endurance athletes to recreational cyclists, and its prevalence estimates vary enormously depending on the sport, the population studied, the definition applied, and whether lifetime, annual, or in-event prevalence is measured [2].

The clinical importance of EAMC extends beyond simple discomfort. In endurance events, cramping is among the most frequent reasons for medical encounters and can force athletes to slow, stop, or withdraw entirely from competition [2]. In occupational and industrial settings, historical accounts describe cramping among miners, steelworkers, and dam construction workers subjected to heavy physical exertion in hot environments, observations that shaped the earliest theories of causation [1]. In clinical populations such as those undergoing haemodialysis, cramping is a frequent and distressing complication that can compromise treatment adherence [3]. The condition thus spans a spectrum from a benign inconvenience in recreational exercisers to a marker of more complex neuromuscular or metabolic derangement in specific clinical contexts.

Historically, two competing explanatory frameworks have dominated discussion of EAMC pathophysiology. The dehydration and electrolyte depletion theory, dating to observations among

miners and industrial workers in the early twentieth century, proposes that sweat-induced losses of water and electrolytes—principally sodium and chloride—create a contracted interstitial fluid space that sensitises motor nerve terminals and precipitates cramping [1]. This theory dominated clinical thinking for decades and continues to inform much of the popular and even some professional advice given to athletes regarding hydration and electrolyte supplementation. The competing altered neuromuscular control theory, formalised by Schwellnus and colleagues in the late 1990s, proposes instead that muscle fatigue disturbs the normal balance between excitatory afferent input from muscle spindles and inhibitory input from Golgi tendon organs, producing sustained and abnormal alpha motor neuron discharge at the level of the spinal cord [1,4]. This theory has garnered increasing support from laboratory studies of electrically induced cramping and from large epidemiological cohorts that have failed to demonstrate consistent associations between cramping and measures of dehydration or serum electrolyte concentration [5].

More recently, additional layers of complexity have emerged. Neurophysiological work employing high-density surface electromyography has begun to dissect the specific alterations in motoneuron discharge behaviour that distinguish cramp-susceptible individuals from controls, implicating persistent inward currents and muscle-specific rather than generalised excitability changes [6]. A parallel line of investigation has proposed that cramping might be better conceptualised as a failure of muscle relaxation rather than purely a disorder of excessive activation, integrating neural, metabolic, and calcium-handling mechanisms into a unified framework relevant across both exercise-associated and disease-associated cramping contexts, such as haemodialysis [3,7]. Genetic and biomechanical hypotheses have further diversified the field, proposing connective tissue polymorphisms and even the mechanical properties of playing surfaces as upstream contributors to cramp susceptibility [8].

Superimposed on this mechanistic uncertainty is a substantial body of epidemiological research identifying risk factors for EAMC across diverse athletic populations, including distance runners, cyclists, and triathletes. These studies consistently implicate prior cramping history and higher relative exercise intensity as robust predictors, while offering more equivocal support for the role of chronic disease, allergy history, training experience, and previous injury [2,9,10]. Understanding these risk factors is clinically important because effective prevention strategies are likely to depend on correctly identifying the dominant mechanism operating in a given individual

or population, rather than applying a uniform hydration or electrolyte protocol to all cramp-prone athletes.

This narrative review aims to synthesise the current evidence regarding the pathophysiology of EAMC, critically evaluate the historical and contemporary theories of causation, examine the epidemiological evidence for risk factors across athletic and clinical populations, and assess the evidence base for prevention and treatment strategies ranging from hydration and electrolyte supplementation to neuromuscular electrical stimulation and stretching. Given the persistent controversy surrounding EAMC aetiology, particular emphasis is placed on identifying where the evidence is strong, where it is weak or contradictory, and where clinically relevant gaps remain.

2. Materials and Methods

This article was conceived as a narrative review rather than a systematic review, and accordingly no review protocol was registered, and no formal risk-of-bias appraisal or quantitative meta-analytic synthesis was undertaken. Sources were identified through targeted searches of Open Access repositories and aggregators, including OpenAlex, Europe PMC, and Crossref, focusing on peer-reviewed, English-language publications addressing exercise-associated muscle cramping, electrolyte disturbances in athletes, magnesium physiology and deficiency, and heat-related illness, with priority given to material published from 2015 onward and available in full text through open access; each digital object identifier was verified against its registry entry prior to inclusion. Sources spanning earlier publication dates were retained where they provided foundational epidemiological or mechanistic data of continued clinical relevance, such as the original prospective cohort studies establishing the altered neuromuscular control theory and the genetic disorder literature underpinning current understanding of magnesium homeostasis. Material was grouped thematically into sections addressing historical and contemporary pathophysiological theories, epidemiological risk factors across distinct athletic populations (distance runners, cyclists, triathletes), the role of electrolyte and magnesium disturbances, heat-related illness as a differential consideration, neurophysiological and genetic mechanisms, and evidence-based prevention and treatment strategies, including hydration, electrolyte and magnesium supplementation, stretching, and neuromuscular electrical stimulation. Because source selection, thematic grouping, and interpretive emphasis were, by design, undertaken narratively rather than systematically, this review may be subject to selection and emphasis bias,

and its conclusions should be understood as a clinically oriented synthesis rather than an exhaustive or formally graded account of all available evidence.

3. Definitions, Clinical Presentation, and Terminology

Exercise-associated muscle cramps are most commonly defined as a painful, spasmodic, involuntary contraction of skeletal muscle occurring during or immediately after muscular exercise [1,4]. This definition, first articulated in the context of marathon running research, has been widely adopted across the epidemiological literature and forms the basis for most subsequent risk-factor studies [9]. Clinically, EAMC is characterised by acute onset of pain, visible or palpable muscle knotting or tautness, and a joint often locked in an end-range position, features that help distinguish it from other causes of exercise-related muscle pain [8]. Some patients report subtle muscle fasciculations preceding the onset of a full cramp, a phenomenon termed the cramp-prone state, during which resting electromyographic activity is elevated relative to non-cramping muscle even though the individual has not yet developed an overt cramp [8].

Severity classification distinguishes a spectrum ranging from the cramp-prone or precramping state, through mild-to-moderate (benign) cramps that are self-limiting and typically resolve with cessation of activity or gentle stretching, to severe or serious cramps that occur in conjunction with systemic symptoms such as dizziness, collapse, nausea, vomiting, dark urine, or altered consciousness, indicating an underlying medical condition such as a serum electrolyte abnormality or acute kidney injury that requires urgent evaluation [8]. This distinction has practical importance: the vast majority of EAMC episodes encountered on the field of play fall into the mild-to-moderate category, but clinicians supervising endurance events must remain alert to the minority of presentations that signal a more serious underlying derangement.

Terminological confusion further complicates the literature, particularly regarding the relationship between muscle cramps and muscle spasms, especially in neurological populations. A scoping review examining muscle cramps and spasms in patients with upper motor neuron disorders—encompassing spinal cord injury, cerebral palsy, traumatic brain injury, and stroke—screened 4,202 studies and found that the overwhelming majority (217 of 253 included studies) used the term "spasm" rather than "cramp," with only seven studies using "cramp" exclusively and 29 using both terms [11]. Of the 253 studies reviewed, approximately half provided no

explicit description of the phenomenon they were reporting, and among those that did, the clinical features described for spasms in upper motor neuron disease overlapped substantially with the classical features of cramps in healthy individuals, including onset, duration, electromyographic characteristics, susceptibility to fatigue and exercise, pain, and relief through stretching [11]. This finding raises the possibility that cramping is systematically under-recognised and potentially misclassified as spasticity in patients with central nervous system lesions, a distinction that carries direct treatment implications since spasms are conventionally managed with central nervous system-depressing medications, whereas cramps are more often addressed with non-pharmacological approaches such as stretching [11]. The authors of this scoping review explicitly caution that more than twenty-five different methods are used to quantify spasms or cramps in the upper motor neuron disease literature, the majority relying on patient self-report without objective corroboration, and that no existing measure reliably distinguishes between the two phenomena [11].

4. Historical Perspective: The Dehydration-Electrolyte Depletion Theory

The earliest systematic descriptions of exercise- and heat-associated cramping emerged from occupational medicine in the early twentieth century, particularly among miners, dam construction workers, and steelworkers subjected to intense physical exertion in hot underground or industrial environments [1]. These large-scale industrial observations, though limited by the analytical methods available at the time, carried the substantial advantage of access to very large worker populations with carefully maintained medical and productivity records [1]. Early investigators attributed cramping in this setting to a combination of high ambient temperature, excessive drinking of plain water in response to thirst, and continued hard physical work, describing the phenomenon as a form of "water poisoning of the muscles brought about by the combination of great loss of chloride by sweating, excessive drinking of water, and temporary paralysis of renal excretion" [1]. Notably, this original formulation did not attribute cramping simply to dehydration, as is sometimes retrospectively claimed, but rather to the specific combination of substantial sweat electrolyte losses combined with inappropriate, excessive intake of electrolyte-free water, a subtlety often lost in later summaries of this literature [1].

The strongest historical evidence supporting a role for water and salt balance disturbances derives from large prospective intervention studies conducted at the Hoover Dam construction site and in

Ohio steel mills, where researchers characterised the biochemical profile of cramping workers as showing dehydration, lowered serum sodium and chloride concentration, minimal urinary sodium or chloride excretion, increased serum protein concentration and red cell count, yet normal osmotic pressure—a complex and partially contradictory pattern combining features of both dehydration and relative overhydration [1]. Critically, in the largest of these intervention studies, involving approximately 12,000 workers at one steel mill, the addition of saline to drinking water while a comparable population at neighbouring mills continued to receive plain water was reported to have almost completely abolished cases of muscle cramping, whereas in previous years and at mills continuing to provide plain water, up to twelve cases of cramp-related hospitalisation occurred in a single day [1]. This intervention trial remains, even by contemporary standards, one of the most compelling pieces of evidence supporting a causal role for electrolyte disturbance in a specific occupational heat-stress context.

