University of Potsdam

Faculty of Human Sciences

DIVISION OF TRAINING AND MOVEMENT SCIENCES

Acute Effects of Exercise Order in Concurrent Training on Immunological Stress Responses and Measures of Muscular Fitness in Youth Athletes of Both Sexes

An academic thesis submitted to

the Faculty of Human Sciences of the University of Potsdam

for the degree

Doctor of Philosophy (**Dr Phil)**

by

Adrian Markov

born in Hennigsdorf, Germany

2023

Published online on the
Publication Server of the University of Potsdam:
https://doi.org/10.25932/publishup-61851
https://nbn-resolving.org/urn:nbn:de:kobv:517-opus4-618517

Statutory Declaration

Affidavits according to the doctoral degree regulations (§ 4 (2), sentences No. 4 and 7) of the Faculty of Human Sciences, University of Potsdam, I hereby declare that this thesis entitled “Acute Effects of Concurrent Training Exercise Order on Immunological Stress Responses and Measures of Muscular Fitness in Youth Athletes” or parts of it have not yet been submitted for a doctoral degree to this or any other institution, neither in identical nor in similar form. The work presented in this thesis is the original work of the author. I did not receive any help or support from commercial consultants. All parts or single sentences, which have been taken analogously or literally from other sources, are identified as citations.

_____ _____

Place, Date Adrian Markov

Table of contents

Acknowledgements

I would like to thank my first supervisor **Dr. Helmi Chaabene**. He is an exceptional human being. His kindness and humbleness, combined with his tremendous knowledge and skills, make him an example par excellence of mentorship. I am grateful for having the opportunity to be taught by him and to work with him. Prospectively, I will do my very best to pass all what I have learned from him to others.

The intellectual content and represented data of this thesis is the result of the effort of many. Accordingly, I would like to thank **Dr. Tom Krüger, Dr. Jens Bussweiler, Dr. Norman Helm, Dr. Harry Kappell, Dr. Philipp Baumert, Lukas Hauser**, **Arnau Sacot**, and **Michael Rex**. All have made a substantial contribution to this piece of work, and I am grateful for all their support during this journey.

I would like to thank **Ines Beischmidt**. In simple words, if I would be MJ, she would be Phil. If she would be Keith, I would be Ronnie. If, I would be Pierre, she would be Marie. She is the one who makes my life easy and her contribution to all this is by far bigger than she would believe.

Finally, I would like to thank my parents, **Reinhild Anna Markov** (**geb. Schwannecke**) und **Dr. Helmuth Markov**. This is a milestone in my life but at the same time a reflection of their parental greatness. In this regard, Dwayne Johnson said: “If something stands between you and your success, move it. Never be denied.” While it is easy to state a powerful sentence, it is in fact difficult to live it. But the way my parents have raised me -with love and fortitude- enabled me to do so. That is why a lot about this milestone belongs to them.

“Ich kann nichts dafür, ich bin ein Kind von dir.“

Abstract

Background and aims: To succeed in competition, elite team and individual athletes often seek the development of both, high levels of muscle strength and power as well as cardiorespiratory endurance. In this context, concurrent training (CT) is a commonly applied and effective training approach. While being exposed to high training loads, youth athletes (≤ 18 years) are yet underrepresented in the scientific literature. Besides, immunological responses to CT have received little attention. Therefore, the aims of this work were to examine the acute (< 15min) and delayed (≥ 6 hours) effects of different exercise order in CT on immunological stress responses, muscular fitness, metabolic response, and rating of perceived exertion (RPE) in highly trained youth male and female judo athletes.

Methods: A total of twenty male and thirteen female participants, with an average age of 16 ± 1.8 years and 14.4 ± 2.1 years, respectively, were included in the study. They were randomly assigned to two CT sessions; power-endurance versus endurance-power (i.e., study 1), or strength-endurance versus endurance-strength (i.e., study 2). Markers of immune response (i.e., white-blood-cells, granulocytes, lymphocytes, monocytes, and lymphocytes, granulocyte-lymphocyte-ratio, and systemic-inflammation-index), muscular fitness (i.e., counter-movement jump [CMJ]), metabolic responses (i.e., blood lactate, glucose), and RPE were collected at different time points (i.e., PRE12H, PRE, MID, POST, POST6H, POST22H).

Results (study 1): There were significant time*order interactions for white-blood-cells, lymphocytes, granulocytes, monocytes, granulocyte-lymphocyte-ratio, and systemic-inflammation-index. The power-endurance order resulted in significantly larger PRE-to-POST increases in white-blood-cells, monocytes, and lymphocytes while the endurance-power order resulted in significantly larger PRE-to-POST increases in the granulocyte-lymphocyte-ratio and systemic-inflammation-index. Likewise, significantly larger increases from PRE-to-POST6H in white-blood-cells and granulocytes were observed following the power-endurance order compared to endurance-power. All markers of immune response returned toward baseline values at POST22H. Moreover, there was

a significant time*order interaction for blood glucose and lactate. Following the endurance-power order, blood lactate and glucose increased from PRE-to-MID but not from PRE-to-POST. Meanwhile, in the power-endurance order blood lactate and glucose increased from PRE-to-POST but not from PRE-to-MID. A significant time*order interaction was observed for CMJ-force with larger PRE-to-POST decreases in the endurance-power order compared to power-endurance order. Further, CMJ-power showed larger PRE-to-MID performance decreases following the power-endurance order, compared to the endurance-power order. Regarding RPE, significant time*order interactions were noted with larger PRE-to-MID values following the endurance-power order and larger PRE-to-POST values following the power-endurance order.

Results (study 2): There were significant time*order interactions for lymphocytes, monocytes, granulocyte-lymphocyte-ratio, and systemic-inflammation-index. The strength-endurance order resulted in significantly larger PRE-to-POST increases in lymphocytes while the endurance-strength order resulted in significantly larger PRE-to-POST increases in the granulocyte-lymphocyte-ratio and systemic-inflammation-index. All markers of the immune system returned toward baseline values at POST22H. Moreover, there was a significant time*order interaction for blood glucose and lactate. From PRE-to-MID, there was a significantly greater increase in blood lactate and glucose following the endurance-strength order compared to strength-endurance order. Meanwhile, from PRE-to-POST there was a significantly higher increase in blood glucose following the strength-endurance order compared to endurance-strength order. Regarding physical fitness, a significant time*order interaction was observed for CMJ-force and CMJ-power with larger PRE-to-MID increases following the endurance-strength order compared to the strength-endurance order. For RPE, significant time*order interactions were noted with larger PRE-to-MID values following the endurance-power order and larger PRE-to-POST values following the power-endurance order.

Conclusions: The primary findings from both studies revealed order-dependent effects on immune responses. In male youth judo athletes, the results demonstrated greater immunological stress responses, both immediately (≤ 15 min) and delayed (≥ 6 hours),

following the power-endurance order compared to the endurance-power order. For female youth judo athletes, the results indicated higher acute, but not delayed, order-dependent changes in immune responses following the strength-endurance order compared to the endurance-strength order. It is worth noting that in both studies, all markers of immune system response returned to baseline levels within 22 hours. This suggests that successful recovery from the exercise-induced immune stress response was achieved within 22 hours. Regarding metabolic responses, physical fitness, and perceived exertion, the findings from both studies indicated acute (≤ 15 minutes) alterations that were dependent on the exercise order. These alterations were primarily influenced by the endurance exercise component. Moreover, study 1 provided substantial evidence suggesting that internal load measures, such as immune markers, may differ from external load measures. This indicates a disparity between immunological, perceived, and physical responses following both concurrent training orders. Therefore, it is crucial for practitioners to acknowledge these differences and take them into consideration when designing training programs.

Keywords: Combined strength and endurance, Risk of infection, White blood cells, Leukocytosis, Adolescents, Combat sports

Zusammenfassung

Hintergrund und Ziele: Um im Wettkampf erfolgreich zu sein, streben Elitesportler oft die Entwicklung einer hohen Muskelkraft und -leistung als auch der kardiorespiratorischen Ausdauer an. In diesem Zusammenhang ist das gleichzeitige Training von Kraft- und Ausdauer (CT) ein häufig angewandter und effektiver Trainingsansatz. Während Jugendliche (≤ 18 Jahre) hohen Trainingsbelastungen ausgesetzt sind, sind sie in der wissenschaftlichen Literatur noch unterrepräsentiert. Außerdem haben immunologische Reaktionen auf CT bisher wenig Aufmerksamkeit erhalten. Daher waren die Ziele dieser Arbeit, die akuten (< 15min) und verzögerten (≥ 6 Stunden) Auswirkungen unterschiedlicher Übungsreihenfolgen im CT auf immunologische Stressreaktionen, muskuläre Fitness, Stoffwechselreaktionen und empfundene Anstrengung (RPE) bei hochtrainierten jugendlichen männlichen und weiblichen Judosportlern zu untersuchen.

Methoden: In die Studie wurden insgesamt zwanzig männliche und dreizehn weibliche Teilnehmer im Alter von durchschnittlich 16 ± 1,8 Jahren bzw. 14,4 ± 2,1 Jahren aufgenommen. Sie wurden zufällig zwei CT-Einheiten zugewiesen: Muskelpower-Ausdauer im Vergleich zu Ausdauer-Muskelpower (d. h. Studie 1) oder Kraft-Ausdauer im Vergleich zu Ausdauer-Kraft (d. h. Studie 2). Marker der Immunantwort (d. h. weiße Blutkörperchen, Granulozyten, Lymphozyten, Monozyten und Lymphozyten, Granulozyten-Lymphozyten-Verhältnis, und systemischer Entzündungsindex), muskuläre Fitness (d. h. counter-movement jump [CMJ]), Stoffwechselreaktionen (d. h. Blutlaktat, Blutglukose) und RPE wurden zu verschiedenen Zeitpunkten (d. h. PRE12H, PRE, MID, POST, POST6H, POST22H) erhoben.

Ergebnisse (Studie 1): Es gab signifikante Zeit*Reihenfolge-Interaktionen für weiße Blutkörperchen, Lymphozyten, Granulozyten, Monozyten, das Granulozyten-Lymphozyten-Verhältnis und den systemischen Entzündungs-index. Die Reihenfolge Muskelpower-Ausdauer führte zu signifikant größeren PRE-bis-POST-Anstiegen bei weißen Blutkörperchen, Monozyten und Lymphozyten, während die Reihenfolge Ausdauer-Muskelpower zu signifikant größeren PRE-bis-POST-Anstiegen im Granulozyten-Lymphozyten-Verhältnis und dem systemischen Entzündungsindex führte. Ebenso wurden

nach der Reihenfolge Muskelpower-Ausdauer signifikant größere Anstiege von PRE-bis-POST6H bei weißen Blutkörperchen und Granulozyten im Vergleich zur Reihenfolge Ausdauer-Muskelpower beobachtet. Alle Marker des Immunsystems kehrten bis POST22H wieder auf das Ausgangsniveau zurück. Darüber hinaus wurde eine signifikante Zeit*Reihenfolge-Interaktion für Blutglukose und Blutlaktat beobachtet. Nach der Reihenfolge Ausdauer-Kraft stiegen Blutlaktat und Blutglukose von PRE-bis-MID, aber nicht von PRE-bis-POST. Außerdem wurde eine signifikante Zeit*Reihenfolge-Interaktion für CMJ-Kraft beobachtet. Entsprechend zeigten sich größere PRE-bis-POST Verminderungen in der Ausdauer-Muskelpower Reihenfolge im Vergleich zu Muskelpower-Ausdauer. Außerdem zeigte die CMJ-Leistung einen größeren Leistungsverlust von PRE-bis-MID in der Muskelpower-Ausdauer Reihenfolge, im Vergleich zu Ausdauer-Muskelpower. Mit Blick auf RPE gab es ebenfalls signifikante Zeit*Reihenfolge-Interaktionen. Entsprechend waren die RPE-Werte höher von PRE-bis-MID nach der Ausdauer-Muskelpower Reihenfolge und von PRE-bis-POST nach der Muskelpower-Ausdauer Reihenfolge.

Ergebnisse Studie 2: Beobachtet wurde eine signifikante Zeit*Reihenfolge-Interaktion für Lymphozyten, Monozyten, das Granulozyten-Lymphozyten-Verhältnis und den systemischen Entzündungsindex. Die Reihenfolge Kraft-Ausdauer hat zu signifikanten Steigerungen der Lymphozyten von PRE-bis-POST geführt, während die Ausdauer-Kraft Reihenfolge signifikante Anstiege des Granulozyten-Lymphozyten-Verhältnis und des systemischen Entzündungsindex zur Folge hatte. Alle Marker des Immunsystems kehrten bis POST22H wieder auf das Ausgangsniveau zurück. Darüber hinaus wurde eine signifikante Zeit*Reihenfolge-Interaktion für Blutglukose und Blutlaktat beobachtet. Von PRE-bis-MID gab es nach der Reihenfolge Ausdauer-Kraft im Vergleich zur Reihenfolge Kraft-Ausdauer einen signifikant größeren Anstieg von Blutlaktat und Blutglukose. Darüber hinaus gab es von PRE-bis-POST einen signifikant höheren Anstieg der Blutglukose nach der Reihenfolge Kraft-Ausdauer im Vergleich zur Reihenfolge Ausdauer-Kraft. In Bezug auf die körperliche Fitness wurde eine signifikante Zeit*Reihenfolge-Interaktion für CMJ-Kraft und CMJ-Leistung beobachtet, wobei größere PRE-

bis-MID-Anstiege nach der Reihenfolge Ausdauer-Kraft im Vergleich zur Reihenfolge Kraft-Ausdauer zu verzeichnen waren. In Bezug auf die empfundene Anstrengung wurden signifikante Zeit*Reihenfolge-Interaktionen festgestellt. Hier kam es zu größeren PRE-bis-MID-Werten in Folge von Ausdauer-Kraft und größere PRE-bis-POST-Werte nach Kraft-Ausdauer.