Subsequent smaller-scale observational work in athletic populations offered some corroborating evidence for a role of sweat sodium losses. Comparative studies of American football players found that those with a self-reported history of cramping had substantially higher sweat sodium losses during training sessions, on the order of 1.18 g or more, compared with non-cramping teammates, and were estimated to be approximately nine times more likely to be cramp-prone when sweat sodium losses exceeded this threshold [8]. A case series comparing cramp-prone footballers with matched controls further found that the cramp-prone group derived a greater percentage of their fluid intake from plain water rather than electrolyte-containing sports drinks, despite only a modest difference in total sodium intake, and exhibited higher sweat sodium concentrations, incurring a substantially greater cumulative sodium deficit over a training session [8].

However, the dehydration-electrolyte depletion theory has faced substantial and mounting challenges over subsequent decades. A frequently cited internal inconsistency is that the theory requires cramping to result from both significant sweat-induced plasma volume contraction, which would be expected to increase plasma osmolality and draw fluid from the interstitial space into the vasculature, and simultaneous substantial sodium loss as a "salty sweater," which would conversely lower plasma osmolality and reduce this same fluid shift—a physiologically contradictory combination that has never been satisfactorily reconciled [8]. Multiple observational studies of endurance runners and triathletes have failed to demonstrate meaningful

differences in plasma volume, red cell volume, body mass loss, or plasma electrolyte concentration between athletes who developed cramping during competition and those who did not [8]. Even under conditions of substantial induced dehydration, controlled laboratory studies have found no measurable change in skeletal muscle resting membrane potential, undermining the proposed mechanistic link between fluid loss and altered neuromuscular excitability [8]. Furthermore, if cramping were fundamentally a systemic disturbance of electrolyte balance, it would be expected to manifest across multiple muscle groups rather than being overwhelmingly confined to the specific muscles actively engaged in the exercise task, which is the pattern most consistently observed clinically [1,8].

5. The Altered Neuromuscular Control Theory

In direct response to the accumulating inconsistencies in the dehydration-electrolyte hypothesis, Schweltnus and colleagues proposed in 1997 an alternative mechanistic framework centred on disturbed neuromuscular control at the spinal level [4]. This theory holds that muscle fatigue, arising from unaccustomed exercise intensity, insufficient conditioning, or prolonged repetitive contraction, produces an imbalance between excitatory afferent input from muscle spindles and inhibitory afferent input from Golgi tendon organs, with the net effect being sustained and abnormal firing of the alpha motor neuron [4,8]. The theory originated from observations in animal models that fatiguing electrical stimulation altered the firing characteristics of both muscle spindle and Golgi tendon organ afferents, with muscle spindle afferent discharge increasing and Golgi tendon organ inhibitory discharge decreasing and being delayed following fatiguing stimulation protocols [8].

Several lines of clinical and experimental evidence have been marshalled in support of this framework. Cramping is observed to occur predominantly in muscles that span two joints and that are therefore susceptible to contracting in an already shortened position, such as the gastrocnemius, hamstrings, and quadriceps—a biomechanical configuration in which tension on the muscle tendon, and consequently inhibitory feedback from the Golgi tendon organ, is reduced, thereby favouring an unopposed excitatory drive to the alpha motor neuron [4,8]. Clinically, EAMC most frequently occurs toward the end of prolonged exercise bouts, when fatigue is presumed to be greatest, a temporal pattern documented across marathon runners, ultramarathon runners, and triathletes [8,9]. The single most consistently effective acute

treatment for an active cramp—passive stretching of the affected muscle—is mechanistically explained within this framework by the resulting increase in tendon tension, which activates the Golgi tendon organ and increases inhibitory input to the alpha motor neuron, thereby restoring the disturbed excitatory-inhibitory balance and terminating the cramp [4,8].

Laboratory models employing either voluntary maximal contraction of a muscle held in a shortened position, or electrically evoked contractions delivered at progressively increasing stimulation frequencies, have been used to induce cramping reliably enough for experimental study, given the notorious unpredictability of spontaneously occurring EAMC in the field [12]. These studies have established the concept of the cramp threshold frequency, defined as the minimum electrical stimulation frequency required to elicit a cramp in a given muscle, and have consistently demonstrated that individuals with a self-reported history of cramping exhibit a significantly lower cramp threshold frequency than non-cramping controls, with one foundational study reporting mean values of 14.9 ± 1.3 Hz in cramp-history-positive individuals compared with 25.5 ± 1.6 Hz in cramp-history-negative individuals [8,13]. This objective electrophysiological marker of individual cramp susceptibility has since underpinned a substantial body of subsequent mechanistic and interventional research.

Nonetheless, the altered neuromuscular control theory is not without its own limitations and unresolved questions. The original animal studies demonstrating fatigue-induced changes in muscle spindle and Golgi tendon organ discharge employed supramaximal electrical stimulation frequencies, of the order of 100 Hz, that considerably exceed the physiological recruitment frequencies observed during normal voluntary human muscle activation, raising questions about the direct applicability of these findings to naturally occurring exercise-induced fatigue [13]. It also remains unclear precisely how much neuromuscular fatigue is required before cramping is triggered, whether this fatigue must be predominantly peripheral or central in origin, and why well-conditioned, highly trained athletes—who might be expected to exhibit greater fatigue resistance—nonetheless continue to experience cramping, indicating that training status and fatigue resistance alone cannot fully account for individual susceptibility [8]. A further complication is that at least one controlled laboratory study found that localised, fatiguing muscle contractions actually decreased electrically induced cramp susceptibility rather than increasing it as the theory would predict, a finding that has not been satisfactorily reconciled with the broader framework [8].

6. The Multifactorial Model and Emerging Integrative Frameworks

Given the persistent limitations of both the dehydration-electrolyte and the purely neuromuscular explanatory models, several authors have proposed multifactorial frameworks that integrate multiple contributing pathways rather than positing a single unifying mechanism. Miller's multifactorial model, building explicitly on the Schwellnus altered neuromuscular control framework, proposes that numerous distinct intrinsic factors—such as prior muscle injury, deconditioning, and pain—interact with extrinsic factors—such as hot or humid environmental conditions and repetitive exercise demands—through multiple converging pathways to alter neuromuscular control and precipitate cramping [8]. Central to this model is the concept of a factor threshold: an individual accumulates risk from multiple intrinsic and extrinsic sources simultaneously, and cramping occurs only once this cumulative threshold is exceeded, with the threshold itself capable of being raised or lowered by the interaction of co-occurring risk factors [8]. This framework offers a plausible explanation for the observation that identical environmental and exercise conditions produce cramping in some individuals but not others, and that a given individual may cramp in some situations but not in others of apparently similar demand.

A more recent and mechanistically ambitious integrative proposal reframes muscle cramps not primarily as disorders of excessive neuromuscular activation, but as disorders of impaired termination of muscle contraction, a concept the author terms "failure of relaxation" [3]. This framework, developed initially in the context of dialysis-associated muscle cramping but explicitly extended to exercise-associated cramping given the shared physiological stresses involved, integrates three interacting layers: a chemical layer in which metabolic alkalosis alters extracellular ionised calcium availability and lowers the activation threshold of excitable membranes; a metabolic layer in which impaired energetic support—including reduced availability of adenosine triphosphate for calcium reuptake into the sarcoplasmic reticulum via the sarcoplasmic reticulum calcium-ATPase, and disturbances in phosphocreatine-mediated rapid energy buffering—compromises the efficiency of ATP-dependent relaxation processes; and a neural layer in which sustained motor unit activity and diminished inhibitory control, mediated through gamma-aminobutyric acid and glycine, prevent appropriate termination of alpha motor neuron discharge [3]. Within this framework, sustained motor unit activity and altered inhibitory control are identified as central and strongly supported mechanisms, while calcium handling,

metabolic constraints, and cross-bridge kinetics are proposed as contributory factors that may modulate the persistence and severity of a cramp once neural disinhibition has been initiated, rather than as independent primary causes [3]. Notably, this model draws explicitly on experimental evidence that relaxation slowing can occur despite relatively preserved calcium reuptake capacity, implicating altered cross-bridge kinetics as an additional contributing mechanism beyond simple impaired calcium clearance [3]. The author explicitly frames this integrative concept as hypothesis-generating rather than definitively established, emphasising that many components of the proposed framework remain speculative and require further investigation to clarify the relative contribution of neural, metabolic, and peripheral mechanisms across different cramp-associated conditions [3].

7. Neurophysiological Mechanisms: Motoneuron Discharge and Persistent Inward Currents

Advances in high-density surface electromyography and motor unit decomposition techniques have enabled direct examination of motoneuron discharge behaviour in cramp-susceptible individuals, moving the field beyond inferential animal models toward direct human physiological measurement. A cross-sectional study comparing fourteen individuals with self-reported cramp susceptibility against fourteen non-cramping controls employed a validated cramp threshold frequency protocol to experimentally classify participants, and found a significant association between self-reported cramp history and experimentally induced cramping, with the odds of cramping during testing being eightfold higher in self-reported crampers than in controls (Fisher's exact test, $p = 0.046$, odds ratio 8.0) [6]. This finding both validates the cramp threshold frequency protocol as a meaningful experimental proxy for real-world cramp susceptibility and confirms that not all self-reported crampers will cramp under laboratory conditions, underscoring that susceptibility is likely to depend on the interaction between acute physiological state and prior cramp history rather than being a fixed, invariant trait [6].

This study examined discharge rate hysteresis (denoted ΔF), a paired motor unit analysis technique used as an indirect estimate of the contribution of persistent inward currents to motoneuron discharge, alongside other metrics including brace height, acceleration and attenuation slopes, and self-sustained discharge duration, in both the soleus and gastrocnemius medialis muscles before and after a cramp-inducing protocol [6]. At baseline, most motor unit

discharge metrics did not differ significantly between crampers and controls in either muscle, and spinal reflex excitability at rest, as reflected in the Hmax/Mmax ratio, was likewise comparable between groups, arguing against a model in which cramp susceptibility arises from a generalised, uniform elevation of spinal excitability [6]. However, a muscle-specific difference emerged: ΔF in the gastrocnemius medialis, but not the soleus, was significantly lower in crampers than in controls at baseline, suggesting a somewhat reduced contribution of persistent inward currents to discharge modulation specifically in this muscle, which is notably more frequently implicated in both experimental and spontaneous cramping than the soleus [6]. Following the cramp-inducing protocol, ΔF and normalised ΔF increased in the gastrocnemius medialis and self-sustained discharge duration increased in both muscles, changes that occurred similarly in both crampers and controls and thus appear to represent a general neuromodulatory response to intense repetitive activation rather than a cramp-specific phenomenon [6]. The single clearly group-dependent finding was that maximal discharge rate in the gastrocnemius medialis increased following the protocol in controls but not in crampers, suggesting a constrained capacity of cramp-prone motoneurons to further increase firing output following intense activation, potentially reflecting stronger recurrent inhibition, altered ion channel conductances, or differences in descending neuromodulatory input [6]. Wide-pulse, high-frequency neuromuscular electrical stimulation-evoked torque responses, extra torque, sustained electromyographic activity, and the tendon vibration-induced warm-up effect—all indices intended to probe centrally mediated persistent inward current contributions—did not differ significantly between groups, further reinforcing that cramp susceptibility is not associated with a global upregulation of spinal reflex excitability but rather with subtle, muscle-specific alterations in the dynamics and adaptability of motor unit discharge [6].

These neurophysiological findings carry an important implication for the broader theoretical debate: they demonstrate that cramp susceptibility cannot be reduced to a single, generalisable measure of "hyperexcitability" applicable across all muscles in a given individual, but instead appears to reflect localised, muscle-specific differences in motoneuron behaviour that may interact with the mechanical and biomechanical characteristics particular to frequently cramping muscles such as the gastrocnemius [6].

8. Genetic and Biomechanical Contributors to Cramp Susceptibility

Beyond acute physiological and neural mechanisms, evidence has accumulated for a heritable component to individual cramp susceptibility. A case-control genetic study recruiting 116 ultra-endurance athletes with a recent self-reported history of exercise-associated muscle cramping and 150 control participants with no such history examined variants in the COL5A1 gene, encoding a component of type V collagen involved in connective tissue structure, based on the hypothesis that variation in tendon and connective tissue properties might influence susceptibility to cramping through altered mechanical loading characteristics [8]. This study found that the COL5A1 CC genotype was significantly overrepresented among the control group (21.8%) relative to the cramping group (11.1%; $p = 0.031$), although no other related gene variants examined showed a differential distribution between groups, offering preliminary but not conclusive support for a genetic contribution to cramp susceptibility mediated through connective tissue mechanics [8]. This genetic association is further corroborated by independent epidemiological findings from a large case-control study of Ironman triathletes, in which a family history of cramping and previous tendon or ligament injury were identified as factors associated with a self-reported history of cramping, consistent with a role for connective tissue characteristics, whether genetically or injury-mediated, in individual susceptibility [10].

A more recent and conceptually novel hypothesis proposes that the mechanical properties of the athletic playing surface itself may function as an underrecognised upstream contributor to cramp susceptibility, operating through a proposed pathway in which exposure to unfamiliar or mismatched surface stiffness, energy dissipation, and energy return characteristics alters an athlete's muscle recruitment patterns and increases localised neuromuscular demand, thereby accelerating the onset of the fatigue-related state that precipitates the excitatory-inhibitory imbalance central to the altered neuromuscular control theory [8]. This hypothesis draws on studies employing surface electromyography during sprinting on fields with differing standardised mechanical properties—characterised using American Society for Testing and Materials protocols measuring force reduction, vertical deformation, and energy restitution—which found that muscle activation patterns differed measurably between surface types even before fatigue was induced, and that these differences were further amplified after a sport-specific fatigue protocol, with biceps femoris activity differing by approximately 50% between sexes and post-fatigue activation patterns differing by 13% from pre-fatigue conditions [8]. The

proposed mechanism suggests that athletes who train predominantly on one surface type but compete on a mechanically dissimilar surface are exposed to unaccustomed loading patterns that the neuromuscular system has not adapted to, potentially producing premature localised fatigue in the biarticular muscles—gastrocnemius, hamstrings, quadriceps—most commonly implicated in cramping [8]. The authors of this hypothesis explicitly acknowledge that it remains untested with respect to a direct relationship between surface mechanical mismatch and actual cramp incidence, and predict that any such effect would be conditional on high-intensity, competition-level exertion sufficient to approach an individual's cramp threshold following repeated or sustained exposure, rather than manifesting after a single brief exposure to an unfamiliar surface [8]. This remains, at present, a theoretical framework requiring direct experimental validation rather than an established mechanism.

9. Epidemiology of EAMC in Distance Runners

The largest epidemiological investigations of EAMC risk factors have been conducted in mass-participation distance running events, benefiting from very large sample sizes that permit robust multivariable analysis. A cross-sectional study drawing on 76,654 consenting race entrants from the 2012–2015 Two Oceans Marathon events in South Africa, encompassing both 21.1 km and 56 km race distances, found an overall lifetime prevalence of a history of EAMC of 12.8% (95% confidence interval 12.6–13.1), with the lifetime prevalence being significantly higher among 56 km entrants (16.0%) than among 21.1 km entrants (8.8%; $p < 0.0001$) [9]. In multivariable analysis adjusted for age and sex, independent risk factors associated with a history of EAMC in both race distances included a composite chronic disease score (prevalence ratio 1.9 for 21.1 km and 1.6 for 56 km entrants, for every two additional chronic diseases reported), a history of any running injury within the preceding twelve months (prevalence ratio 1.7 for 21.1 km and 1.4 for 56 km), and a history of any allergies (prevalence ratio 1.4 for 21.1 km and 1.2 for 56 km), together with several training-related variables including years of recreational running, average weekly training frequency, and average training speed, each showing prevalence ratios in the range of 1.0 to 1.1 [9]. Male sex and older age were also significantly associated with a higher prevalence of EAMC in both race distances, with the prevalence ratio for male versus female entrants being approximately 1.9 to 2.0 across both distances [9].

The mechanism underlying the association between chronic disease and allergy history and EAMC remains speculative. The authors of this study suggest that both the underlying chronic conditions themselves and, more plausibly, the medications used to treat them—such as antihistamines, which are known to cause fatigue and drowsiness as side effects—might contribute to premature muscle fatigue during exercise and thereby predispose to the altered neuromuscular control pathway implicated in cramping, although this remains a hypothesis requiring direct investigation rather than an established causal chain [9]. Notably, this same research group's earlier and larger cross-sectional study of 15,778 distance runners had similarly identified underlying chronic disease, medication use, a history of running injuries, and greater running experience as independent factors associated with a history of exercise-associated muscle cramping, providing a degree of internal replication for these findings across overlapping but distinct study populations [9].

The relationship between EAMC and race distance—and, by extension, exercise duration and cumulative fatigue—receives further support from an independent 161 km ultramarathon study, in which muscle cramping or "near cramping" (a controllable, sub-threshold sensation of impending cramp) affected 14.3% and 26.8% of surveyed finishers, respectively, for a combined prevalence of 41.1% [14]. This study found that the calf, quadriceps, and hamstring muscles were the most commonly affected sites, together accounting for over 130% of reported cramp locations when summed across the survey population (reflecting that many runners experienced cramping in more than one muscle group), a pattern consistent with the biomechanical hypothesis that muscles under the greatest exercise demand and susceptibility to shortened-position contraction are preferentially affected [14]. Critically, this study found no significant relationship between EAMC or near-cramping and either percentage body weight change during the race or post-race serum sodium concentration, but did find that runners with cramping or near-cramping had significantly higher post-race blood creatine kinase concentrations (a marker of muscle damage) and significantly higher post-race blood urea nitrogen than those without cramping, interpreted by the authors as indicating that cramping individuals were placing greater relative demands on their muscles during the race relative to their current state of training, rather than experiencing a distinct fluid or electrolyte disturbance [14]. A prior history of muscle cramping during an ultramarathon was strongly associated with both cramping and near-cramping in this event, with

previously cramp-affected runners being 2.5 times more likely to experience cramping or near-cramping during the study race than those without such a history [14].

10. Epidemiology of EAMC in Cyclists and Triathletes

While distance running has generated the largest epidemiological datasets, cycling and triathlon populations offer complementary and sometimes contrasting evidence regarding risk factor profiles. A descriptive cross-sectional study of 21,460 consenting entrants in the 2016 Cape Town Cycle Tour, a 109 km mass-participation road cycling event, reported a substantially higher retrospective lifetime prevalence of a history of EAMC than has been documented in comparable running populations, at 30.51%, with a retrospective annual incidence of 18.6% [15]. The quadriceps muscle group was overwhelmingly the most commonly affected site in this cycling population (47.7% of cramping episodes), followed by the calf (27.8%) and hamstring muscles (20.4%), a distribution the authors attribute to the specific biomechanical demand placed on the knee extensors as the prime movers generating force during the downstroke phase of the pedal cycle, in contrast to the more evenly distributed pattern of calf, quadriceps, and hamstring involvement typically reported in running populations [15]. Cramping most frequently occurred during the final quarter of the race (63.4% of episodes), a temporal pattern consistent with cumulative fatigue as a precipitating factor and closely mirroring the pattern documented in distance running populations [15].

Independent risk factors identified in multivariable regression analysis, adjusted for age and sex, in this cycling cohort included an increased number of years participating as a recreational cyclist (prevalence ratio 1.03 per five-year increase), a higher chronic disease composite score (prevalence ratio 1.36 for every two additional chronic diseases, described by the authors as demonstrating a "dose-dependent" relationship), a history of any allergies (prevalence ratio 1.18), a history of medication use before or during the event (prevalence ratio 1.41), and a history of either an acute injury (prevalence ratio 1.29) or a gradual-onset injury (prevalence ratio 1.30) [15]. These findings substantially replicate the risk factor profile identified in the distance running literature—chronic disease, allergy history, and previous injury each emerging as independent predictors across both sporting disciplines—lending cross-sport support to the plausibility of these associations, even though the precise causal mechanisms remain speculative [9,15]. The authors of the cycling study explicitly note that this represents, to their knowledge,

the first study to report independent risk factors for EAMC specifically in cyclists, and highlight the methodological limitation that a significant proportion of race entrants did not provide follow-up data, alongside the inherent limitation that self-reported, cross-sectional data cannot establish causal directionality [15].