Schlussfolgerungen: Die Hauptergebnisse beider Studien zeigten reihenfolgeabhängige Auswirkungen auf Immunreaktionen. Bei männlichen jugendlichen Judosportlern zeigten die Ergebnisse größere immunologische Stressreaktionen, sowohl unmittelbar (≤ 15 min) als auch verzögert (≥ 6 Stunden), nach der Reihenfolge Muskelpower-Ausdauer im Vergleich zur Reihenfolge Ausdauer-Muskelpower. Bei weiblichen jugendlichen Judosportlern deuteten die Ergebnisse auf höhere akute, aber nicht verzögerte, reihenfolgeabhängige Immunreaktionen nach der Reihenfolge Kraft-Ausdauer im Vergleich zur Reihenfolge Ausdauer-Kraft hin. Es ist erwähnenswert, dass in beiden Studien alle Marker der Immunreaktion innerhalb von 22 Stunden auf das Ausgangsniveau zurückkehrten. Dies deutet darauf hin, dass eine erfolgreiche Erholung von der durch Bewegung verursachten Immunstressreaktion innerhalb von 22 Stunden erreicht wurde. In Bezug auf Stoffwechselreaktionen, körperliche Fitness und empfundene Anstrengung zeigten die Ergebnisse beider Studien akute (≤ 15 Minuten) Veränderungen, die von der Übungsreihenfolge abhängig waren. Diese Veränderungen wurden hauptsächlich durch die Ausdauerübungskomponente beeinflusst. Darüber hinaus lieferte Studie 1 Hinweise darauf, dass interne Belastungsmessungen, wie Immunmarker, von externen Belastungsmessungen wie beispielsweise RPE abweichen können. Dies deutet auf eine Diskrepanz zwischen immunologischen Reaktionen, körperlichen Leistungsfähigkeiten und empfundener Ermüdung nach beiden Trainingsreihenfolgen hin. Daher ist es für Praktiker wichtig, sich dieser Unterschiede bewusst zu sein und bei der Gestaltung von Trainingsprogrammen zu berücksichtigen.

Schlüsselwörter: Kombination aus Kraft und Ausdauer, Infektionsrisiko, weiße Blutkörperchen, Leukozytose, Jugendliche, Kampfsport, Profisportler

Abbreviations

Concurrent training	CT
Counter-movement jump	CMJ
Granulocytes	GRAN
Granulocyte-lymphocyte-ratio	GLR
Lymphocytes	LYM
Monocytes	MONO
Rating of perceived exertion	RPE
Systemic-inflammation-index	SII
White blood cells	WBC

1 Introduction

Acute immunological responses to exercise are complex and involve systemic alterations in hormone and innate immune cell concentrations [1, 2]. Compelling evidence suggests that chronic exposure to exercise has anti-inflammatory effects [3-7]. However, the acute immunological responses to exercise have not been extensively discussed [8]. Nonetheless, it is well-established that exercise can cause acute leukocytosis in healthy individuals [5]. Leukocytosis is a clinically accepted marker of inflammation and is often associated with infection [9] and exercise-induced stresses [5]. Recent literature suggests that the acute inflammatory response to exercise is primarily mediated by the magnitude of muscle damage (i.e., disruption of the myofibrillar structure) and the required time for tissue repair [10, 11]. This would make the extent of leukocytosis dependent on several training variables such as the applied exercise intensity, frequency, duration, order, as well as type of exercise [5, 12-14].

To succeed in competition, elite team and individual elite athletes often seek the development of high levels of muscle strength and power as well as cardiorespiratory endurance [15-19]. In this context, concurrent training (CT) which combines strength/power and endurance exercises, is a commonly applied and effective training approach to improve measures of muscle strength, muscle power, and cardiorespiratory endurance (e.g., maximal oxygen consumption or aerobic capacity) [19-21]. Immunological responses to CT have received little attention in the literature, with most studies focused on either strength training or endurance training alone. For example, a recent study by Senna and colleagues [22] showed that a single resistance training session induced significant increases in white-blood-cells (WBC) along with other prominent markers of muscle tissue damage (e.g., creatine kinase, interleukin-6, tumour-necrosis-factor-α) in healthy trained men aged 26 years. Interestingly, the same authors reported an increased inflammatory response when the rest period between sets was reduced from 3 to 1 min. Similar findings have been reported for endurance-based exercises [23, 24], although a very recent study comparing the effects of strength versus endurance exercises on cellular immune responses (i.e., WBC) in healthy men

aged 24 years found higher immune cell mobilization following endurance exercises compared to strength exercises [13].

Unlike adult athletes, youth athletes (≤ 18 years) are underrepresented in the scientific literature. Generally, youth experience growth and maturation processes, which are associated with changes within tissues, organs, body systems, body composition, and physical fitness [25]. Additionally, youth athletes are commonly exposed to high training loads, making them vulnerable to an increased risk of infection [6, 26] and dropout due to training-related acute or chronic injuries [27, 28]. Of note, very few studies have investigated the acute immunological responses to exercise in youth [29-31], leading to a relatively deficient understanding of the matter. Furthermore, none of the few available studies have specifically addressed the acute immunological responses to CT in youth athletes. Moreover, compared to males, female athletes are largely underrepresented in the scientific literature [32-34]. It is important to note that evidence gained from studies on males cannot be directly generalized to females due to their distinct biology [35]. Therefore, future studies that include female athletes are urgently needed.

Several factors, including the type of exercise, exercise order, intensity, and duration are likely to influence the effects of CT on markers of immunological stress responses [36-38]. There are indications that the applied exercise order during CT can affect the underlying physiological events [39-41]. However, there is a lack of studies that have examined the acute effects of CT exercise order on markers of immunological stress responses (i.e., WBC, lymphocytes [LYM], granulocytes [GRAN], monocytes [MONO], granulocyte-lymphocyte-ratio [GLR] and the systemic inflammation index [SII]), in youth athletes.

1.1 Aims of the thesis

The primary objective of this thesis was to investigate the effects of CT exercise order (i.e., power/strength-endurance versus endurance-power/strength) on acute (< 15min) and delayed (≥ 6 hours) immunological stress responses (i.e., WBC, LYM, GRAN, GLR, and SII) in male and female youth judo athletes. The secondary goal was to evaluate the effects of CT exercise order on measures of muscular fitness (i.e., jump height, force, power), metabolic response (i.e., blood glucose, blood lactate), and rating of perceived exertion (RPE) in the same group.

1.2 Hypothesis

Hypothesis 1: The order of CT exercises (i.e., power/strength-endurance versus endurance-power/strength) will result in different acute (< 15 min) and delayed (≥ 6 hours) changes in peripheral immune cell counts (e.g., WBC) in youth male and female judo athletes [40, 41].

Hypothesis 2: CT exercise order will differently affect measures of muscular fitness (i.e., jump height, force, power), metabolic response (i.e., blood glucose, blood lactate), and RPE in youth male and female judo athletes [40, 41].

1.3 Contribution of the thesis

The findings of this thesis will be beneficial for practitioners working with youth athletes by assisting them in selecting the most suitable CT exercise order that minimizes disruptions to the immune function. Furthermore, this study provides additional insights into the lack of consensus between immunological, perceived, and physical fitness responses following both CT exercise orders, indicating the need for concurrent measurement of internal and external training load to gain a comprehensive understanding of the athlete's physical and physiological state. In general, these results will aid practitioners optimizing their CT interventions for youth athletes.

2 Literature Review

2.1 Concurrent Training

2.1.1 Historical background

The development of muscle strength and endurance capacity is crucial from a performance optimisation and health perspective [21, 42, 43]. In this sense, the combination of strength- and endurance training is known as CT. In 1980, Robert C. Hickson [20] investigated for the first time the effects of 10 weeks of CT compared to single-mode strength and single-mode endurance training on measures of muscle strength and cardiorespiratory endurance in recreationally active adults. Hickson reported that the level of muscle strength gains within the CT group was comparable to the strength group during the first seven weeks of training. However, during the 9th and 10th weeks, the same author noted that the gain in muscle strength within the CT group levelled off and even decreased. Meanwhile, cardiorespiratory endurance (i.e., maximal oxygen consumption) did not differ between the CT group and endurance training group [20]. These findings demonstrated that CT does not affect cardiorespiratory endurance but does compromise muscle strength adaptations. Hickson's study constitutes the first proof of evidence of the existence of an "interference effect". In fact, the term interference refers to an attenuated adaptive potential of CT to improve muscle strength compared to single-mode strength training. Then, nearly a decade later it was hypothesised that residual fatigue resulting from endurance training may compromise the ability to produce high levels of muscle tension during the subsequent strength training when both exercises are performed within the same session and in close proximity [44]. The reduced ability to generate a high level of muscle tension would limit the potential for strength adaptations. In fact, this was partly confirmed within a very recent systematic review with meta-analysis by Markov et al. [42] in which the authors reported that endurance-based exercises acutely reduce measures of muscle strength. Based on advanced methods within the molecular exercise physiology domain, another important milestone within the CT domain was originally set by Atherton and colleagues in the early 21st century [45] and further developed by Coffey and Hawley [39, 46] alongside

others [47, 48]. These studies highlighted the importance of the adenosine monophosphate-activated kinase (i.e., AMPK) and the mechanistic target of rapamycin (i.e., mTOR or mTORC1 [complex1]). These two key enzymes are directly involved in exercise-induced signalling pathways that regulate muscle protein synthesis and mitochondrial biogenesis. However, there is evidence showing that in response to CT, AMPK and mTORC1 tend to interfere with each other, which in turn may cause alterations within the pattern of skeletal muscle adaptations. In fact, since Robert C. Hickson's original work in the early 80s, CT has been one of the most studied topics in the sports and exercise science literature with an ever-growing number of publications. Thereby, the current literature generally suggests that CT can be an effective and time-efficient method to improve both, muscle strength and aerobic capacity [48, 49]. However, the question of how to appropriately combine strength and endurance exercises and/or training to avoid or at least minimise the level of interference remains the major challenge [36, 50, 51].

2.1.2 Methodological considerations: Modifiable Factors

The occurrence and magnitude of the interference effect are influenced by the interaction between numerous factors [37]. These factors should be considered by practitioners for the appropriate planning and prescription of CT. Among the most prominent training variables, we can denote training intensity, volume, mode of exercise, exercise order, and recovery time between endurance and strength exercises [36, 52] (Figure 1). Also, characteristics inherent to the training individual, mainly training status, constitutes another important factor that moderates the effects of CT-inducing strength and aerobic performance changes [37].

The intensity of exercise is a crucial variable that moderates the effects of CT [36]. This applies to endurance training (i.e., high- vs low-intensity continuous exercise or high-intensity intermittent exercise (HIIE) vs moderate-/high-intensity continuous exercise) and strength training (i.e., high- vs moderate-/low-intensity strength exercises). Particularly, there is compelling evidence that HIIE is a time-efficient method for improving

mitochondrial biogenesis and oxidative capacity [36]. However, little is known about the effects of HIIE on aerobic performance as well as the interference phenomena in the context of long-term CT programs. Earlier studies addressing the molecular aspects demonstrated that HIIE may exacerbate acute molecular interference compared with lower-intensity continuous endurance exercise [36, 53-55].

Training volume is another factor that could have an impact on the interference effect. In this sense, previous studies indicated that the total volume of endurance exercise, rather than the intensity *per se*, is probably a more prominent mediator of the interference effect [56, 57]. In fact, a volume-dependent interference was supported by studies revealing no interference with lower endurance training frequencies (≤ 2 sessions per week) [58-60] while others reported decreased maximal strength with increasing training volume (≥ 2 sessions per week) [57, 61, 62]. In another study, authors [63] reported an association between increasing daily endurance training duration and attenuated resistance training-induced strength improvements. Overall, it seems that increasing training volume, either by increasing the frequency or the duration of training negatively impacts long-term strength training adaptations.

Regarding the mode of exercise, there is evidence that the type of endurance exercise could modulate the interference effect following long-term CT [63, 64]. Of note, most of the existing CT studies that reported an interference effect have used running-type exercises [63, 64]. In this context, Gergley [65] investigated the effects of two different endurance exercise modes (i.e., running vs cycling) combined with strength training compared to strength training alone on measures of lower body muscle strength in healthy untrained adults aged between 18 to 24 years. Following nine weeks of training, the author reported that strength gains were significantly lower in the strength with running group but not in the strength with cycling group when compared to strength training alone. Meanwhile, other studies found no effect of exercise mode on measures of muscle strength [66].