Triathlon populations, and Ironman-distance events in particular, provide the most extensively studied evidence base regarding the specific predictive value of prior cramping history and relative exercise intensity, given the pioneering role of this population in the development of the altered neuromuscular control theory. A prospective cohort study of 210 Ironman triathletes found that increased running speed during the event and a previous history of cramping, rather than measures of dehydration or serum sodium concentration change, predicted the occurrence of exercise-associated muscle cramping, a finding widely cited as key evidence against the dehydration-electrolyte hypothesis and in favour of the exercise-intensity-mediated fatigue pathway [8]. A separate case-control study similarly found that Ironman triathletes with a self-reported history of EAMC were distinguished from non-cramping controls by greater body composition, shorter race completion time (indicating relatively higher exercise intensity), a positive family history of cramping, and a history of previous tendon or ligament injury [10].

More recent longitudinal work in this population has begun to explore the relationship between cramp frequency (rather than simply binary cramp history) and race-day hydration adherence. A longitudinal study of 136 triathletes completing a full Ironman-distance race, in which 33 participants developed EAMC during or after the race, found in exploratory logistic regression modelling that triathletes who reported a history of "infrequent" prior cramping had approximately 3.2-fold higher odds of experiencing EAMC during the study race compared with those reporting no prior cramping history, while those reporting a history of "frequent" prior cramping had approximately 19.7-fold higher odds [16]. This finding suggests a dose-response gradient in which the granularity of cramp frequency information may carry more clinically useful predictive information than a simple binary history variable, potentially reflecting an individual's underlying cramp threshold in a more nuanced manner [16]. This same study found that triathletes who did not adhere to their pre-planned race-day hydration strategy had approximately threefold higher odds of developing EAMC compared with those who adhered to their plan, although the authors are careful to note that they did not assess the specific characteristics of the hydration strategies employed—such as fluid volume, composition, or

timing—nor did they collect objective physiological hydration measures, meaning that the observed association reflects adherence to a self-defined strategy rather than an established causal link to hydration status itself, and should accordingly be interpreted with appropriate caution given the modest number of observed cramping events [16]. Age, sex, height, body mass, flexibility training, and race completion time relative to expectation were not significantly associated with EAMC occurrence in this cohort, consistent with prior triathlon research failing to identify these variables as robust risk factors [10,16].

Table 1 summarises representative epidemiological studies examining risk factors for EAMC across these three major athletic populations, illustrating both the consistency of certain risk factors across disciplines and the population-specific differences in affected muscle groups and prevalence estimates.

Table 1. Representative epidemiological studies of exercise-associated muscle cramp (EAMC) risk factors across athletic populations.

Source [ref]	Population / design	Sample size	Principal findings
de Jager et al. [9]	Distance runners (21.1 km and 56 km), cross-sectional, South Africa	76,654 entrants	Lifetime prevalence 12.8%; independent risk factors: chronic disease composite score (PR 1.6–1.9), running injury in past 12 months (PR 1.4–1.7), allergy history (PR 1.2–1.4), training variables (PR 1.0–1.1); higher prevalence in males and older entrants
Pohl et al. [15]	Recreational cyclists, cross-sectional, South Africa	21,460 entrants	Lifetime prevalence 30.5%; quadriceps most commonly

			affected (47.7%); independent risk factors: years as recreational cyclist (PR 1.03/5 yr), chronic disease score (PR 1.36), allergy history (PR 1.18), medication use (PR 1.41), acute (PR 1.29) and gradual-onset injury (PR 1.30)
Hoffman & Stuempfle [14]	161 km ultramarathon finishers, observational	280 survey respondents	Cramping/near-cramping in 41.1%; calf, quadriceps, hamstrings most affected; prior cramp history strongly associated (2.5-fold higher likelihood); no association with weight change or serum sodium; higher creatine kinase in crampers
Schwellnus et al. (cited in [8,10])	Ironman triathletes, prospective cohort and case-control	210 (cohort)	Increased running speed and prior cramp history predicted EAMC; dehydration and serum sodium change

			did not predict EAMC
Hauptenthal et al. [16]	Ironman-distance triathletes, longitudinal	136 (33 with EAMC)	Frequent prior cramping associated with ~19.7-fold higher odds; infrequent prior cramping with ~3.2-fold higher odds; non-adherence to hydration plan with ~3.0-fold higher odds

PR: prevalence ratio.

11. The Role of Sodium, Potassium, and Fluid Balance

Given the historical prominence of the dehydration-electrolyte theory, sodium metabolism and fluid balance warrant dedicated consideration, particularly since the relevant literature encompasses both cramping specifically and the broader spectrum of exercise-associated electrolyte disturbance. Sodium is the principal extracellular electrolyte, its concentration driving plasma tonicity and playing a central role in neuromuscular signal transmission via the neuromuscular junction [17,18]. Sweat sodium losses during exercise are highly variable between individuals, with reported losses ranging from approximately 0.51 g to 6.7 g per hour of exercise, meaning that in a single hour of intense exercise an athlete may lose an amount of sodium approaching or exceeding commonly cited total daily recommended intakes [17]. This substantial variability in individual sweat composition, influenced by genetics, diet, heat acclimatisation, and hydration status, likely explains much of the heterogeneity observed across studies examining sodium's relationship to cramping [17].

The physiological rationale for sodium's proposed protective role against cramping centres on its capacity to expand plasma volume and delay dehydration through enhanced fluid retention, a phenomenon termed sodium-induced hyperhydration. Controlled experimental studies in which participants ingested sodium prior to exercise have demonstrated measurable physiological

benefits along this pathway: one study found that sodium-supplemented cyclists exhibited significantly lower dehydration (0.7% versus 1.6% body mass loss) and improved subsequent time-trial performance compared with non-supplemented controls, an effect attributed to greater voluntary fluid consumption and retention following sodium loading [17,18]. Similarly, controlled studies in runners exercising in heat found that sodium administration before exercise extended the average time to exhaustion, both due to thermoregulatory limits and due to reaching a critical core body temperature threshold, compared with trials without sodium supplementation [18]. Research examining moderately trained women in a high-hormone menstrual phase similarly found that sodium administration extended time to exhaustion during cycling in warm conditions relative to non-supplemented trials [18].

Despite this body of evidence supporting a role for sodium in delaying dehydration and modestly enhancing endurance performance, the direct causal link between sodium status and cramping specifically remains considerably weaker and more contested than the link between sodium and general dehydration outcomes. As detailed in Section 4, large observational studies in marathon runners, ultramarathon runners, and Ironman triathletes have repeatedly failed to demonstrate significant differences in serum sodium concentration between athletes who cramp and those who do not [8,14]. This apparent paradox—sodium clearly influences hydration status and endurance capacity, yet shows inconsistent association with cramping specifically—suggests that whatever protective effect sodium supplementation confers against cramping in some contexts may operate indirectly, perhaps by delaying the onset of fatigue that ultimately triggers the neuromuscular pathway, rather than through a direct electrolyte-mediated mechanism at the level of the neuromuscular junction [1,8].

Potassium, the principal intracellular cation with a normal reference range of approximately 3.5–5 mmol/L, plays an essential role in muscle contraction, resting membrane potential regulation, and carbohydrate metabolism, and has been proposed to contribute to reducing lactic acid accumulation and associated fatigue [17]. Survey data examining micronutrient intake in athletes found that more than 50% of both male and female athletes failed to meet recommended potassium intake thresholds, a deficiency that has been linked to impaired training capacity and increased susceptibility to heat exhaustion, although a direct, specific link between potassium deficiency and EAMC has not been as extensively documented in controlled studies as has been the case for sodium [17]. Given that potassium is lost in sweat alongside sodium, albeit typically

in substantially smaller quantities, inadequate replacement during prolonged exercise represents a plausible contributory factor to overall neuromuscular fatigue susceptibility, though the evidence base directly linking potassium status to cramping incidence remains considerably less developed than that for sodium.

The clinical entity of exercise-associated hyponatraemia (EAH), while mechanistically and clinically distinct from EAMC, deserves consideration given the historical tendency to conflate cramping with broader electrolyte-related complications of endurance exercise. EAH is defined as a serum sodium concentration falling below 135 mmol/L, and its severity can range from mild and largely asymptomatic through to profound hyponatraemia below approximately 110–115 mmol/L, which carries a risk of cerebral oedema, central nervous system failure, and death [17,18]. Notably, the pathophysiology of severe EAH is understood to arise predominantly from overconsumption of hypotonic fluids relative to sweat losses, resulting in dilutional hyponatraemia, rather than from sodium depletion per se—a mechanism essentially opposite to the traditional dehydration theory of cramping, which posits that inadequate fluid and electrolyte replacement, rather than excessive intake, precipitates the problem [17,18]. This distinction underscores an important clinical point: prevention strategies for EAH (avoiding excessive hypotonic fluid intake) and the historically proposed prevention strategies for EAMC (ensuring adequate salt intake to prevent depletion) are not merely different but can, if uncritically applied, work at cross purposes, reinforcing the importance of individualised, evidence-based rather than blanket hydration advice for endurance athletes [17,18].

12. Magnesium Physiology and Its Proposed Role in Neuromuscular Excitability

Magnesium occupies a distinctive position in the muscle cramp literature: it is among the most commonly recommended supplements for cramp prevention in popular and even some clinical advice, yet the direct evidence connecting magnesium status specifically to exercise-associated cramping is considerably more equivocal than its broader, well-established roles in neuromuscular physiology would suggest. Magnesium is the second most abundant intracellular cation after potassium and serves as an essential cofactor for several hundred enzymatic reactions, including all reactions involving adenosine triphosphate, protein and nucleic acid synthesis, and the maintenance of normal neuromuscular excitability [17,19,20]. At the neuromuscular level, magnesium functions as a physiological calcium antagonist, competing with

calcium for binding sites on relevant transport proteins and channels, and critically, magnesium occupies the calcium channel of the N-methyl-D-aspartate receptor, blocking ion flow at resting membrane potential and thereby suppressing excessive excitatory neurotransmission [19,21]. Magnesium deficiency correspondingly reduces this inhibitory blockade, amplifying calcium influx and increasing neuronal excitability, a mechanism directly relevant to the broader concept of a hyperexcitable neuromuscular state predisposing to cramping [19,21].

At the level of the neuromuscular junction specifically, magnesium regulates the release of the principal excitatory neurotransmitter acetylcholine and modulates the release of inhibitory neurotransmitters including glycine and gamma-aminobutyric acid, functioning as what has been described as a systemic "harmonizer" of neuromuscular excitability across multiple levels of the nervous system, from peripheral nerve terminals through spinal interneuronal circuits to central regulatory structures such as the basal ganglia [21]. Magnesium deficiency has specifically been shown to reduce the normal inhibitory capacity over acetylcholine release from motor nerve terminals, and to reduce cholinesterase-mediated acetylcholine degradation, both changes that would theoretically be expected to increase susceptibility to sustained or excessive neuromuscular excitation of the type implicated in cramping [21]. Magnesium deficiency has similarly been implicated in reducing gamma-aminobutyric acid-mediated inhibition at the spinal level, potentially contributing to the hyperactivity of alpha and gamma motor neurons that characterises the altered neuromuscular control model of cramping [1,21]. From a purely mechanistic standpoint, therefore, magnesium deficiency represents a biologically plausible contributor to precisely the type of neuromuscular hyperexcitability that the altered neuromuscular control theory implicates in EAMC.

Despite this strong mechanistic rationale, the epidemiological and interventional evidence directly linking magnesium status to exercise-associated cramping specifically, as opposed to cramping in other clinical contexts such as pregnancy or nocturnal leg cramps in older adults, remains notably limited and inconsistent. Systematic review evidence addressing magnesium supplementation for exercise-associated muscle cramps specifically has found no clinically meaningful reduction in cramp frequency, intensity, or duration compared with placebo, a finding at odds with the strength of the underlying neurophysiological rationale [8,22]. This apparent disconnect between plausible mechanism and inconsistent clinical effect may reflect several factors: overt magnesium deficiency severe enough to produce measurable neuromuscular

hyperexcitability may be relatively uncommon among the generally well-nourished athletic populations studied in cramp research; serum magnesium concentration, the biomarker most readily measured, correlates poorly with total body or intracellular magnesium stores, since only approximately 1% of total body magnesium resides in the extracellular fluid compartment, meaning that many individuals with normal serum magnesium may nonetheless harbour clinically relevant intracellular deficits that remain undetected [19,23,24]; and the pathophysiology of EAMC, as detailed extensively in the preceding sections, appears to be dominated by acute fatigue-related neuromuscular dysregulation and mechanical factors specific to the exercise task, mechanisms that may simply be less amenable to correction through chronic magnesium repletion than would be the case for cramping arising primarily from a sustained deficiency state.

Magnesium homeostasis itself is tightly regulated through the coordinated actions of intestinal absorption, renal reabsorption, and skeletal storage, with approximately 99% of total body magnesium residing intracellularly, distributed between bone (50–65%), skeletal muscle, and soft tissue, and less than 1% present in the extracellular fluid compartment measured as serum magnesium [19,20,23-25]. Intestinal absorption occurs through both a passive, non-saturable paracellular route predominating in the jejunum and ileum, and an active, saturable transcellular route mediated principally by the transient receptor potential melastatin 6 and 7 channels, which becomes proportionally more important when luminal magnesium concentrations are low [19,20,26,27]. Renal handling is dominated by reabsorption in the thick ascending limb of the loop of Henle, accounting for 50–70% of filtered magnesium via a paracellular pathway dependent on the tight junction proteins claudin-16 and claudin-19, with fine-tuning of the final urinary excretion occurring in the distal convoluted tubule via active transcellular transport, again principally through transient receptor potential melastatin 6 [19,26,27]. This distal convoluted tubule segment represents the decisive regulatory site determining net magnesium balance, and disruption of its function—whether through inherited channelopathies or acquired causes such as diuretic or proton pump inhibitor use—is responsible for the majority of clinically significant hypomagnesaemic states [26-28].

13. Genetic Causes of Hypomagnesaemia: Insights into Neuromuscular Excitability

Although inherited hypomagnesaemic disorders represent rare conditions rather than a common contributor to typical EAMC, the substantial body of genetic research characterising these disorders has provided valuable mechanistic insight into the specific molecular pathways governing magnesium reabsorption and, by extension, the physiological consequences of magnesium deficiency on neuromuscular function. These genetic disorders are broadly classifiable into four categories based on the renal segment and pathophysiological mechanism affected: hypercalciuric hypomagnesaemias, arising from disrupted paracellular divalent cation transport in the thick ascending limb (including mutations in claudin-16, claudin-19, the calcium-sensing receptor, and the chloride channel ClC-Kb underlying Bartter syndrome type 3); Gitelman-like hypomagnesaemias, arising from disturbances in sodium, potassium, or chloride transport in the distal convoluted tubule that secondarily impair the transmembrane voltage gradient required for transcellular magnesium reabsorption via transient receptor potential melastatin 6 (including Gitelman syndrome itself, caused by mutations in the sodium-chloride cotransporter gene, and several rarer conditions); mitochondrial hypomagnesaemias, of uncertain precise mechanism but presumed related to the high mitochondrial density and energy demand of the distal nephron; and other hypomagnesaemias arising from direct mutations in transient receptor potential melastatin 6 itself or its regulatory pathways, including epidermal growth factor and its receptor [26,28].

Clinically, patients with hypomagnesaemia with secondary hypocalcaemia, caused by loss-of-function mutations in transient receptor potential melastatin 6, illustrate the profound neuromuscular consequences of severe magnesium deficiency in its most extreme form, typically presenting in infancy with serum magnesium concentrations that may fall to 0.2 mmol/L or lower, precipitating generalised seizures within the first months of life if untreated [26]. Gitelman syndrome, the most prevalent genetic cause of hypomagnesaemia with an estimated prevalence of approximately 1 in 40,000, characteristically presents later in childhood or adolescence with symptoms including muscle cramps, paresthesias, and in severe cases cardiac arrhythmia, occurring in the context of concurrent hypokalaemia and metabolic alkalosis [26,28]. The isolated dominant hypomagnesaemia caused by mutations in the gamma-subunit of the sodium-potassium-ATPase pump, though documented in only a small number of families, is notable for presenting with muscle cramps as an essentially universal clinical feature [26]. Similarly,

autosomal dominant hypomagnesaemia arising from mutations in the voltage-gated potassium channel Kv1.1 produces severe hypomagnesaemia accompanied by muscle cramps, tetanic episodes, tremor, and generalised muscle weakness, attributed to loss of the channel's normal role in maintaining the apical membrane voltage gradient that drives magnesium reabsorption via transient receptor potential melastatin 6 in the distal convoluted tubule [26,28].

The clinical presentations of these inherited disorders—muscle cramps, tetany, seizures, and generalised neuromuscular hyperexcitability—provide direct, if extreme, physiological confirmation that severe magnesium deficiency can indeed produce the type of neuromuscular hyperexcitability that has long been hypothesised to contribute to cramping in the general athletic population. However, the substantial gap between the profound serum magnesium depletion characteristic of these genetic disorders (often below 0.4 mmol/L, and in some cases essentially unmeasurable) and the much more modest magnesium status changes that might plausibly occur in an otherwise healthy athlete during a single competitive event underscores the biological implausibility of a direct mechanistic equivalence, and helps explain why the modest and often unremarkable magnesium fluctuations documented in athletic populations translate so inconsistently into a demonstrable relationship with EAMC.

14. Hypomagnesaemia in Broader Clinical and Nutritional Context

Beyond its rare genetic causes, acquired hypomagnesaemia is a considerably more common finding in general and hospitalised populations, with reported prevalence estimates in the general population ranging from approximately 1.5% to 15%, and reaching approximately 10% among hospitalised patients [24]. Recognised acquired causes include inadequate dietary intake—of particular relevance given that Western dietary patterns are frequently characterised by insufficient consumption of magnesium-rich foods such as green leafy vegetables, legumes, nuts, and whole grains—together with gastrointestinal losses from chronic diarrhoea or malabsorptive conditions, and increased renal losses associated with diabetes mellitus, chronic alcohol use, and a range of commonly prescribed medications including loop and thiazide diuretics, proton pump inhibitors, and certain chemotherapeutic and immunosuppressive agents [19,20,23-25]. Proton pump inhibitor-associated hypomagnesaemia, in particular, has been recognised as a class-related adverse effect since a formal regulatory safety communication was issued in 2011, with prevalence estimates among long-term users ranging from approximately 13% to over 50%,

particularly among elderly patients and those receiving concurrent diuretic therapy, and arising through impairment of transient receptor potential melastatin 6-mediated intestinal magnesium absorption secondary to elevation of intestinal luminal pH [23]. This mechanism is of practical relevance to sports medicine given the not infrequent use of proton pump inhibitors and diuretics among older recreational athletes and those with concurrent cardiovascular or gastrointestinal comorbidities, populations that overlap with those identified in the epidemiological literature as having elevated EAMC risk related to chronic disease and medication use [9,15].

Clinical manifestations of hypomagnesaemia span a spectrum from entirely asymptomatic mild deficiency through to severe, life-threatening presentations, with symptoms generally becoming clinically apparent once serum magnesium falls below approximately 0.5 mmol/L [19,20,24,25]. Mild-to-moderate deficiency most commonly manifests with nonspecific symptoms including lethargy, muscle cramps, and generalised muscle weakness, while moderate-to-severe deficiency produces more pronounced neuromuscular irritability—tremor, carpopedal spasm, and in severe cases generalised seizures—together with characteristic electrocardiographic changes including peaked T waves, prolongation of the PR and QT intervals, and QRS widening [19,20,25]. Severe hypomagnesaemia frequently coexists with, and can precipitate, concurrent hypocalcaemia and hypokalaemia, a combination that further complicates the clinical picture and increases the risk of malignant cardiac arrhythmia, and this clustering of electrolyte disturbances underscores the importance of considering magnesium status whenever unexplained or treatment-refractory hypokalaemia or hypocalcaemia is encountered clinically [19,20,25].