The recovery time between the strength and endurance exercises is another key factor given that residual fatigue and/or substrate depletion (i.e. muscle glycogen) caused by endurance exercise may negatively influence subsequent force/power production [44, 64]. In this context, earlier studies showed reduced force production for at least six hours of the involved muscles following a bout of endurance exercise [67-69]. The decreased ability of the muscle to produce a high amount of force/power during strength exercise would limit the capacity to activate higher-threshold motor units and fibres [69], which are the most sensitive to muscle hypertrophy [70]. Additionally, there is evidence that the anabolic signalling response to subsequent resistance exercise is impaired [71]. This appears to be due to the residual fatigue from prior endurance exercise which reduces the total volume and quality of the subsequent resistance exercise [69], compromising the anabolic response. On the other hand, it is well-established that endurance exercise particularly stimulates AMPK that tend to inhibit mTORC1 pathway activation and therefore the rate of muscle protein synthesis [36]. In summary, there is strong evidence to suggest that performing strength exercises in closer proximity to endurance exercises may hinder the anabolic response to strength exercises [36].

Another important aspect is the applied exercise order (i.e., endurance prior to strength vs strength prior to endurance). In fact, combining strength and endurance exercises within the same session is a common practice. While this topic was addressed in several studies [36, 43, 72-76], it is yet very difficult to draw a comprehensive conclusion. From a performance perspective, it was previously suggested to favour the strength-endurance order to minimize interference [43, 72, 73]. This is primarily based on the assumption that substrate depletion and/or neuromuscular fatigue may compromise strength exercises if these are performed after the endurance exercises [64, 77, 78]. In fact, several studies showed reduced measures of muscle strength after several weeks of CT when strength was applied after endurance exercises [43, 72, 73]. Nonetheless, current CT studies related to the underlying molecular mechanisms suggest applying strength after endurance exercises [39, 48, 74, 79, 80]. This is due to the inhibiting

potential of AMPK on the mTORC1 signalling pathway. Accordingly, there is evidence showing reduced mTORC1 activity when endurance exercises were applied immediately after strength exercises [80, 81]. This highlights a discrepancy between performance- and molecular-related CT investigations.

Training status is an additional moderating factor that should be considered. In this regard, Petre et al. [21] recently meta-analysed the effects of CT on lower-body maximal dynamic strength in healthy untrained, moderately trained, and trained individuals (18 to 40 years) and reported a significant effect of training status. More specifically, the same authors reported that trained individuals experienced an interference effect while moderately trained as well as untrained did not. Concerning the underlying physiological mechanisms, studies considering athletes are yet limited. In fact, some studies indicate that CT stimulates both muscle protein synthesis and mitochondrial biogenesis [82-86]. Fyfe et al. [36] highlighted that most of the available studies investigating the acute molecular responses to CT generally used non-athlete populations (i.e., sedentary, recreationally active, untrained). Meanwhile, there is evidence showing that in untrained individuals, the mTORC1 pathway –which is critical for muscle hypertrophy– is activated due to strength and/or endurance-based exercises while in trained athletes mTORC1 is primarily stimulated by strength but not endurance-based exercises [87-89]. This would strengthen the assumption that trained individuals differ in their molecular responses to CT when compared to their untrained counterparts. However, this needs to be investigated in future studies.

2.1.3 Methodological considerations: Non-modifiable Factors

In addition to the modifiable factors, there are several non-modifiable factors that must be considered (Figure 1). The most prominent ones are age, sex, genetics, and epigenetics. In fact, studies investigating the effects of these factors on CT-related outcomes are yet lacking. Nonetheless, there is evidence from recent meta-analyses [19, 43, 90] indicating that the magnitude of the effects of CT is moderated by sex and age to a certain extent. For instance, Seipp and colleagues [19] systematically reviewed the

effects of CT on measures of muscular fitness in team sports athletes and reported improvements in measures of muscle strength (e.g., one-repetition maximum, muscle power) and endurance performance (e.g., maximum oxygen consumption). However, the same authors stressed that training status and recovery time modulate the magnitude of interference and that this in turn, is determined by maturity level [19], highlighting the interdependency between modifiable and non-modifiable factors. In support, Markov et al. [43] recently meta-analysed the effects of CT in older adults and found higher effects of CT on measures of muscle strength in adults aged > 65 compared to those ≤ 65 years. The same authors reported higher effects of CT on measures of muscle strength and endurance in female older adults compared to males. In this context, it is generally accepted that physiological responses to exercise in males cannot be generalized to females due to their distinct biology [35]. In fact, the available literature [91-93] indicates that strength exercise-induced anabolic responses, satellite cell activity, and/or the rate of muscle protein synthesis and breakdown are strongly affected by female sex hormones (e.g., oestrogen). Another critical factor seems to be the genetic profile of an individual. Accordingly, there is cumulative evidence showing the importance of genetic variability in the context of sport and exercise [94-96]. For instance, a recent systematic review identified common genes associated with cardiovascular fitness, muscle strength, and anaerobic power and reported that the inter-individual differences in responses to strength and/or endurance-based exercises are explained by genetic variations by up to 72% [97].

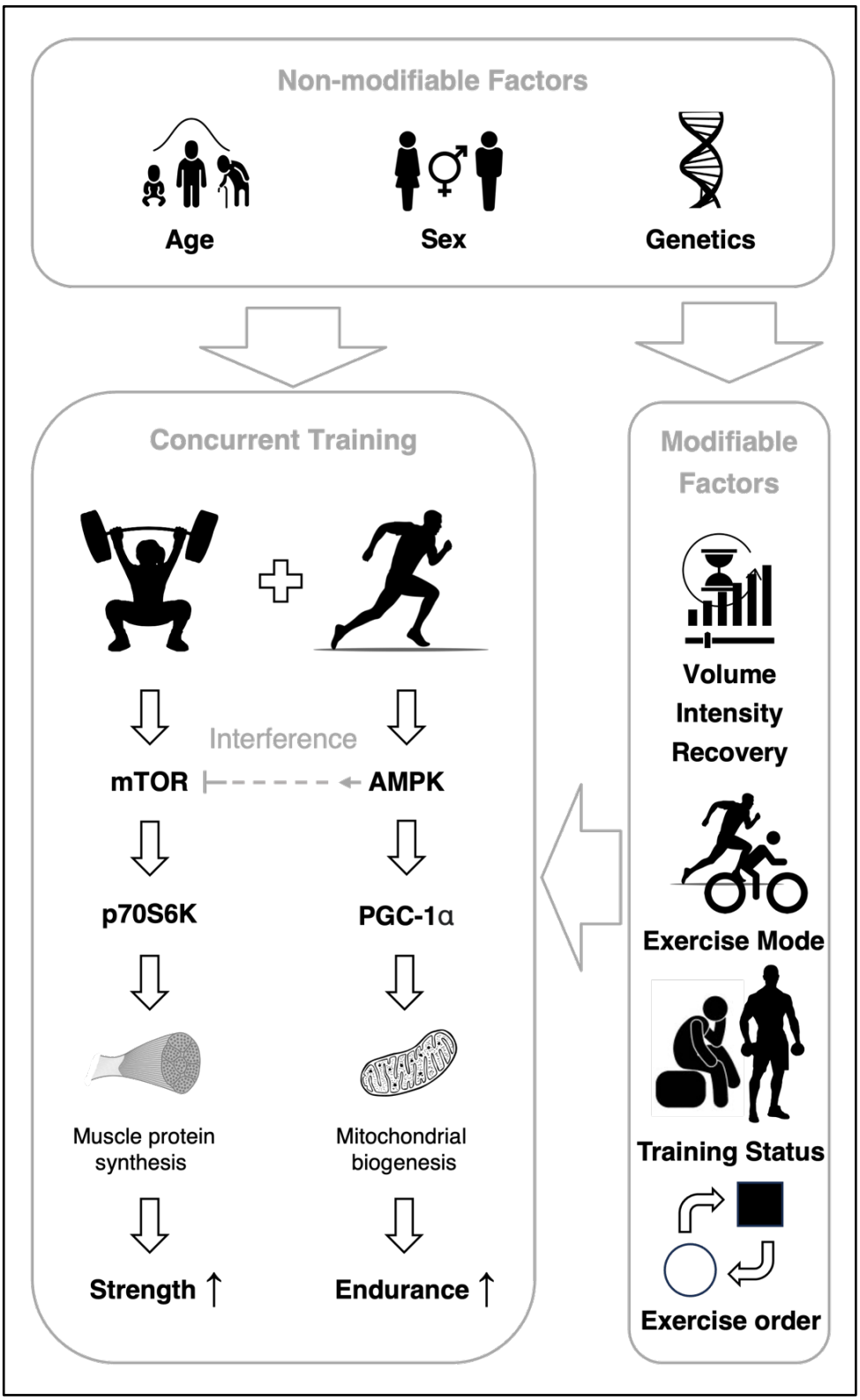

***Figure 1**. A simplified illustration of the holistic concept of concurrent training. AMPK = AMP-activated protein kinase, mTOR = mammalian target of rapamycin, p70S6K = ribosomal protein S6 kinase, PGC-1α = Peroxisome proliferator-activated receptor gamma coactivator 1-alpha. Strength and endurance exercises acutely stimulate molecular mechanisms of adaptation such as the mTOR and/or AMPK pathway. This increases the rate of muscle protein synthesis and mitochondrial biogenesis which in turn leads to increased levels of strength and endurance. Based on the available literature, AMPK and mTOR interfere with each other. The interference effect in turn, is moderated by several non-modifiable (e.g., age, sex, genetics) and/or modifiable (e.g., volume, intensity, recovery time, exercise mode, training status, exercise order) factors. The graph was generated by use of Pixabay [98].*

2.1.4 The effects of Concurrent Training on measures of physical fitness

2.1.4.1 Chronic effects

Generally, the literature suggests that CT is an effective method to improve muscle strength, muscle power, and cardiorespiratory endurance in healthy individuals, regardless of age and sex [19, 43, 90]. For instance, Schumann et al. [99] conducted a systematic review with meta-analysis on the effects of CT on measures of muscle strength/power and muscle hypertrophy in healthy adults of any age or sex. The authors reported that, irrespectively of age (i.e., < 40 years vs. > 40 years), training history (i.e., trained vs untrained), type of endurance exercise (i.e., cycling vs running), training frequency (i.e., < 5 sessions/week vs. > 5 sessions/week) and training modality (i.e., same session vs separate days), CT does not compromise the development of muscle strength and muscle hypertrophy [99]. However, the authors found a negative effect on muscle power, indicating that CT may attenuate the capacity to develop a high level of explosive strength, particularly when strength and endurance exercises were combined within the same session [99]. Murlasits and colleagues [73] meta-analysed the literature related to the long-term effects of two different intra-session exercise orders (i.e., strength-endurance vs endurance-strength) during CT on lower-body muscle strength and maximal aerobic capacity in healthy individuals aged 14 to 66 years. These authors reported that strength before endurance exercises is more effective to improve muscle strength than endurance exercise before strength. However, the development of aerobic capacity (i.e., maximum oxygen consumption) remained unaffected by the applied exercise order. Using a similar meta-analytical approach, Eddens and colleagues [72] confirmed the findings of Murlasits et al. [73] for lower limbs maximal strength in healthy individuals aged 18 to 65 years. It should be mentioned though, that the inclusion criteria of the forenamed studies were marked by a high heterogeneity related to the age, sex, and training status of the included participants.

2.1.4.2 Acute effects

Little is known about the acute effects of CT on measures of physical fitness. In this context, the term 'acute' refers to the short-term or immediate effect of one exercise on the subsequent when strength and endurance exercises are combined within the same session. The findings on the acute effects of endurance exercises on measures of muscle strength and power have shown inconsistent results. More specifically, while some studies reported attenuated strength and power outcomes [41, 100, 101], others showed post-activation performance enhancement most likely triggered by the previous endurance exercises [102-104]. Besides the complexity of the underpinning mechanisms of training and adaptation in general, the observed discrepancy in the literature is most likely due to several factors such as the rest between endurance and strength exercises as well as the type of exercises (e.g., cycling vs running) applied [36, 39, 48]. Other key aspects, seem to be the applied exercise order [36, 39] and participants' training status [36, 105]. In this regard, Markov et al. [42] meta-analysed the literature on the acute effects of endurance exercises on measures of muscle strength and power in trained individuals. The main findings of this meta-analysis showed that endurance exercise applied right before a strength exercise results in acute significant declines in muscle strength but not power of the involved muscles in trained male individuals. The findings further indicated that not only higher compared with lower intensity endurance exercises but also extended durations (i.e., > 30 minutes) exacerbate declines in muscle strength. Moreover, the authors reported that cycling compared with running exercise causes larger decrements in lower limb muscle strength. Based on their findings, Markov et al. [42] speculated endurance exercise-related neuromuscular fatigue [106, 107] to be the main driver of the observed results. From a performance perspective, that would be an explanation for the previously reported negative long-time effects of CT on muscle strength when endurance exercises are performed prior to strength exercises [72, 73]. However, Markov and colleagues [42] also indicated that performance measures do not necessarily reflect the underlying physiological mechanisms.