Beyond its direct neuromuscular effects, magnesium has been epidemiologically and mechanistically linked to a remarkably broad range of chronic disease states relevant to the general athletic and ageing population, including type 2 diabetes mellitus and insulin resistance, hypertension and broader cardiovascular disease, osteoporosis, migraine, depression, and asthma, reflecting magnesium's fundamental roles in glucose metabolism, vascular tone regulation, bone mineralisation, and bronchial smooth muscle relaxation [19,20,23-25]. Meta-analytic evidence indicates that oral magnesium supplementation produces modest but clinically relevant reductions in blood pressure among hypertensive and hypomagnesaemic individuals, and modest improvements in glycated haemoglobin among patients with type 2 diabetes, effects that appear most pronounced in individuals with documented baseline magnesium deficiency rather than in magnesium-replete populations [24]. This pattern—modest benefit concentrated in deficient

subgroups rather than a generalisable effect across all supplemented individuals—mirrors the pattern observed for cramp-specific outcomes and reinforces the broader principle that magnesium supplementation is most rationally targeted at individuals with a demonstrated or strongly suspected deficiency state, rather than applied indiscriminately as a universal cramp-prevention strategy in athletic populations without an identified risk factor for magnesium depletion.

15. Heat-Related Illness as a Differential Consideration

Heat-related illness represents an important differential and, in some cases, comorbid consideration in the clinical assessment of the exercising athlete presenting with muscle cramping, given both the historical conflation of "heat cramps" with EAMC and the shared environmental context in which both conditions typically arise. Heat cramps are formally classified as the mildest point on the spectrum of heat-related illness, positioned below heat syncope, heat exhaustion, and the most severe manifestation, heatstroke, which is clinically defined by a core body temperature exceeding 40°C accompanied by central nervous system dysfunction such as confusion, seizures, or coma [29]. Heatstroke itself is further subdivided into classic (non-exertional) heatstroke, typically affecting elderly or chronically ill individuals during passive environmental heat exposure, and exertional heatstroke, affecting predominantly younger, otherwise healthy individuals—including athletes, military personnel, and outdoor labourers—undergoing intense physical exertion, frequently but not invariably in combination with elevated ambient temperature [29,30].

It is important to emphasise, however, that contemporary evidence has substantially revised the traditional understanding of heat cramps as being causally driven primarily by elevated body temperature. Heat cramps are now understood not to be directly related to core body temperature per se, occurring across a range of ambient thermal conditions, and importantly, they are not relieved by the application of cooling modalities in the way that would be expected if hyperthermia were the direct causal mechanism, a finding that argues strongly against a simple thermal explanation and instead situates heat cramps mechanistically much closer to the fatigue- and electrolyte-related pathways discussed throughout this review than to a distinct thermoregulatory disorder [8]. This revision carries direct clinical relevance: the historically common practice of labelling exercise-associated cramping occurring in hot conditions as "heat

cramps" and treating it primarily through cooling interventions is not well supported by contemporary pathophysiological understanding, and such episodes should instead be approached using the same framework of fatigue, prior cramp history, and individual risk factor assessment applied to EAMC occurring in any thermal environment.

Nonetheless, the distinction between simple EAMC and evolving heat exhaustion or heatstroke remains of critical clinical importance, since the latter conditions carry substantially greater morbidity and mortality and require fundamentally different emergency management. Heat exhaustion is characterised by fatigue, headache, nausea, dizziness, hypotension, and tachycardia in the setting of an elevated but generally sub-40°C core temperature, with preserved neurological function, whereas the presence of central nervous system dysfunction alongside a core temperature of 40°C or greater signifies the transition to heatstroke, a genuine medical emergency requiring rapid cooling as the single most critical determinant of survival and neurological outcome [29,30]. Laboratory findings in heatstroke, reflecting the systemic inflammatory and multiorgan consequences of severe hyperthermia, may include haemoconcentration, leukocytosis, elevated creatine kinase reflecting rhabdomyolysis (frequently exceeding 10,000 IU/L), acute kidney injury, hepatocellular injury with transaminases sometimes exceeding 1,000 IU/L, and disseminated intravascular coagulation in severe cases—laboratory derangements considerably more extensive than would ever be expected in simple EAMC and that should prompt immediate escalation of care [29,30]. From a practical field-management perspective, the international consensus guidance developed for elite sporting events emphasises that clinicians and event medical staff should be trained to distinguish athletes with benign exhaustion, who can be directed toward a supervised recovery area, from those exhibiting central nervous system dysfunction, who require immediate transfer for core temperature assessment and, where indicated, rapid whole-body cooling using cold-water immersion, the single most effective cooling modality currently available [30].

Heat acclimatisation—the process of repeated heat exposure over one to two weeks, inducing physiological adaptations including enhanced sweat response, reduced plasma volume loss, and improved electrolyte conservation—represents a further consideration of direct relevance to cramp prevention discussions, since athletes who are inadequately acclimatised to anticipated competition heat conditions are recognised to be at substantially elevated risk of a range of heat-related complications, and by extension may plausibly be at elevated risk of the premature fatigue

that the altered neuromuscular control theory implicates in cramping, even though heat acclimatisation protocols have not been directly and specifically evaluated as an EAMC prevention strategy in the reviewed literature [30]. International consensus recommendations for elite competition in hot environments accordingly emphasise individualised hydration planning tailored to sweat rate and composition, avoidance of hypohydration exceeding 2% body mass loss, and the use of sodium-containing fluids at rates of approximately 0.5–0.7 g of sodium per litre for exercise exceeding one hour, escalating to 1.5 g per litre for athletes specifically prone to cramping, reflecting a pragmatic, individualised approach that acknowledges the persistence of clinical practice favouring sodium supplementation for cramp-prone individuals despite the mechanistic uncertainty discussed throughout this review [30].

16. Rhabdomyolysis and the Differential Diagnosis of Exercise-Induced Muscle Pain

A further important differential consideration when evaluating exercise-related muscle symptoms is exertional rhabdomyolysis, a condition that shares some superficial clinical overlap with severe or recurrent EAMC—both present with exercise-associated muscle pain and can occur in the context of unaccustomed or excessive physical exertion—but which represents a mechanistically and clinically distinct entity involving frank myocyte breakdown rather than a transient, reversible neuromuscular event. Exertional rhabdomyolysis is characterised biochemically by a substantial rise in serum creatine kinase, typically peaking 24–36 hours after the precipitating exercise and then declining at a rate of approximately 40% per day, accompanied by myalgia, muscle swelling, and weakness, with the diagnostic threshold for creatine kinase elevation debated in the literature but most commonly proposed to fall in the range of five to fifty times the upper limit of normal depending on the specific criteria applied [31]. Notably, most cases occurring in the context of unaccustomed but not extreme exercise represent a physiological, self-limiting response rather than a manifestation of underlying disease, as demonstrated in a large military training cohort study in which no cases meeting a strict definition of clinically symptomatic exertional rhabdomyolysis (requiring concurrent weakness and myoglobinuria in addition to elevated creatine kinase) were identified despite creatine kinase elevations exceeding ten times the upper limit of normal in 11% of participants at the peak of a demanding training period [31].

The relevance of exertional rhabdomyolysis to the differential diagnosis of EAMC lies principally in the recognition that recurrent, unusually severe, or atypically prolonged cramping-type symptoms—particularly when accompanied by dark urine, disproportionate muscle swelling, or persistent weakness extending well beyond the immediate post-exercise period—should prompt consideration of underlying muscle breakdown rather than simple cramping, and, in cases of recurrent presentation without a clear precipitating pattern of unaccustomed exertion, should raise suspicion for an underlying genetic myopathy predisposing to exercise intolerance [31]. The mnemonic "RHABDO," proposed to guide clinical screening for a genetic predisposition, incorporates recurrent episodes, hyperCKaemia persisting beyond expected resolution, accustomed (rather than unaccustomed) exercise precipitating the episode, blood creatine kinase exceeding fifty times the upper limit of normal, drugs or other exogenous factors being insufficient to explain the severity of presentation, and other family members being similarly affected or the individual reporting other exertional symptoms including cramps [31]. This framework, while developed specifically for the evaluation of rhabdomyolysis, offers a useful conceptual template for sports medicine clinicians assessing any athlete with recurrent or atypically severe exercise-associated muscle symptoms, reinforcing the broader principle articulated throughout this review that a detailed individual history—encompassing prior episode frequency, precipitating exercise characteristics, and family history—is central to appropriate clinical evaluation of muscle cramping in all its presentations.

17. Nutritional and Training-Related Preventive Considerations

Beyond the specific electrolyte and magnesium considerations addressed in preceding sections, a broader constellation of nutritional and training-related factors merit consideration within a comprehensive approach to EAMC prevention, reflecting the multifactorial model of cramp aetiology discussed in Section 6. Adequate carbohydrate availability during prolonged exercise is recognised to play a role in delaying the onset of fatigue, and given the centrality of fatigue to the altered neuromuscular control theory of cramping, ensuring sufficient carbohydrate intake—broadly in the range of 30 to 90 grams per hour depending on exercise duration and intensity, consistent with established sports nutrition guidance for endurance events exceeding approximately one hour—represents a physiologically plausible, if not cramp-specific, component of a broader fatigue-mitigation strategy [17,32]. Adequate pre-race hydration status, achieved through a structured pre-exercise fluid intake protocol rather than acute pre-competition

fluid loading, together with individualised fluid replacement during exercise guided by estimated sweat rate rather than a fixed volumetric target, forms the foundation of contemporary sports nutrition guidance for endurance athletes, reflecting the recognition that both underhydration and overhydration carry distinct performance and safety risks [17,32].

From a training perspective, the epidemiological literature reviewed in Sections 9 and 10 consistently identifies measures of relative rather than absolute exercise intensity—running or cycling faster than habitual training pace, or completing a race distance in less time than typically achieved—as more robust predictors of cramping than absolute measures of training volume or experience, a pattern that lends direct support to the fatigue-mediated pathophysiological framework and carries a practical implication for athletes and coaches: appropriate pacing strategies that avoid a mismatch between planned race intensity and an individual's current state of conditioning may represent one of the more evidence-supported, if underappreciated, preventive strategies available, in contrast to the disproportionate clinical and popular attention historically directed toward hydration and electrolyte supplementation [8,9,15]. This is further reinforced by findings that a history of running injury within the preceding twelve months constitutes an independent risk factor for cramping across multiple athletic populations, plausibly reflecting either localised muscle weakness and altered biomechanics predisposing to premature fatigue in the previously injured muscle group, or an increased reflex alpha motor neuron activity triggered by the local soft tissue injury itself, though the precise mechanism linking prior injury to subsequent cramp susceptibility remains to be directly elucidated [9,15].

18. Treatment and Prevention Strategies: Stretching, Pharmacological, and Nutritional Approaches

The management of an acute EAMC episode is most consistently and effectively addressed through gentle static stretching of the affected muscle, a strategy that, as detailed in Section 5, is mechanistically explained by the resulting activation of the Golgi tendon organ and consequent restoration of inhibitory input to the alpha motor neuron [4,8]. This intervention enjoys the strongest evidentiary support of any acute treatment strategy for EAMC and is uniformly recommended across the reviewed literature as the first-line approach for an ongoing cramp episode [4,8]. However, it is important to note that the evidence for stretching as a prophylactic, rather than acute treatment, strategy is considerably less robust: laboratory studies employing pre-

exercise stretching protocols have generally failed to demonstrate a reduction in subsequently measured electrically induced cramp susceptibility, and observational studies of stretching frequency and habitual flexibility among distance runners have similarly failed to identify a consistent protective association with cramp occurrence, suggesting that the beneficial mechanical effect of stretching may be specific to its acute, reflexive action during an active cramp rather than reflecting a durable prophylactic training adaptation [8].

A range of oral remedies—including pickle juice, mustard, and various commercially marketed electrolyte products—have attracted considerable popular and some clinical interest as acute cramp treatments, and the evidence for pickle juice in particular merits specific mention given the relatively rigorous experimental characterisation it has received. Controlled laboratory studies employing electrically induced cramping have found that small volumes of pickle juice can reduce the duration of an induced cramp by approximately 35–45% relative to no fluid or plain water, an effect that occurs far more rapidly than would be plausible for a fluid or electrolyte absorption-mediated mechanism, since it manifests before the ingested volume could plausibly reach and influence systemic circulation [8]. This observation has led to the proposed mechanism that constituents of pickle juice, most likely the acetic acid responsible for its characteristic taste, may trigger a reflexive inhibitory response originating from oropharyngeal or gastric sensory receptors, acting via afferent pathways to reduce alpha motor neuron firing rather than via any systemic electrolyte or hydration effect [8]. This mechanistic interpretation is corroborated by studies demonstrating that ingestion of small volumes of pickle juice produces no measurable change in plasma sodium, potassium, magnesium, calcium concentration, plasma osmolality, or plasma volume, definitively excluding a systemic electrolyte-mediated explanation for the observed acute therapeutic effect [8]. It is important to emphasise, however, that this body of evidence pertains specifically to cramping induced experimentally through electrical stimulation of a small isolated foot muscle held in a shortened position, and cannot be directly extrapolated as proof of efficacy for spontaneously occurring EAMC in the field, a caveat the original investigators explicitly acknowledge.

Quinine, historically among the most widely used pharmacological agents for muscle cramp prophylaxis, has fallen substantially out of favour following regulatory restriction of its over-the-counter availability due to safety concerns, and contemporary systematic review evidence indicates that while quinine does produce a statistically significant reduction in cramp frequency

and intensity, the magnitude of this effect is clinically modest—amounting to a mean reduction of fewer than two cramp episodes over a two-week treatment period in pooled meta-analytic estimates—while carrying a documented risk of both minor and, less commonly, serious adverse events including gastrointestinal disturbance and thrombocytopenia [8]. On this basis, quinine cannot be recommended as a routine prophylactic strategy for EAMC given its unfavourable risk-benefit profile relative to its modest demonstrated efficacy.

Bananas, frequently recommended anecdotally as a potassium-rich prophylactic or treatment food for cramping, have received limited direct experimental scrutiny, but the available evidence indicates that ingestion of one or two servings does not produce a measurable increase in plasma potassium concentration or plasma volume until approximately sixty minutes following consumption, a delay that renders this intervention implausible as an effective acute treatment for an active cramp episode, though it may retain a role within a broader strategy of ensuring adequate overall dietary potassium intake as discussed in Section 11 [8].

19. Neuromuscular Electrical Stimulation as a Preventive Intervention

Among the various prevention strategies evaluated in the reviewed literature, targeted neuromuscular electrical stimulation protocols designed specifically to raise an individual's cramp threshold frequency represent the intervention with the most direct mechanistic rationale and the most compelling controlled experimental support currently available, distinguishing this approach from the generally weaker or inconsistent evidence base underpinning hydration, electrolyte, and stretching-based strategies. The foundational randomised controlled trial in this area allocated fifteen healthy male participants to either an intervention group receiving unilateral electrical stimulation of the calf musculature delivered in a shortened position specifically designed to induce repeated experimental cramping (with the contralateral limb serving as a within-subject comparator stimulated in a neutral, non-cramping position), or a non-treatment control group, applying the protocol twice weekly over a six-week period [12]. This trial found that the cramp threshold frequency in the calf muscles stimulated in the cramp-inducing shortened position increased significantly, from a baseline mean of 23.3 ± 5.7 Hz to 33.3 ± 6.9 Hz after three weeks of training ($p < 0.001$), and further to 35.3 ± 6.0 Hz after six weeks, whereas no significant change occurred in either the contralateral limb stimulated in the neutral position or in the control group's untrained limbs [12]. Critically, this study identified a clear dose-response

relationship between the cumulative electrical stimulation energy delivered across the training period and the magnitude of cramp threshold frequency improvement achieved (Pearson correlation coefficient $r = 0.92$, $p < 0.001$), indicating that the training-induced adaptation was directly related to the intensity of the cramp-inducing stimulus applied rather than representing a non-specific effect of electrical stimulation per se [12]. The authors of this trial propose that repeated cramp induction under controlled conditions may adaptively alter the set-point sensitivity of muscle spindle and Golgi tendon organ afferents to forceful contraction occurring at short muscle length, thereby increasing inhibitory feedback to the alpha motor neuron pool and directly addressing the excitatory-inhibitory imbalance central to the altered neuromuscular control theory, although the authors explicitly caution that the precise underlying neural mechanism remains speculative and that this proof-of-concept trial requires replication in larger, more diverse populations, including individuals with genuinely elevated baseline cramp susceptibility rather than the asymptomatic healthy volunteers studied [12].

This foundational proof-of-concept finding has since been extended and clinically translated in a subsequent randomised controlled trial specifically targeting adults with a documented history of nocturnal leg cramps, which compared a structured neuromuscular electrical stimulation protocol delivered to the bilateral calf musculature against a comparator group performing a standardised lower-extremity static stretching program, with both interventions delivered three times weekly for twenty minutes per session over a four-week period, and outcomes assessed using electromyography-based cramp threshold frequency measurement alongside a visual analogue pain scale [22]. This trial found that both interventions produced statistically significant within-group improvements in cramp threshold frequency and pain severity following the four-week intervention period, but that the magnitude of improvement was significantly greater in the electrical stimulation group than in the stretching comparator group for both outcomes: cramp threshold frequency increased by 9.20 ± 6.75 Hz in the stimulation group compared with 1.80 ± 1.75 Hz in the stretching group (between-group difference $p = 0.007$), while visual analogue pain scores decreased by 5.20 ± 0.92 points in the stimulation group compared with 1.60 ± 0.84 points in the stretching group (between-group difference $p < 0.001$) [22]. These findings suggest that structured neuromuscular electrical stimulation confers superior benefit to conventional stretching for both objective electrophysiological cramp susceptibility and subjective pain outcomes in a clinical population with established cramp history, although this trial was

conducted in a population characterised by nocturnal leg cramps rather than exercise-associated cramping specifically, and the comparator condition employed static stretching rather than a true no-treatment or sham-stimulation control, meaning that the observed between-group difference cannot be unambiguously attributed to a specific mechanistic effect of electrical stimulation as distinct from the general benefit of any structured, repeated lower-limb intervention; the authors of this trial explicitly acknowledge this limitation and call for future studies incorporating active contraction-based comparator groups to more clearly isolate the mechanism underlying the observed benefit [22].

Taken together, these two studies—separated by roughly a decade and differing in their target population (healthy volunteers without a cramp history versus clinically affected patients with established nocturnal cramping)—provide a converging and internally consistent body of evidence that repeated, targeted electrical stimulation of cramp-susceptible musculature can produce a measurable, dose-dependent increase in the objective electrophysiological threshold for cramp induction, alongside clinically meaningful reductions in cramp-associated pain, positioning this approach as among the more promising and mechanistically well-grounded prevention strategies currently available for cramp-prone individuals, notwithstanding the continued need for larger trials directly evaluating its efficacy in reducing spontaneously occurring EAMC during actual athletic competition rather than laboratory-induced or nocturnal cramping.

20. Discussion

The body of evidence reviewed across the preceding sections converges on several clear and clinically actionable conclusions, while simultaneously exposing the persistence of substantial mechanistic uncertainty that has characterised research into EAMC for well over a century. The single most consistent and robust finding across the epidemiological literature, replicated independently across distance runners, cyclists, and Ironman-distance triathletes studied on different continents and using different methodologies, is that a prior history of cramping constitutes the strongest available predictor of subsequent cramping, with the effect size increasing in a clear dose-response manner according to the reported frequency of prior episodes, from approximately threefold increased odds for infrequent prior cramping to nearly twentyfold increased odds for frequent prior cramping in the most granular analysis available [9,15,16]. This

consistency across such heterogeneous populations, sports, and study designs lends this particular risk factor a degree of evidentiary weight that few other proposed mechanisms or risk factors in this literature can match, and it should arguably form the cornerstone of any individualised clinical risk assessment for an athlete presenting for pre-participation counselling regarding cramp prevention.