2.1.5 Molecular mechanisms of concurrent Training

The underlying physiological mechanisms of exercise and training, including CT, are highly complex. Therefore, an in-depth analysis of all molecular players (e.g., proteins, enzymes, kinases, hormones), involved in the process of adaptation to exercise is beyond the scope of this work. In this context, it is crucial to stress that several factors are likely to alter the molecular training response [36, 108]. Comprehensive systematic reviews and/or meta-analyses concerning the molecular responses to CT are yet missing. Nonetheless, there are several narrative review articles describing/summarizing the current state of the knowledge [36, 39, 47, 48, 50]. In general, exercise-induced adaptation is subjected to the principle of signal transduction (Figure 1, [109]). In the context of skeletal muscle, there are several studies including human [110, 111] and animal models [45, 80, 112] which highlight the importance of the AMPK and the mTOR/mTORC1 signalling pathways. These pathways are directly involved in the exercise-induced regulation of muscle protein synthesis (mTOR) and mitochondrial biogenesis (AMPK) [47]. For instance, in a rodent study, Bolster and colleagues [113] found that strength training acutely increases the rate of phosphorylation of several proteins (e.g., protein kinase B; mTOR; Eukaryotic translation initiation factor 4E-binding protein 1; Ribosomal protein S6 kinase beta-1 [p70S6K]) which are directly linked to the mTOR pathway and thus, the regulation of muscle protein synthesis. Meanwhile, there is evidence showing that a rapamycin-induced inhibition of the mTOR pathway directly blocks the phosphorylation of its downstream targets (i.e., p70S6k) which in turn attenuates muscle hypertrophy [114]. This was reported by data collected between two [111, 115] to 24 hours [110] following strength training in human subjects.

On the other hand, endurance exercise changes the ratio of adenosine-diphosphate/adenosine-triphosphate (ADP/ATP) and calcium levels within skeletal muscle. In turn, this stimulates the phosphorylation of AMPK [116, 117]. AMPK regulates important downstream targets such as the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) or nuclear respiratory factor 1 and 2 (NRF1/2)

[118]. PGC-1α is an important transcription regulator that regulates mitochondrial biogenesis by stimulating NRF-1/2 and mitochondrial transcription factor A, which in turn increases mitochondrial DNA replication and thus, gene transcription [119]. In this context, evidence from animal studies shows that the expression of PGC-1α correlates with muscle fiber-type formation [120, 121] and mitochondrial biogenesis [83, 112]. Taken together, both the mTOR as well as the AMPK networks are directly involved in skeletal muscle phenotype alteration.

With respect to the CT literature, it is critical to note that the AMPK and mTOR pathways tend to interfere with each other which in turn may cause alterations within the magnitude of skeletal muscle growth and other tissue [47]. For instance, an animal model by Bolster and colleagues showed that, when the activity of the AMPK pathway increased due to an injection of 5-aminoimidazole-4-carboxamide 1-β-d-ribonucleoside, phosphorylation levels of mTOR, p70S6K and other regulator proteins of muscle protein synthesis were significantly decreased [80]. In fact, other animal studies support the assumption that endurance exercise attenuates mTOR pathway activity [81]. In this context, it should be mentioned that there are studies that showed no interference between the mTOR/AMPK network. For instance, de Souza and colleagues [122] reported that 8 weeks of CT, compared to strength training alone, did not hamper the development of muscle strength and hypertrophy in healthy men aged 24 years. Generally, several factors determine the underlying physiological process of adaptation (compare to section 2.1.2 and 2.1.3). Regarding human skeletal muscle, frequently discussed factors are exercise volume and intensity [36]. Accordingly, Jones et al. [57] reported that the rate of muscle growth decreased with increased endurance exercise frequency. Meanwhile, Fyfe and colleagues [123] showed increased phosphorylation of mTOR and p70S6K when the endurance exercise intensity was increased. Interestingly, other studies did not find attenuated effects on muscle strength, regardless of endurance exercise type and/or intensity [66, 124]. Another important factor, most likely altering the molecular response to CT is the applied exercise order. Accordingly, there is evidence showing significant increases in the phosphorylation of mTOR and p70S6K

as well as mRNA expression of PGC-1α when strength exercises were performed immediately after endurance exercises [83]. This is in line with other studies investigating either the acute (i.e., ≤ 24 hours [125-127]) or chronic (≥ 7 weeks) effects of endurance before strength exercises (i.e., endurance-strength order) on measures of muscle hypertrophy [82, 128, 129]. Meanwhile, the strength-endurance order resulted in attenuated mTOR pathway activity [74, 79]. Unfortunately, the literature lacks studies representing high-performance athletes, which makes it difficult to draw causal conclusions for this group. Generally, it should be mentioned that many of the regulating mechanisms were studied in animal models while conclusive evidence from human models is yet rare. However, from a current molecular perspective, it seems reasonable to perform endurance before strength exercises to avoid or at least minimize the level of interference [39, 48, 74, 79, 80]. Of note, this is contrary to what is recommended in the studies that focus on the effects of CT on performance measures [72, 73], highlighting the need for future studies considering measures of physical fitness and the respective underlying physiological mechanisms.

2.1.6 Concurrent training and youth athletes

The body of literature regarding youth athletes is yet limited. This accounts particularly for studies investigating the effects of CT on the underlying physiological mechanisms together with measures of physical fitness. Generally, it is well-evidenced that maturation difference in youth is a key aspect affecting not only growth but also physical fitness performance, regardless of sex [25, 130]. Also, there is evidence that growth and maturation affect not only performance measures but also the capacity to adapt to training (i.e., trainability) [131]. Alves and colleagues investigated the effects of the applied exercise order and frequency (i.e., same session vs different sessions) on muscle power and maximal oxygen consumption, following 8 weeks of CT, in prepubertal children aged 10 to 11 years [132, 133]. Generally, the authors reported that CT is an effective method to improve both muscle power and maximal oxygen consumption. However, these effects were higher when strength and endurance exercises were performed on different days [132]. Also, when sessions were combined, the authors found beneficial

effects of the strength-endurance order for the development of muscle power while the endurance-strength order seems to be advantageous to induce increases in aerobic capacity [133]. Currently, there is only one meta-analysis available [90] that covers the effects of CT on cardiorespiratory endurance, muscular fitness, and athletic performance (i.e., time-trial, kicking/throwing velocity) in trained and untrained youth individuals. The main findings of the meta-analysis indicated [90] that CT is more effective to increase athletic performance (e.g., time-trial performance) in endurance-trained youth when compared to endurance exercise alone. Further, for untrained individuals, the authors reported higher increases in lower-body muscle power in the CT group compared to the strength training group. However, it must be mentioned that the main results of the study of Gäbler and colleagues [90] should be interpreted with caution due to the limited number of studies included, their low methodological quality, and the heterogeneous data they displayed. More recently, Seipp et al. [19] systematically reviewed the effects of CT on measures of muscular fitness in team sports athletes. Generally, the authors reported that CT improves both strength and endurance performance in team sport athletes. More specifically, results indicated superior effects in youth soccer players (≤ 18 years) when combining strength- and endurance exercises within a single session compared to separated sessions while no effect was observed regarding the applied exercise order [19]. Meanwhile, for highly trained youth soccer athletes (≤ 18 years) there was an order-effect, showing larger improvements in muscular fitness when plyometric jump training preceded sport-specific soccer training. Controversially, the authors reported attenuated muscle strength and endurance performance capacity in adolescent trained handball players (≤ 15 years) when strength exercises preceded endurance exercises within a single session [19].

2.1.7 Concurrent training and combat sports

Most combat sports demand both high levels of muscle strength/power and cardiorespiratory endurance [15-18]. Therefore, CT appears to be an appropriate approach to develop muscle strength/power and cardiorespiratory endurance in combat sports, including judo. Yet, there are very few original studies investigating the effects of CT in

combat sports [15]. For instance, Radovanovic et al [134] examined the effects of CT on measures of physical fitness and oxidative stress in trained male judo players aged 23 years. Following 12 weeks of training, authors reported significant increases in anaerobic power, maximal oxygen consumption, and markers of oxidative stress (i.e., erythrocyte malondialdehyde and plasma catalase). Another study by Ghahramani and colleagues [16] investigated the effects of the applied exercise order and the duration of rest between strength and endurance exercises following 8 weeks of CT in young male wrestling athletes aged 18 to 25 years. The study included five different groups, that is strength-endurance, endurance-strength, strength-8h rest- endurance, endurance-8h rest-strength, and control. The main findings indicated that upper-body muscle strength significantly increased in all groups apart from the endurance-strength group. Further, the authors revealed significant lower-body muscle strength increases when strength and endurance exercises were separated by 8 hours in between. Meanwhile, cortisol levels solely decreased significantly within the strength-8h rest-endurance group. In fact, it is generally accepted that breaks ≥ 3 hours reduce potential interference effects when applying strength and endurance exercises concurrently [19, 36, 48].

2.2 The Immune System

The immune system is a complex network spreading throughout the entire body, serving as both an external and internal shield against every potential source of threat such as viruses, bacteria, and damaged cells. Its primary function is to maintain the biological integrity of the organism. Of note, immune responses are crucial not only in the context of disease but also in response to physical exercise [135, 136]. In this sense, one notable mechanism involves the infiltration of WBC into the skeletal muscle to counteract exercise-induced muscle damage. Briefly, exercise stimulates inflammatory processes which enable certain immune cells (e.g., monocytes, lymphocytes, and complementary proteins) to infiltrate skeletal muscle, activating mechanisms of tissue repair [135-137]. Generally, the immune system comprises two distinct subsystems: the innate (non-specific) and the adaptive (specific) immune systems. It is fundamental to

understand that the two subsystems act together in harmony whenever an immune response is needed. Various cells, including macrophages and dendritic cells, which are part of the innate immune system, play a crucial role by presenting foreign substances (e.g., antigens) to the respective cells from the adaptive immune system (e.g., T-lymphocytes). This interaction subsequently triggers specific immune responses [138].

2.2.1 The innate immune system

The main function of the innate (non-specific) immune system is to fight harmful substances and germs that get access to the body through the skin or digestive system. As such, the innate immune system provides a general defense against harmful germs or substances. It mostly acts using defense cells such as natural killer cells and phagocytes. The innate immune system operates via two major lines of defense. The first line includes the skin and the mucous membrane [139] and the second line pertains to the inflammatory processes which are regulated due to the activity of certain cells (e.g., mast cells) and hormones (e.g., histamine) [138]. Briefly, inflammation causes blood vessels to dilate to increase permeability which in turn drives WBC subsets (i.e., GRAN, MONO), and other complementary proteins (e.g., complement component 3) to migrate to the area concerned. Simultaneously activated, the complement system (i.e., serum proteins, cell membrane receptors) co-regulates the entire process of inflammation [138]. For instance, it attracts other phagocytes (i.e., GRAN, macrophages) – a process which is known as chemotaxis – and/or induces the release of further histamine from mast cells, which in turn stimulates the entire inflammatory process [140].

2.2.2 The adaptive immune system

The adaptive (specific) immune response reflects the third line of defense. Adaptive immune responses are either cell- (i.e., cytotoxic T-lymphocytes) and/or humoral- (i.e., B-lymphocytes) mediated. When being activated, mainly due to pathogenic signals, T-lymphocytes destroy pathogens due to the release of several signals (e.g., perforin) which in turn, drive the pathogenic cell to undergo apoptosis [141]. Meanwhile, B-lymphocytes primarily serve the function of producing specific antibodies (known as immunoglobins) that bind to antigens presented on the pathogen's membrane. This interaction subsequently leads to the disruption of the pathogen's cellular integrity [142]. Importantly, T- and B-lymphocytes possess the ability to build memory cells when exposed to non-self-substances. This remarkable mechanism enables the adaptive immune system to launch specific responses to any source of threat, providing the body with a heightened level of protection.

2.2.3 Exercise and upper-respiratory-tract-infection

Exercise immunology is an ever-growing discipline within the sports science domain [143]. However, due to the general complexity of biology, it is often difficult to draw causal conclusions from original studies and transfer the respective findings to the field. Current exercise immunology studies could be separated into two different subareas, where one would cover upper-respiratory-tract-infections (URTI) and their occurrence following different endurance exercise frequencies and/or intensities [144] while the other focus on cellular immune responses to exercise [145]. With respect to URTI, the most recognized concept may be the open window theory [5, 144]. This theory is based on the assumption that the immune system is suppressed as a consequence of (endurance) exercise, which in turn causes an increased likelihood of URTI [146, 147]. In this context, the J-curve proposed by David Niemann [146], one of the pioneers within the scientific domain of exercise immunology, indicates a correlation between the risk of URTI and the applied exercise intensity and frequency. Accordingly, Niemann suggested that exercise at moderate frequencies and intensities may reduce the risk for URTI while exercising more frequently at higher intensities increases the risk for

URTI [146]. Consequently, that would mean that particularly athletes, who perform up to 4 training sessions per day [148], may be at higher risk for URTI than for instance recreationally active individuals. In fact, the open window theory is currently under debate [149] with recent literature suggesting other causes than viral or respiratory pathogens for URTI in athletes [150-152].

2.2.4 Cellular immune responses to exercise

A second area would cover cellular immune responses to exercise, for instance, changes within the number of circulating WBC (i.e., GRAN, LYM, MONO). Nonetheless, the literature indicates that the magnitude and the time course of the acute immune response and thus, any alteration within circulating immune cell counts is dependent on several factors such as the type of exercise applied, intensity and duration as well as training status [5, 13, 23, 153] while chronic exercise training at higher intensities may even reduce the number as well as the function of several immune cells (e.g., GRAN, LYM) [154]. Within this holistic concept, an exercise that involves repetitive muscle contraction acutely stimulates the activity of the central nervous system and causes systemic substrate metabolism [145]. This would alter immune cell activity/function and further, stimulate the release of glucocorticoid hormones (e.g., cortisol), catecholamine (e.g., adrenaline, cytokines such as Interleukin-6), and WBC into peripheral circulation [145, 155]. Thereby, the increase in WBC (i.e., leukocytosis) seems to be due to demarginating from the vessel walls and to cell releases from organic storage (e.g., liver, lung), as well as the thymus gland, bone marrow, lymph nodes, and skeletal muscle [156]. Previous studies reported acute leukocytosis after strength [157, 158] and endurance exercises [24, 159-161] in trained [24, 160, 161] and recreationally active [157-159] adults.

2.2.5 Cellular immune responses to Concurrent Training

Compared to strength or endurance-based exercises alone, studies investigating the effects of CT on immune system responses are yet scarce, highlighting a critical gap in the present literature.

2.2.5.1 Acute effects

From an acute perspective, Donges and colleagues [162] contrasted the level of cytokine mRNA expression following either strength-, endurance-, or concurrent exercises in sedentary middle-aged men and reported a significant increase, one-hour post-exercise, in the expression of Interleukin-6 and tumour-necrosis-factor-α, irrespective of the training method applied. Further, the same authors reported a significant difference between groups four hours post-exercise, showing that both Interleukin-6 and tumour-necrosis-factor-α went back toward baseline following CT while staying elevated following strength or endurance exercises alone. Supporting literature that contrasts the acute effects of CT on immune responses to strength and/or endurance exercises alone is yet missing. However, Bessa et al. [14] examined the acute effects of CT on markers of muscle damage and inflammation in elite cyclists aged 28 years And reported significant increases in WBC, neutrophils, LYM, MONO, and creatine kinase from ≤ 3 to ≤ 12 hours post-exercise. Meanwhile, the neutrophil-lymphocyte-ratio peaked 3 hours after the CT protocol and dropped significantly below baseline 12 hours post-exercise. The observed results were accompanied by significant decreases in upper-body muscle strength lasting from ≤ 3 to ≤ 12 hours post-exercise. In another study, Inoue et al. [163] investigated the effects of the applied CT order on acute immune responses in recreational male weightlifters and found similar acute alterations for interleukin-6, interleukin-10 and tumour-necrosis-factor-alpha immediately post-exercise, regardless of the applied exercise order.

2.2.5.2 Chronic effects

Concerning the chronic effects of CT, the available literature is yet inconclusive [164-167]. Nonetheless, Ihalainen et al. [165] recently reported that 24 weeks of CT reduces markers of inflammation in healthy men aged 31 years. In support, Stuart and colleagues stated that 12 weeks of CT reduce the risk of cardiovascular disease development due to a reduction in inflammatory cytokines and the C-reactive-protein in healthy adults, irrespective of age. Yet, there are no studies reflecting the effects of CT on chronic immune responses in athletes. In general, the number of studies in this area is limited but the available ones indicate that the immune responses to CT may differ from those known after single-mode strength- or endurance training [162], yet supportive evidence is missing.

3 Methods

3.1 Participants

A total of thirty-nine youth judo athletes participated in this study. Details of the recruited sample are provided in Table 1. To be included, participants had to be free from injuries or any signs of infectious diseases before and throughout the entire experimental period. All participants were members of the federal and/or national judo squad and can therefore be classified as highly trained athletes [168]. Additionally, they were all actively engaged in national and/or international judo competitions. Their general training routine consisted of two sessions per day, lasting one to two hours each on ≥ 5 days a week. The maturity status of participants was determined using the maturity offset method, which was estimated using the respective predictive equation of Mirwald et al. [169] for males and females. During the wash-out period, four male- and two female individuals dropped out. Thus, twenty males completed the entire protocol of study 1 (i.e., power-endurance versus endurance-power) while thirteen females completed the entire protocol of study 2 (strength-endurance versus endurance-strength). All participants as well as their legal guardians gave written informed consent to participate in the study. The Human Ethics Committee at Potsdam University approved the experimental procedures (No. 45/2020).

***Table 1**: Characteristics of the included participants across both studies.*

Characteristics	Study 1	Study 2
Number of participants	20	13
Sex	Male	Female
Age (years)	16 ± 1.8	14.4 ± 2.1
Maturity offset (years)	1.8 ± 1.4	2.0 ± 1.2
Sitting height (cm)	89.2 ± 3.8	85.9 ± 3.6
Standing height (cm)	171.2 ± 8	162.9 ± 6.3
Body mass (kg)	64.7 ± 11.6	57.1 ± 10.7
Training age (years)	9.1 ± 1.5	7.5 ± 1.4
Training volume (hours/week)	17 ± 4	17 ± 4

3.2 Experimental Procedures

Both study 1 and study 2 were designed after consultation with the head coaches of the male and female judo teams. In fact, within this period of the year, one of the main goals for the male head coach was to optimize muscle power performance and sport-specific aerobic performance while the female head coach aimed for the development of muscle strength and sport-specific aerobic performance. In this sense, we opted for a concurrent training intervention that combines a sport-specific aerobic task (i.e., repeated special judo fitness test) and power or strength-related exercise to be consistent with the objectives of the training schedule of participants. A schematic overview of studies 1 and 2 is shown in Figure 2. The experiments took place between May and June 2021. All participants visited the training/testing area on four different occasions. During the first visit, all participants were familiarised with all exercises and the experimental protocol while during the second visit, the 1-repetition maximum protocol using the leg-press machine was carried out. Thirty-six hours before the third and fourth visits, participants were instructed to avoid any kind of physical activity. Further, all participants were advised to have breakfast on the day of the experiment but to follow their normal filling routine. Due to COVID-19 restrictions, participants were assigned to three groups. For all experimental procedures (i.e., visit three and four), the first group arrived at 7:00 am, the second at 9:30 am, and the third at 11:30 am. All participants performed a standardised warm-up routine, based on selected exercises from the FIFA 11+ program [170]. During study 1 all participants were randomly assigned to either the power-endurance or endurance-power order, while for study 2, all participants were randomly assigned to either the strength-endurance or endurance-strength order. After the end of the protocols, all participants were informed to follow their daily routine but were instructed not to perform any additional sports activities for the rest of the day. Following a wash-out period of two weeks in which all participants followed their normal training routine, the procedure was repeated. More specifically, all participants from study 1, who performed the power-endurance order ran endurance-power and vice versa while all participants from study 2, who performed the strength-endurance order ran endurance-strength and vice versa.

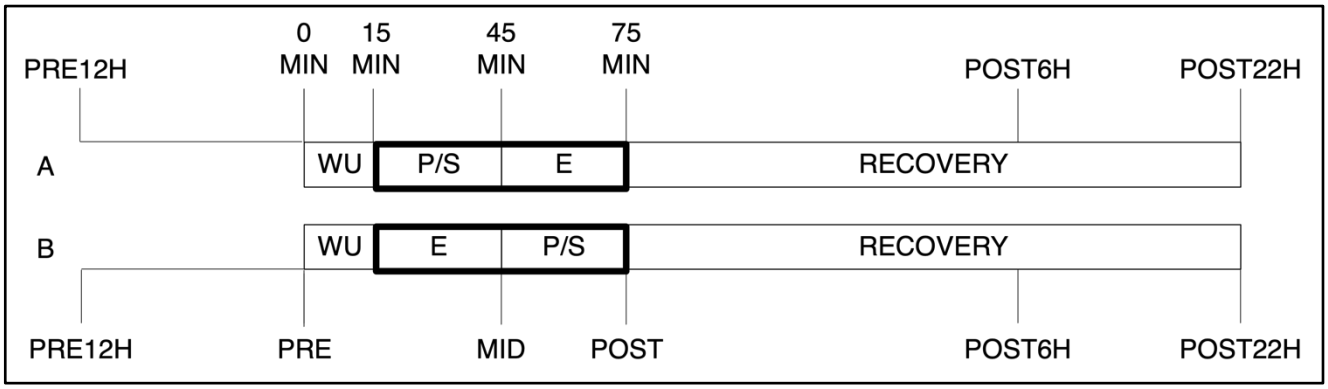

***Figure 2**. Schematic overview of study 1 and study 2. MIN = minutes; WU = warm-up; P = power exercise; S = strength exercise; E = sport-specific endurance exercise.*

3.2.1 Muscle power, muscle strength, and sport-specific endurance exercises

With reference to the recommendations of Faigenbaum et al. [171] for the progression of resistance training in youth athletes, the power exercise within study 1 consisted of 4 sets of 8 repetitions using a leg-press machine (SCHNELL, Peutenhausen, Germany, Figure 3) at 30 to 40% of 1-repetition maximum with 4 minutes break between sets (total work time including breaks and post measures ~ 25 minutes). Participants were instructed to perform each repetition as fast as possible. Meanwhile, in study 2, all participants completed 4 sets to volitional failure at 70 to 80% of their individual 1-repetition maximum [171]. To optimise the time under tension [172], each set lasted for a minimum of 45 seconds. The Break in between sets lasted ~ 4 minutes. For the sport-specific endurance exercise, the previously validated Special-Judo-Fitness-Test [173] was conducted (Figure 3). Specifically, four rounds of the Special-Judo-Fitness-Test with three sets (A = 15 s; B and C = 30 s) per round were carried out. The rest in between sets and rounds was 10 seconds and 4 minutes, respectively. Briefly, during each round, the evaluated participant throws two partners who are positioned 12 m apart as many times as possible using the *ippon-seoi-nage* technique [174]. The total work time including breaks and post measures was ~ 25 minutes. Due to their daily training routine and the previously applied familiarisation sessions, all participants were acquainted with the applied exercises.

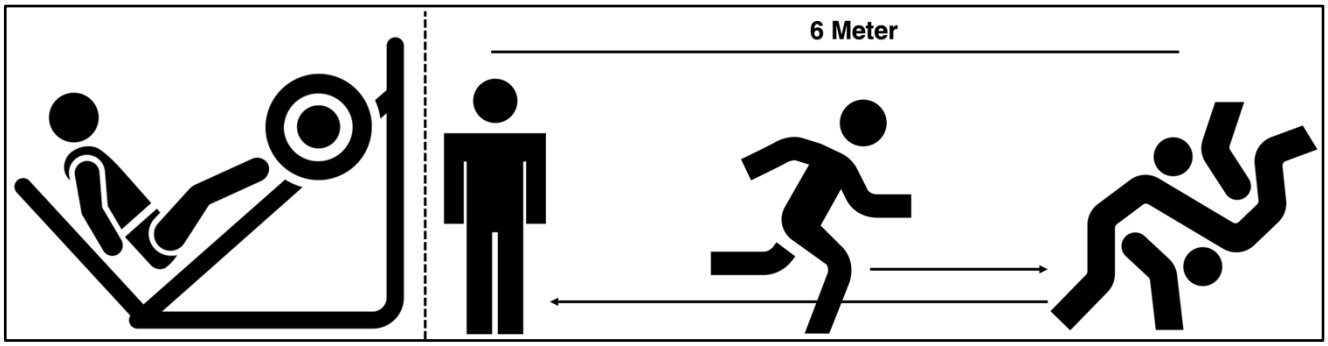

***Figure 3**. Schematic overview of the concurrent training exercises. On the left side, the strength/power exercise using the leg press machine and on the right side the sport-specific endurance exercise using the special judo fitness test.*

3.3 Data collection

All time points of measurement (i.e., PRE12H, PRE, MID, POST, POST6H, POST22H) are illustrated in Figure 2 and Table 2.

3.3.1 Immune responses

Capillary blood markers of immune response were obtained from the earlobe (20 μl) at PRE12H, PRE, POST, POST6H, and POST22H. Particularly, it needs to be emphasized that we did not measure immune responses between the power/strength and sport-specific endurance protocol (i.e., MID). Another measurement at MID would have extended the timeframe between the power/strength and sport-specific endurance exercise, something we wanted to avoid (Table 2). WBC, LYM, GRAN, MONO, and (blood) platelet were analysed immediately after taking the blood sample by using a hematology analyser system (Medonic M32, Boule Medical AB, Sweden). Medonic M32 uses a WBC-discriminator and operates due to the principle of impedance. Thereby, GRAN includes neutrophils, basophils, and eosinophils. MONO reflect on middle-sized-cells estimated, based on the total number of GRAN and LYM.

3.3.2 Indirect markers of immune response

GLR and the SII were calculated for PRE12H, PRE, POST, POST6H, and POST22H. With reference to previous literature [175, 176], the following equation was used:

$$GLR = \mathrm{GRAN/LYM}$$

$$SII = \mathrm{Platelets} * \mathrm{GRAN/LYM}$$

3.3.3 Metabolic response

Additionally, 10 μl blood was taken from the earlobe at PRE, MID, and POST, to measure blood lactate and blood glucose (Biosen S-Line, EKF-Diagnostics, Germany).

3.3.4 Physical fitness and Rating of perceived exertion

Measures of physical fitness and RPE were collected at PRE, MID, POST, and POST6H. CMJ-height, -force, and -power was assessed by using a force plate (Leonardo Jumping Platform, Novotec, Germany) while RPE was measured by use of the BORG scale [177].

***Table 2**: Time point of measurement for all markers of immune response, metabolic response, and measures of physicall fitness and RPE.*

	PRE12H	PRE	MID	POST	POST6H	POST22H
Immune response	✓	✓		✓	✓	✓
Metabolic response		✓	✓	✓		
Physical Fitness		✓	✓	✓	✓	

Legend: The green tick marks the time of the measurement.