The second major point of convergence, and arguably the most important shift in understanding to have occurred over the past several decades, concerns the progressive weakening of evidentiary support for the historical dehydration-electrolyte depletion theory as a primary or generalisable explanation for EAMC, in favour of frameworks emphasising fatigue-mediated alteration of spinal neuromuscular control. This shift is not absolute or uncontested: as detailed in Section 4, genuinely compelling historical evidence from large occupational intervention studies does support a causal role for sodium supplementation in preventing heat-associated cramping in the specific context of prolonged, intense physical labour in hot industrial environments accompanied by excessive plain water consumption [1]. The apparent contradiction between this historical evidence and the largely negative findings of contemporary athletic cohort studies examining serum electrolyte concentrations in relation to cramping [8,14] is most plausibly reconciled not by dismissing either body of evidence, but by recognising that these different literatures may be capturing genuinely distinct phenomena that share a common clinical presentation. Severe, sustained occupational heat exposure combined with substantial free water intake, of the type documented in the historical mining and steel-mill literature, may represent a genuinely distinct pathophysiological entity from the transient, fatigue-related cramping most commonly experienced by athletes during a single competitive event of finite duration, even though both phenomena have historically been grouped under the same clinical label of "cramp." This distinction, if valid, would explain why sodium supplementation demonstrably prevented cramping in the industrial intervention studies while showing little consistent relationship to serum sodium concentration in athletic cohort studies, and it argues for greater precision in future research regarding the specific clinical context and exposure duration under study, rather than treating "muscle cramp" as a single, mechanistically uniform entity across all settings.

A further important tension within the reviewed literature concerns the relative contribution of central neural versus peripheral or metabolic mechanisms, a debate that the emerging "failure of relaxation" integrative framework attempts to resolve by explicitly incorporating both dimensions

rather than favouring one exclusively [3]. The direct neurophysiological evidence reviewed in Section 7, demonstrating muscle-specific rather than generalised alterations in motoneuron discharge dynamics among cramp-susceptible individuals, provides an important corrective to earlier formulations of the altered neuromuscular control theory that implicitly assumed a relatively uniform, generalised increase in spinal excitability would characterise cramp-prone individuals [6]. This more nuanced, muscle-specific finding is consistent with, and helps to mechanistically explain, the clinical and epidemiological observation that cramping is overwhelmingly localised to specific biarticular muscle groups such as the gastrocnemius rather than manifesting diffusely, and it suggests that future research and, eventually, targeted interventions may need to be conceived at the level of the individual muscle rather than the individual athlete as a whole.

The evidence base for prevention and treatment strategies, considered collectively, reveals a striking disproportion between the strength of evidence supporting different approaches and the degree of attention each receives in popular sports medicine practice. Hydration and electrolyte supplementation strategies, despite their historical prominence and continued widespread recommendation, are supported by a genuinely mixed and often contradictory evidence base when evaluated specifically for EAMC prevention, whereas the comparatively less publicised approach of targeted neuromuscular electrical stimulation training has produced the most internally consistent and mechanistically coherent controlled trial evidence currently available, with a clear dose-response relationship and replication across two independently conducted trials separated by a decade [12,22]. This disproportion between evidentiary strength and clinical prominence likely reflects, in part, the practical simplicity and low cost of hydration-based advice relative to the specialised equipment and protocol adherence required for structured electrical stimulation training, a translational gap that future clinical guidance should aim to address as further confirmatory research accumulates.

Finally, the genetic, biomechanical, and connective-tissue-related hypotheses reviewed in Section 8, while individually supported by only limited direct evidence, collectively point toward an important and likely durable conclusion: EAMC susceptibility is unlikely to be reducible to any single unifying mechanism applicable uniformly across all affected individuals, and future research would benefit from explicitly stratifying study populations according to identifiable risk profiles—prior cramp frequency, presence of chronic disease or allergy, injury history, and

potentially genetic connective tissue markers—rather than continuing to treat EAMC as a single, homogeneous clinical entity amenable to a single universal preventive strategy.

21. Limitations of the Evidence Base

Several limitations characterise the evidence base synthesised in this review and should be considered when interpreting its conclusions. First, the field remains heavily reliant on cross-sectional and retrospective observational study designs, particularly the large epidemiological cohort studies underpinning much of the risk factor literature discussed in Sections 9 and 10; these designs, while offering considerable statistical power owing to their large sample sizes, cannot establish causal directionality, and associations identified between variables such as chronic disease, medication use, or training characteristics and EAMC history must accordingly be interpreted as correlative rather than confirmed causal relationships [9,15]. Second, virtually all epidemiological data in this field rely on self-reported cramp history and cramp occurrence, introducing the potential for recall bias, differential reporting between athletes of varying experience or health literacy, and inconsistent application of the underlying case definition across studies, a limitation explicitly acknowledged by several of the primary studies reviewed [9,14-16]. Third, direct experimental studies of cramp physiology, including the neurophysiological work detailed in Section 7 and the electrical stimulation intervention trials detailed in Section 19, have necessarily relied on relatively small sample sizes—ranging from ten to twenty-eight participants across the key studies reviewed—reflecting the inherent practical difficulty of recruiting and retaining participants for demanding, invasive, or repeatedly cramp-inducing laboratory protocols, and consequently these mechanistic findings, however internally consistent, await confirmation in larger and more diverse cohorts before their generalisability can be fully established [6,12,22].

Fourth, a persistent methodological challenge across this literature is the extrapolation of findings from experimentally or electrically induced cramping in controlled laboratory settings to the phenomenon of spontaneously occurring EAMC during real-world athletic competition; while the cramp threshold frequency protocol has demonstrated meaningful, if imperfect, concordance with self-reported cramp history, it remains an imperfect proxy, and interventions shown to elevate this laboratory-derived threshold, such as electrical stimulation training, have not yet been directly evaluated for their capacity to reduce the incidence of spontaneous cramping during

actual endurance competition [6,12]. Fifth, the majority of the reviewed literature focuses on a relatively narrow range of endurance sports—principally distance running, cycling, and triathlon—raising questions about the generalisability of these findings to team sports, strength and power sports, or occupational settings that may involve substantially different patterns of muscular loading, fatigue, and environmental exposure. Sixth, this review is narrative rather than systematic in design, meaning that source selection, thematic organisation, and interpretive emphasis reflect the authors' judgement regarding the material identified through the search strategy described in Section 2, rather than a pre-registered protocol with formal risk-of-bias assessment or quantitative synthesis, and this approach may therefore be subject to selection and emphasis bias despite efforts to represent the full range of perspectives and contradictory findings present in the underlying literature.

Finally, several of the more novel and conceptually interesting frameworks discussed in this review—including the surface mechanical properties hypothesis detailed in Section 8 and the integrative "failure of relaxation" model detailed in Section 6—are explicitly presented by their original authors as hypothesis-generating rather than established mechanisms, and this review has endeavoured to represent them with appropriate epistemic caution; readers should be aware that these frameworks, however biologically plausible, currently rest on considerably more limited direct empirical support than the more extensively replicated epidemiological risk factor findings and the electrical stimulation intervention evidence discussed elsewhere in this review.

22. Conclusions

Exercise-associated muscle cramps remain a common, clinically significant, and mechanistically complex phenomenon that continues to resist explanation by any single unifying theory more than a century after the earliest systematic clinical descriptions. This narrative review has traced the evolution of understanding from the historical dehydration-electrolyte depletion hypothesis, which retains genuine but likely context-specific validity in severe occupational heat-exposure settings, through the altered neuromuscular control theory that has dominated contemporary mechanistic thinking since the late 1990s, to emerging integrative frameworks that incorporate neural, metabolic, and biomechanical contributions within a multifactorial model of individual susceptibility.

The epidemiological evidence reviewed across distance running, cycling, and triathlon populations converges with notable consistency on prior cramping history and higher relative exercise intensity as the most robust identifiable predictors of EAMC, while offering more modest but independently replicated support for the contributory roles of chronic disease, allergy history, and prior musculoskeletal injury. In contrast, the relationship between EAMC and measures of dehydration or serum electrolyte concentration, though intuitively appealing and historically dominant in clinical practice, is supported by considerably weaker and more inconsistent evidence when examined specifically in athletic populations under contemporary study conditions. Direct neurophysiological investigation has begun to reveal that cramp susceptibility reflects subtle, muscle-specific alterations in motoneuron discharge dynamics rather than a generalised state of spinal hyperexcitability, a finding that helps explain the characteristic localisation of cramping to specific biarticular muscle groups and that points toward the need for future research and intervention strategies conceived at the level of the individual muscle rather than the individual athlete alone.

Regarding prevention and treatment, gentle static stretching remains the best-supported acute intervention for an active cramp, mechanistically explained by restoration of Golgi tendon organ-mediated inhibitory input to the alpha motor neuron, although its value as a prophylactic strategy is considerably less well established. Targeted neuromuscular electrical stimulation protocols designed to elevate an individual's cramp threshold frequency represent the most mechanistically coherent and consistently replicated prevention strategy currently available in the controlled trial literature, outperforming conventional stretching in a direct clinical comparison, and warrant further investigation for their capacity to reduce spontaneous cramping during actual athletic competition. Generalised hydration and electrolyte or magnesium supplementation protocols, while retaining a plausible physiological rationale and demonstrated benefit for broader measures of endurance performance and heat tolerance, should not be regarded as a universally effective cramp-prevention strategy in the absence of an identified individual risk factor such as documented sodium-sensitive cramping history or confirmed magnesium deficiency. Clinicians and sports medicine practitioners are accordingly encouraged to move away from uniform, one-size-fits-all hydration or supplementation advice and toward an individualised risk assessment incorporating prior cramp frequency, training and racing intensity relative to habitual conditioning, chronic disease and medication history, and prior musculoskeletal injury, while

remaining alert to the differential diagnosis of more serious exercise-associated conditions, including exertional heatstroke and rhabdomyolysis, that may present with superficially similar but mechanistically and clinically distinct features requiring urgent and fundamentally different management.

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