3.4 Statistical analyses

To examine the effects of CT exercise order on the dependent variables (i.e., WBC; LYM; GRAN; MONO; GLR; SII; blood lactate and glucose; CMJ-performance [i.e., power; force; height] as well as RPE) a two (order [study 1: power-endurance versus endurance-power; study 2: strength-endurance versus endurance-strength]) *five (time [immune]: PRE12H, PRE, POST, POST6H, POST22H) or four (time [performance measures; RPE]: PRE, MID, POST, POST6H) or three (time [metabolic]: PRE, MID, POST) repeated measure analysis of variance (ANOVA) was computed [178]. Data were tested and confirmed for normal distribution using the Shapiro–Wilk test [179]. To correct for violations of sphericity, the degrees of freedom were corrected in the normal way, using the Huynh-Feldt ($\varepsilon > 0.75$) or Greenhouse-Geisser ($\varepsilon < 0.75$) values for ε, as appropriate [180]. In the case of significant order * time interactions, Bonferroni pairwise comparisons were conducted [180, 181]. Delta changes and effect sizes (ES) were calculated from PRE-to-MID, PRE-to-POST, PRE-to-POST6H, and PRE-to-POST22H. Effect sizes are generally expressed as positive values and were interpreted as trivial ($ES < 0.20$), small ($0.2 \leq ES < 0.50$), moderate ($0.50 \leq ES < 0.80$), or large ($ES \geq 0.80$) [181]. The results are presented as mean ± standard deviation (SD). Statistical significance was set at $p < 0.05$. The data were analysed using the Statistical Package for Social Science (SPSS, Chicago, IL, USA, version 29.0).

4 Results

4.1 Study 1

Mean values and standard deviations for all measures are displayed in Table 3. Delta changes and effect sizes are displayed in Table 4. There was no difference observed between PRE12H and PRE. Further, no baseline differences between the two exercise orders for all measurements were observed.

***Table 3**: Mean values and standard deviation for study 1 for all undertaken measures.*

Variable	Condition	PRE12H	PRE	MID	POST	POST6H	POST22H	Condition	Time	Interaction
WBC (10^3/µl)	Power-Endurance	8.52±2.46	7.20±2.10	7.20±2.10	11.80±3.22*	14.25±3.43*	7.22±1.92	$F_{1, 19}$ = 7.23;	$F_{3.93, 74.57}$ = 46.95;	$F_{3.72, 70.71}$ = 2.66;
	Endurance-Power	8.26±1.88	7.60±2.82		10.10±2.53*	11.86±2.30*	7.00±3.13	***p* = 0.015**	***p* < 0.001**	***p* = 0.043**
GRAN (10^3/µl)	Power-Endurance	4.33±1.27	3.75±1.25		5.99±1.79	9.77±2.99*	3.48±1.06	$F_{1, 19}$ = 0.10;	$F_{4, 76}$ = 55.54;	$F_{2.32, 44.15}$ = 3.83;
	Endurance-Power	4.35±1.00	4.11±2.30		6.90±2.57	7.98±2.00*	3.61±2.37	*p = 0.757*	***p* < 0.001**	***p* = 0.024**
LYM (10^3/µl)	Power-Endurance	3.60±1.37	2.97±1.08		4.99±2.05*	3.55±1.10	3.24±1.92	$F_{1, 19}$ = 18.43;	$F_{2.61, 49.58}$ = 4.09;	$F_{2.78, 52.74}$ = 8.92;
	Endurance-Power	3.35±0.95	2.96±0.93		2.59±0.89*	3.11±1.09	2.91±1.30	***p* < 0.001**	***p* = 0.015**	***p* < 0.001**
MONO (10^3/µl)	Power-Endurance	0.59±0.19	0.49±0.19		0.83±0.27*	0.94±0.23	0.52±0.15	$F_{1, 19}$ = 5.65;	$F_{2.94, 55.78}$ = 27.12;	$F_{2.72, 51.72}$ = 3.25;
	Endurance-Power	0.59±0.17	0.53±0.19		0.61±0.15*	0.77±0.27	0.48±0.19	***p* = 0.028**	***p* < 0.001**	***p* = 0.033**
GLR (10^3/µl)	Power-Endurance	1.31±0.41	1.35±0.50		1.36±0.56*	2.91±1.17	1.12±0.33	$F_{1, 19}$ = 6.62;	$F_{2.55, 48.49}$ = 33.36;	$F_{2.36, 44.88}$ = 7.86;
	Endurance-Power	1.35±0.36	1.44±0.74		2.97±1.63*	2.94±1.42	1.32±0.77	***p* = 0.019**	***p* < 0.001**	***p* = 0.001**
SII (10^3/µl)	Power-Endurance	187±75	203±75		209±110*	427±214	149±53	$F_{1, 19}$ = 6.25;	$F_{2.31, 43.83}$ = 25.39;	$F_{2.52, 47.92}$ = 6.73;
	Endurance-Power	180±61	218±116		456±290*	444±252	164±113	***p* = 0.022**	***p* < 0.001**	***p* = 0.001**
LA (mmol/l)	Power-Endurance		0.99±0.29	1.50±0.35*	8.06±2.89*			$F_{1, 19}$ = 22.84;	$F_{1.48, 28.17}$ = 108.65;	$F_{1.13, 21.46}$ = 136.27;
	Endurance-Power		0.97±0.20	9.19±3.02*	2.72±0.94*			***p* < 0.001**	***p* < 0.001**	***p* < 0.001**
GLU (mg/dl)	Power-Endurance		4.74±0.88	4.54±0.63*	5.54±0.93*			$F_{1, 19}$ = 2.13;	$F_{1.29, 24.43}$ = 2.34;	$F_{2, 38}$ = 11.60;
	Endurance-Power		4.92±1.16	5.82±1.18*	4.57±0.71*			*p* = 0.160	*p* = 0.133	***p* < 0.001**
CMJ-H (cm)	Power-Endurance		41.49±6.32	40.68±6.02	40.10±5.46	42.31±6.74		$F_{1, 19}$ = 1.26;	$F_{3, 57}$ = 3.10;	$F_{1.84, 35.01}$ = 0.50;
	Endurance-Power		40.78±5.80	40.73±6.66	39.12±7.68	40.87±6.29		*p* = 0.276	***p* = 0.034**	*p* = 0.595
CMJ-P (W)	Power-Endurance		3.15±0.90	3.12±0.89*	3.17±0.86	3.21±0.93		$F_{1, 19}$ = 1.09;	$F_{3, 57}$ = 2.50;	$F_{2.67, 50.68}$ = 3.80;
	Endurance-Power		3.15±0.93	3.23±0.98*	3.00±0.94	3.16±0.87		*p* = 0.310	*p* = 0.068	***p* = 0.019**
CMJ-F (N)	Power-Endurance		1.56±0.41	1.53±0.43	1.57±0.40*	1.54±0.40		$F_{1, 19}$ = 0.34;	$F_{3, 57}$ = 0.76;	$F_{2.04, 38.84}$ = 3.34;
	Endurance-Power		1.59±0.43	1.57±0.43	1.51±0.39*	1.56±0.39		*p* = 0.567	*p* = 0.521	***p* = 0.045**
RPE	Power-Endurance		7±1	9±1*	18±2*	7±1		$F_{1, 19}$ = 4.02;	$F_{2.17, 41.15}$ = 274.94;	$F_{2.73, 51.82}$ = 285.51;
	Endurance-Power		7±1	18±1*	11±2*	8±2		*p* = 0.059	***p* < 0.001**	***p* < 0.001**

Legend: *Marks a significant difference between exercise orders at the respective time point. WBC = White blood cells; GRAN = Granulocytes; LYM = Lymphocytes; MONO = Monocytes; GLR = Granulocyte-Lymphocyte-ratio; SII = Systemic-inflammation-index; LA = Lactate: GLU = Glucose; CMJ-H = Counter-movement jump height; CMJ-P = Counter-movement jump power; Counter-movement jump force; RPE = Rating of perceived exertion.

***Table 4**: Delta changes and effect sizes for study 1 between all displayed time points.*

Variable	Condition	PRE	MID (Δ%; ES)	POST (Δ%; ES)	POST6H (Δ%; ES)	POST22H (Δ%; ES)	Interaction, ES
WBC (10^3/µl)	Power-Endurance	7.20±2.10		+64; 2.20	+98; 3.40	±0; 0.00	***p* = 0.043**; ES = 0.75
	Endurance-Power	7.60±2.82		+33; 0.90	+55; 1.50	-8; 0.20	
GRAN (10^3/µl)	Power-Endurance	3.75±1.25		+60; 1.79	+160; 4.82	-7; 0.22	***p* = 0.024;** ES = 0.90
	Endurance-Power	4.11±2.30		+68; 1.21	+94; 1.68	-12; 0.22	
LYM (10^3/µl)	Power-Endurance	2.97±1.08		+68; 1.87	+20; 0.54	+9; 0.25	***p* < 0.001**; ES = 1.37
	Endurance-Power	2.96±0.93		-13; 0.40	+5; 0.16	-2; 0.05	
MONO (10^3/µl)	Power-Endurance	0.49±0.19		+69; 1.79	+91; 2.37	+6; 0.16	***p* = 0.033**; ES = 0.83
	Endurance-Power	0.53±0.19		+15; 0.42	+45; 1.26	-9; 0.26	
GLR (10^3/µl)	Power-Endurance	1.35±0.50		+1; 0.02	+116; 3.12	-17; 0.46	***p* = 0.001**; ES = 1.29
	Endurance-Power	1.44±0.74		+106; 2.07	+104; 2.03	-8; 0.16	
SII (10^3/µl)	Power-Endurance	203±75		+3; 0.08	+110; 2.99	-27; 0.72	***p* = 0.001**; ES = 1.19
	Endurance-Power	218±116		+109; 2.05	+104; 1.95	-25; 0.47	
LA (mmol/l)	Power-Endurance	0.99±0.29	+52; 1.72	+814; 24.38			***p* < 0.001,** ES = 5.37
	Endurance-Power	0.97±0.20	+947; 40.50	+280; 8.75			
GLU (mg/dl)	Power-Endurance	4.74±0.88	-4; 0.23	+17; 0.91			***p* < 0.001**, ES = 1.56
	Endurance-Power	4.92±1.16	+18; 0.78	-7; 0.30			
CMJ-H (cm)	Power-Endurance	41.49±6.32	-2; 0.13	-3; 0.22	+2; 0.31		*p* = 0.595, ES = 0.33
	Endurance-Power	40.78±5.80	±0; 0.01	-4; 0.29	±0; 0.02		
CMJ-P (W)	Power-Endurance	3.15±0.90	-1; 0.03	+1; 0.02	+2; 0.07		***p* = 0.019**, ES = 0.90
	Endurance-Power	3.15±0.93	+3; 0.09	-5; 0.16	±0; 0.01		
CMJ-F (N)	Power-Endurance	1.56±0.41	-2; 0.07	+1; 0.02	-1; 0.05		***p* = 0.045**, ES = 0.84
	Endurance-Power	1.59±0.43	-1; 0.05	-5; 0.19	-2; 0.07		
RPE	Power-Endurance	7±1	+29; 2.00	+157; 11.00	±0; 0.00		***p* < 0.001**, ES = 7.78
	Endurance-Power	7±1	+157; 11.00	+57; 4.00	+14; 1.00		

Legend: WBC = White blood cells; GRAN = Granulocytes; LYM = Lymphocytes; MONO = Monocytes; GLR = Granulocyte-Lymphocyte-ratio; SII = Systemic-inflammation-index; LA = Lactate: GLU = Glucose; CMJ-H = Counter-movement jump height; CMJ-P = Counter-movement jump power; Counter-movement jump force; RPE = Rating of perceived exertion; ES = Effect size, ∆% = delta change.

4.1.1 Immune responses

Results showed significant time*order interactions for WBC (p = 0.043), GRAN (p = 0.024), LYM ($p < 0.001$), MONO (p = 0.033), as well as GLR and SII (both $p < 0.01$). More specifically, power-endurance resulted in significantly larger PRE-to-POST (Δ+64%) and PRE-to-POST6H (Δ+98%) increases for WBC compared to endurance-power (Δ+33% and Δ+55%, respectively). In terms of GRAN, results indicated significantly larger PRE-to-POST6H elevations (Δ+160%) for power-endurance compared to endurance-power (Δ+94%). For LYM, significantly larger PRE-to-POST increases (Δ+68%) in power-endurance compared to endurance-power (Δ-13%) were noted. With respect to MONO, the power-endurance order induced significantly larger PRE-to-POST (Δ+69%) increases compared to endurance-power (Δ+15%). Regarding GLR and SII, findings indicated significantly larger PRE-to-POST increases for endurance-power (Δ+106% and Δ+109%, respectively), compared to power-endurance (Δ+1% and Δ+3%, respectively). No significant differences were noted between PRE12H-to-PRE, and PRE-to-POST22H for all parameters, regardless of the exercise order. A graphical representation of these results can be found in Figures 4, 5, and 6.

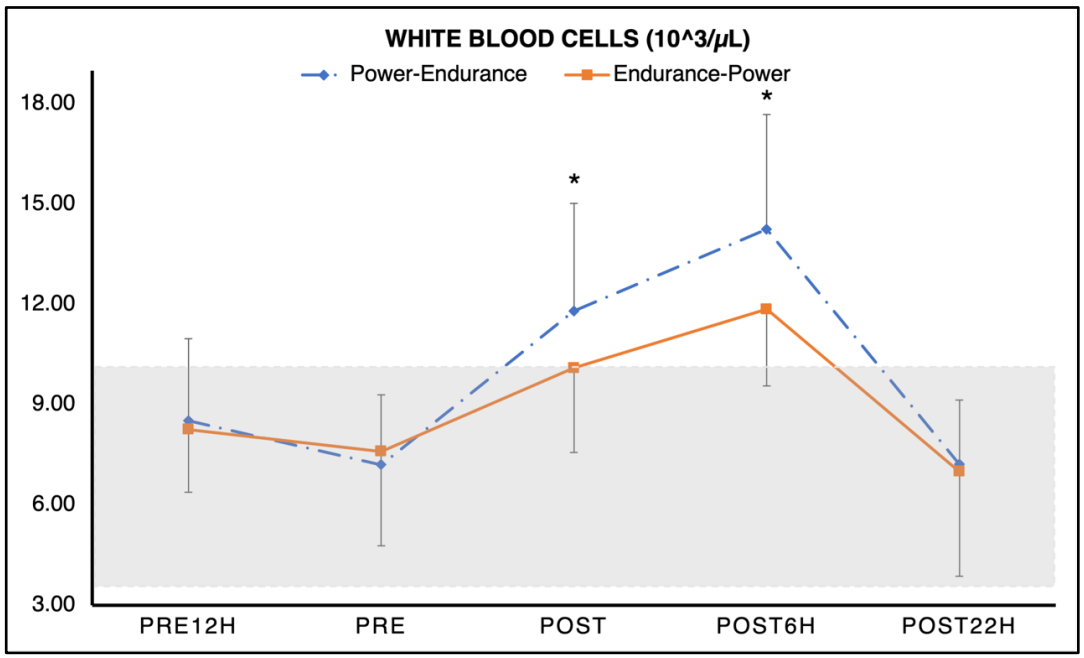

***Figure 4**. Means and standard deviation for white blood cells measured at PRE12H, PRE, POST, POST6H, and POST22H. The grey zone marks lower and upper reference values provided by the manufacturer (Medonic M32 series). ***:** stands for significant difference between the two exercise orders.*

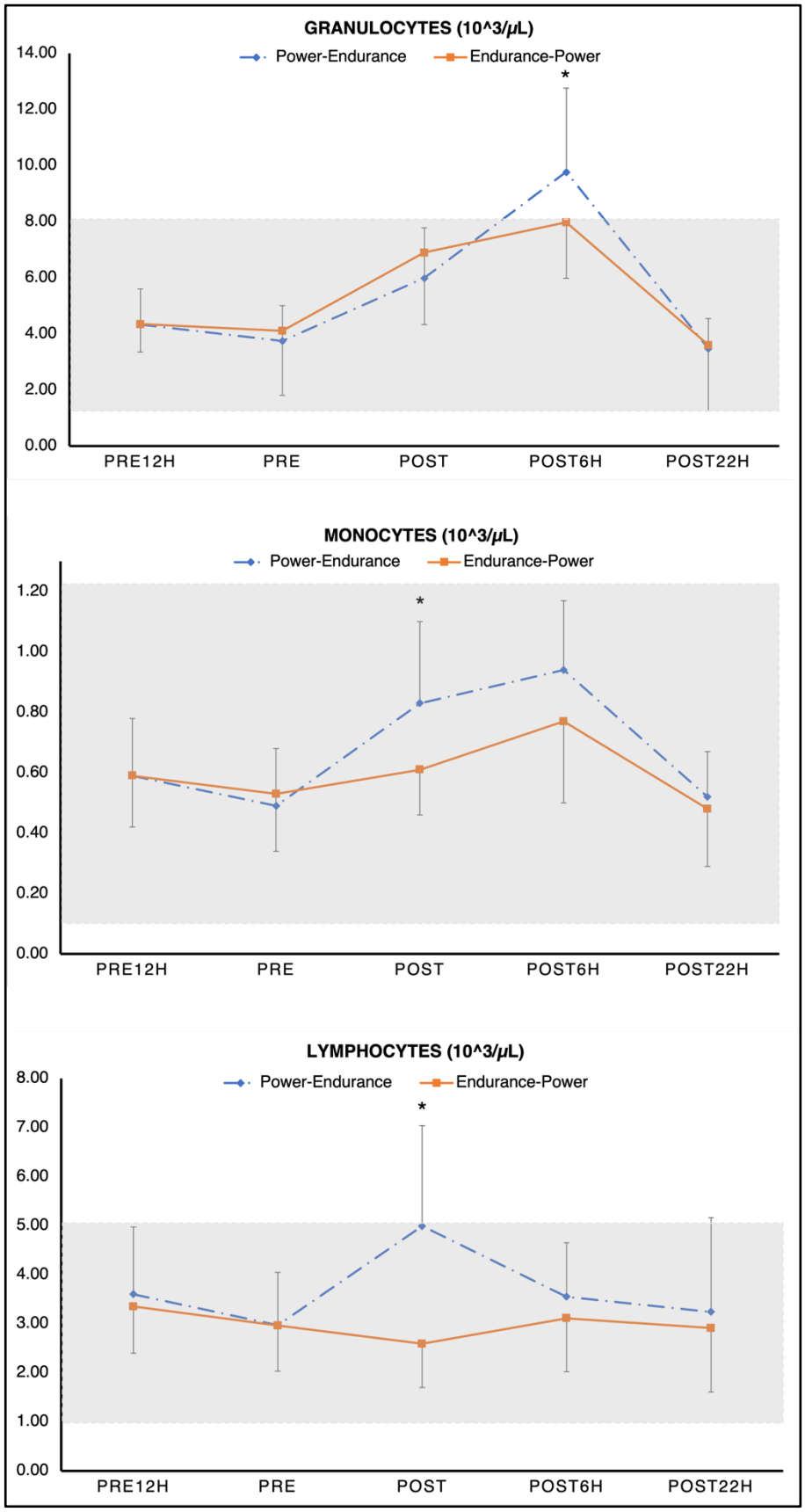

***Figure 5**. Means and standard deviation for granulocytes, monocytes, and lymphocytes, measured at PRE12H, PRE, POST, POST6H, and POST22H. The grey zone marks lower and upper reference values provided by the manufacturer (Medonic M32 series). ***:** stands for significant difference between the two exercise orders.*

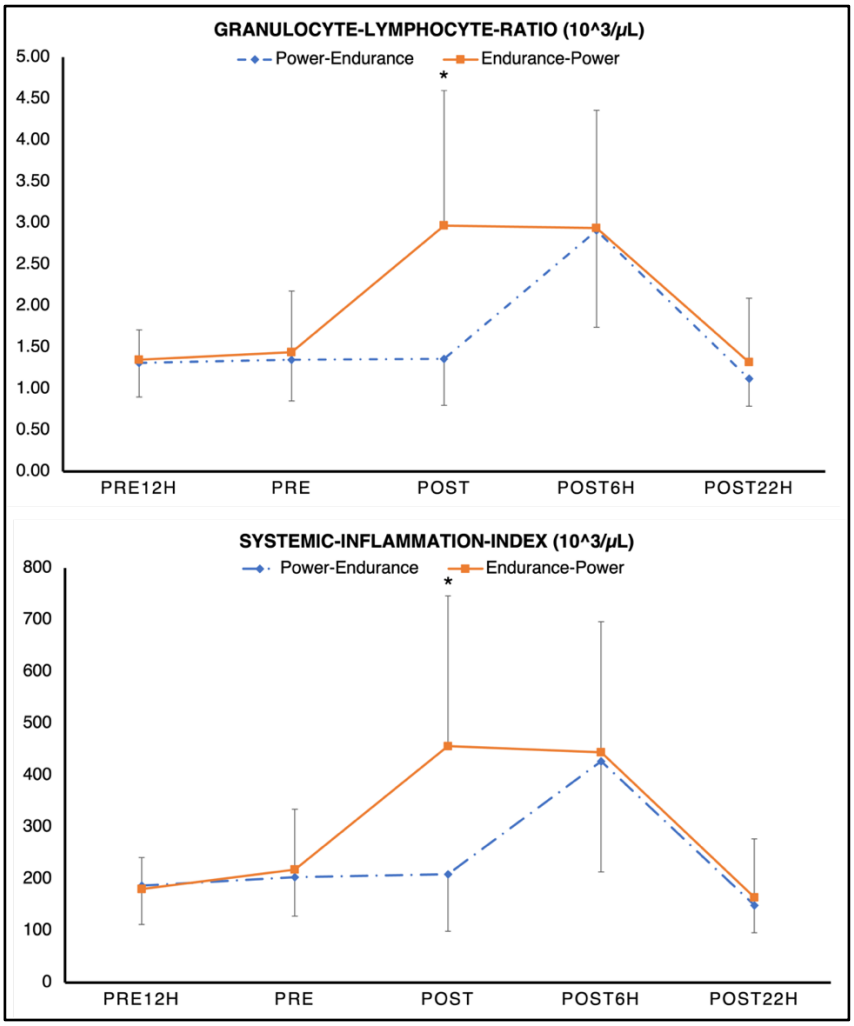

Figure 6**. Means and standard deviation for the granulocytes-lymphocytes-ratio and the systemic-inflammation-index, calculated at PRE12H, PRE, POST, POST6H, and POST22H. ***: stands for significant difference between the two exercise orders.

4.1.2 Metabolic responses

Our findings indicated significant time*order interactions for blood glucose and lactate (both $p < 0.01$). Results showed significantly larger PRE-to-MID increases in blood glucose and lactate following the endurance exercise (as part of the endurance-power order, Δ+18% and Δ+947%, respectively) compared to the power exercise (as part of the power-endurance order, Δ-4% and Δ+52%, respectively). From PRE-to-POST, changes in blood glucose and lactate were significantly larger for the power-endurance order (Δ+17% and Δ+814%, respectively), compared to the endurance-power order (Δ-7% and Δ+280%, respectively). A graphical representation of these results can be found in Figure 7.

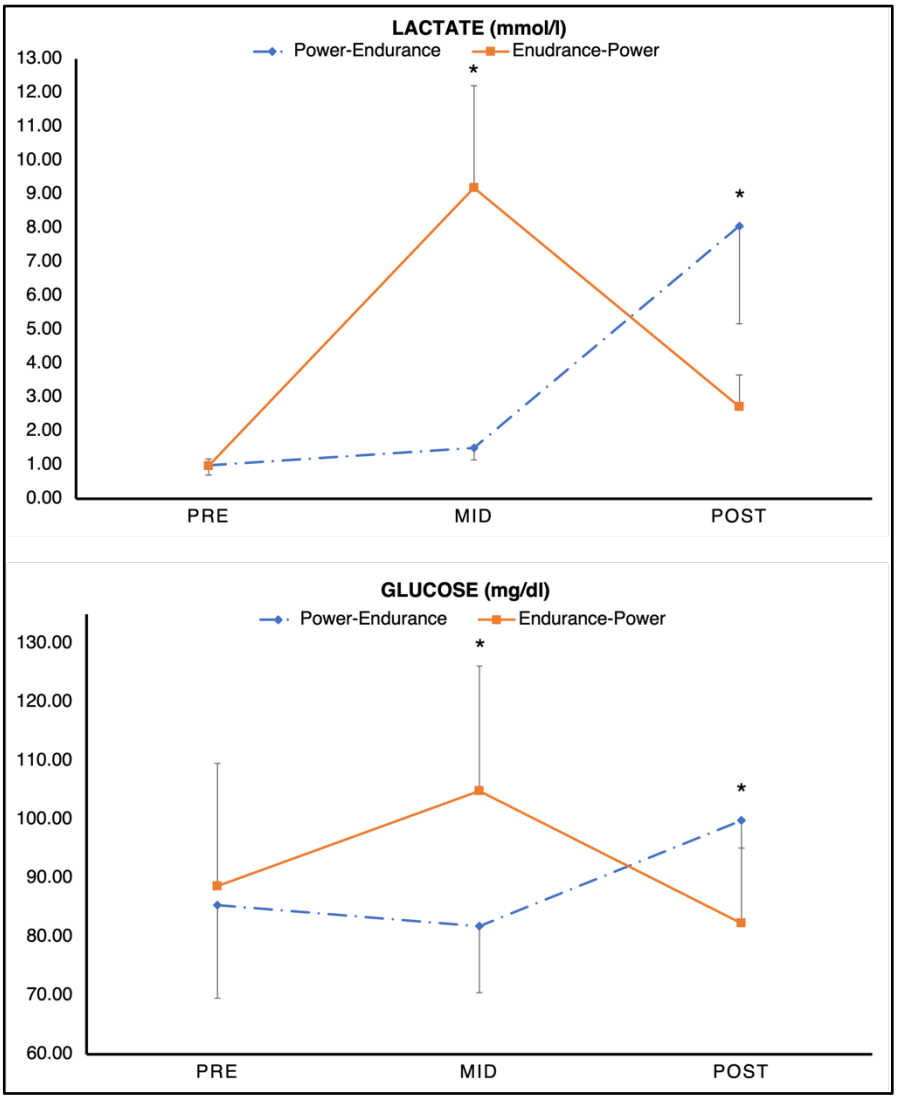

***Figure 7**. Means and standard deviation for blood lactate and blood glucose measured at PRE, MID, and POST. *: stands for significant difference between the two exercise orders.*

4.1.3 Physical fitness and Rating of perceived exertion

For physical fitness, a significant time*order interaction was observed for CMJ-force (p = 0.045) with significantly larger PRE-to-POST performance decreases for the endurance-power order (Δ-5%), compared to the power-endurance order (Δ+1%). Further, there was a significant time*order interaction for CMJ-power (p = 0.019) with larger PRE-to-MID performance decreases following the power exercise (as part of the power-endurance order, Δ-1%), compared to the endurance exercise (as part of the endurance-power order, Δ+3%). Regarding RPE, there was a significant time*order interaction ($p < 0.01$) with larger PRE-to-MID values following the endurance exercise

(as part of the endurance-power order, Δ+157%), compared to the power exercise (as part of the power-endurance order, Δ+29%). Additionally, RPE values were significantly larger from PRE-to-POST following the power-endurance order (Δ+157%), compared to endurance-power (Δ+57%). A graphical representation of these results can be found in Figure 8.

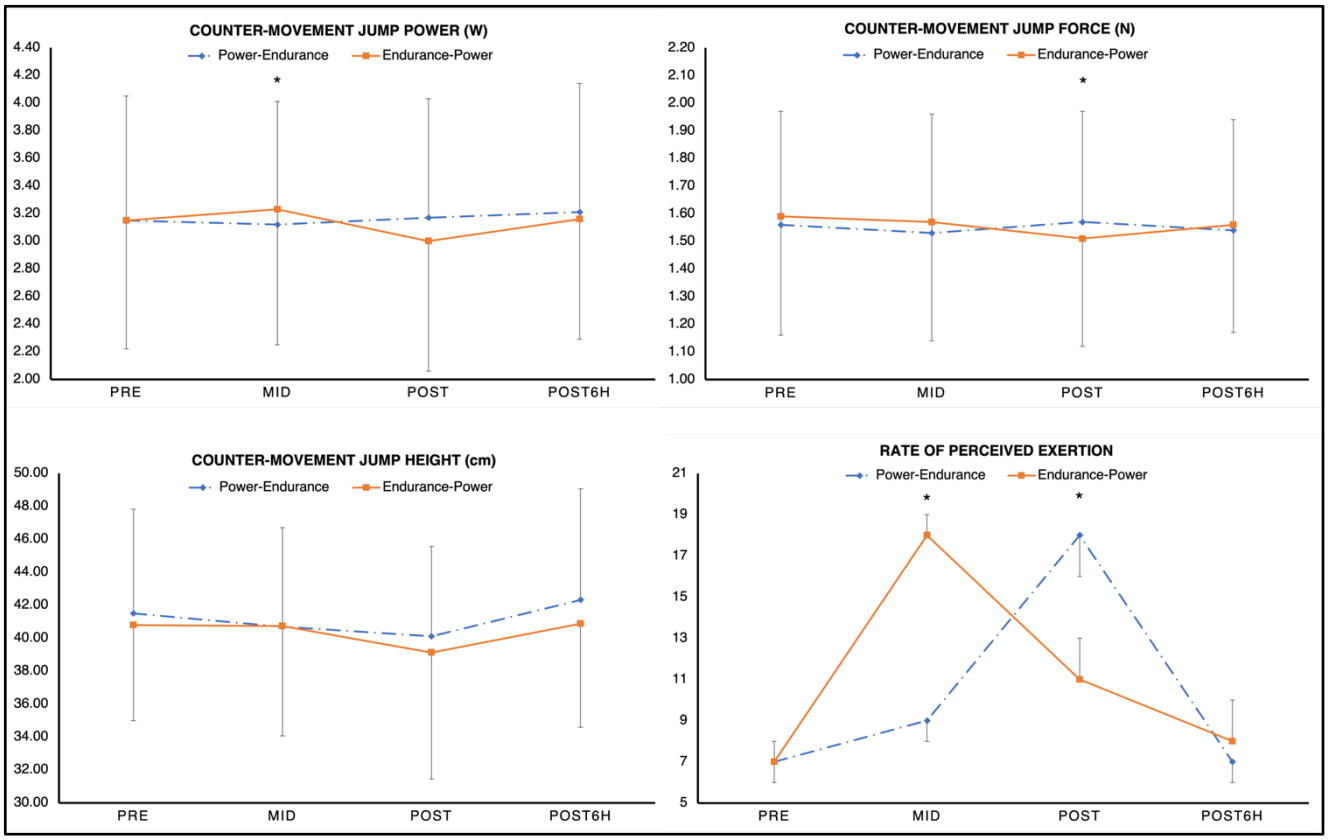

***Figure 8**. Means and standard deviation for Counter-movement jump height, power, force, and rating of perceived exertion measured at PRE, MID, POST, and POST6H. *: stands for significant difference between the two exercise orders.*

4.2 Study 2

Mean values and standard deviations for all measures are displayed in Table 5. Delta changes and effect sizes are displayed in Table 6. There was no difference observed between PRE12H and PRE. Further, no baseline differences between the two exercise orders for all measurements were observed.

***Table 5**: Mean values and standard deviation for study 2 for all undertaken measures.*

Variable	Condition	PRE12H	PRE	MID	POST	POST6H	POST22H	Condition	Time	Interaction
WBC (10^3/µl)	Strength-Endurance	8.35±2.26	8.27±2.29		12.91±4.76	12.84±3.68	6.94±2.07	$F_{1, 12}$ = 1.77;	$F_{2.74, 32.87}$ = 21.82;	$F_{2.71, 32.55}$ = 2.24;
	Endurance-Strength	9.65±3.62	9.03±1.93		11.90±3.52	14.42±3.62	7.83±2.05	p = 0.208	**p < 0.001**	p = 0.107
GRAN (10^3/µl)	Strength-Endurance	4.69±1.61	4.30±1.59		7.31±2.90	8.71±2.82	3.68±1.32	$F_{1, 12}$ = 1.64;	$F_{2.69, 32.33}$ = 36.29;	$F_{2.35, 27.04}$ = 3.26;
	Endurance-Strength	5.07±1.88	4.56±0.66		8.19±2.83	9.31±2.50	3.84±1.07	p = 0.225	**p < 0.001**	p = 0.750
LYM (10^3/µl)	Strength-Endurance	3.41±1.90	3.42±0.92		4.76±2.91*	3.25±0.78	2.78±0.86	$F_{1, 12}$ = 0.31;	$F_{2.20, 26.34}$ = 1.00;	$F_{2.77, 33.27}$ = 5.15;
	Endurance-Strength	3.90±1.71	3.82±1.44		3.02±1.27*	4.10±1.41	3.54±1.36	p = 0.585	p = 0.389	**p = 0.006**
MONO (10^3/µl)	Strength-Endurance	0.56±0.16	0.55±0.16		0.84±0.36	0.87±0.28	0.48±0.12	$F_{1, 12}$ = 2.06;	$F_{2.88, 34.58}$ = 14.05;	$F_{2.66, 31.99}$ = 3.72;
	Endurance-Strength	0.68±0.27	0.65±0.21		0.69±0.24	1.02±0.30	0.57±0.16	p = 0.177	**p < 0.001**	**p = 0.035**
GLR (10^3/µl)	Strength-Endurance	1.57±0.54	1.31±0.48		1.84±1.09*	2.83±1.12	1.35±0.35	$F_{1, 12}$ = 0.52;	$F_{1.86, 22.27}$ = 19.01;	$F_{2.43, 29.20}$ = 7.32;
	Endurance-Strength	1.39±0.44	1.33±0.49		3.02±1.23*	2.44±0.92	1.20±0.55	p = 0.486	**p < 0.001**	**p = 0.002**
SII (10^3/µl)	Strength-Endurance	249±101	216±103		301±203*	461±166	183±66	$F_{1, 12}$ = 0.02;	$F_{1.91, 22.88}$ = 16.11;	$F_{2.51, 30.06}$ = 3.66;
	Endurance-Strength	220±75	209±112		433±209*	389±143	173±76	p = 0.887	**p < 0.001**	**p = 0.029**
LA (mmol/l)	Strength-Endurance		0.96±0.22	4.33±1.64*	6.00±4.15			$F_{1, 12}$ = 0.74;	$F_{1.15, 13.85}$ = 36.19;	$F_{1.14, 13.62}$ = 6.83;
	Endurance-Strength		0.88±0.26	6.35±2.95*	4.62±1.81			p = 0.408	**p < 0.001**	**p = 0.018**
GLU (mg/dl)	Strength-Endurance		4.73±0.50	4.46±0.42*	5.60±1.27*			$F_{1, 12}$ = 0.64;	$F_{2, 24}$ = 1.40;	$F_{1.76, 21.06}$ = 13.08;
	Endurance-Strength		4.81±0.54	5.69±1.27*	4.66±0.65*			p = 0.438	p = 0.266	**p < 0.001**
CMJ-H (cm)	Strength-Endurance		32.26±3.20	30.81±3.88	29.97±4.65	31.86±3.06		$F_{1, 12}$ = 9.67;	$F_{3, 36}$ = 3.14;	$F_{1.84, 22.02}$ = 1.17;
	Endurance-Strength		32.50±2.68	33.23±4.07	32.11±3.15	33.36±4.15		**p = 0.009**	**p = 0.037**	p = 0.326
CMJ-P (W)	Strength-Endurance		2.17±0.57	2.13±0.55*	2.15±0.42	2.17±0.45		$F_{1, 12}$ = 2.40;	$F_{2.12, 25.41}$ = 2.81;	$F_{2.11, 25.33}$ = 5.91;
	Endurance-Strength		2.19±0.93	2.27±0.50*	2.06±0.47	2.24±0.49		p = 0.147	p = 0.076	**p = 0.007**
CMJ-F (N)	Strength-Endurance		1.34±0.35	1.28±0.32*	1.35±0.33	1.31±0.32		$F_{1, 12}$ = 1.51;	$F_{1.34, 16.49}$ = 1.07;	$F_{1.41, 16.90}$ = 4.75;
	Endurance-Strength		1.32±0.34	1.35±0.31*	1.17±0.43	1.31±0.31		p = 0.243	p = 0.340	**p = 0.033**
RPE	Strength-Endurance		7±1	14±2*	17±2*	9±3		$F_{1, 12}$ = 0.38;	$F_{2.95, 35.45}$ = 152.41;	$F_{3, 36}$ = 12.62;
	Endurance-Strength		8±2	17±2*	15±2*	8±2		p = 0.551	**p < 0.001**	**p < 0.001**

Legend: *Marks a significant difference between exercise orders at the respective time point. WBC = White blood cells; GRAN = Granulocytes; LYM = Lymphocytes; MONO = Monocytes; GLR = Granulocyte-Lymphocyte-ratio; SII = Systemic-inflammation-index; LA = Lactate: GLU = Glucose; CMJ-H = Counter-movement jump height; CMJ-P = Counter-movement jump power; Counter-movement jump force; RPE = Rating of perceived exertion.

***Table 6**: Delta changes and effect sizes for study 2 between all displayed time points.*

Variable	Condition	PRE	MID (Δ%; ES)	POST (Δ%; ES)	POST6H (Δ%; ES)	POST22H (Δ%; ES)	Interaction, ES
WBC (10^3/µl)	Strength-Endurance	8.27±2.29		+56; 2.03	+55; 2.00	-16; 0.58	*p* = 0.107; ES = 0.87
	Endurance-Strength	9.03±1.93		+32; 1.49	+60; 2.79	-13; 0.62	
GRAN (10^3/µl)	Strength-Endurance	4.30±1.59		+70; 1.89	+103; 2.77	-14; 0.39	*p* = 0.750**;** ES = 0.33
	Endurance-Strength	4.56±0.66		+80; 5.50	+104; 7.20	-16; 1.09	
LYM (10^3/µl)	Strength-Endurance	3.42±0.92		+39; 1.46	-5; 0.18	-19; 0.70	***p* = 0.006**; ES = 1.31
	Endurance-Strength	3.82±1.44		-21; 0.56	+7; 0.19	-7; 0.19	
MONO (10^3/µl)	Strength-Endurance	0.55±0.16		+53; 1.81	+58; 2.00	-13; 0.44	***p* = 0.035**; ES = 1.06
	Endurance-Strength	0.65±0.21		+6; 0.19	+57; 1.76	-12; 0.38	
GLR (10^3/µl)	Strength-Endurance	1.31±0.48		+40; 1.10	+116; 3.17	+3; 0.08	***p* = 0.002**; ES = 1.56
	Endurance-Strength	1.33±0.49		+127; 3.45	+83; 2.27	-10; 0.27	
SII (10^3/µl)	Strength-Endurance	216±103		+39; 0.83	+113; 2.38	-15; 0.32	***p* = 0.029**; ES = 1.11
	Endurance-Strength	209±112		+107; 2.00	+86; 1.61	-17; 0.32	
LA (mmol/l)	Strength-Endurance	0.96±0.22	+351; 15.32	+525; 22.91			***p* = 0.018,** ES = 1.51
	Endurance-Strength	0.88±0.26	+621; 21.04	+425; 14.38			
GLU (mg/dl)	Strength-Endurance	4.73±0.50	-6; 0.51	+18; 1.64			***p* < 0.001**, ES = 2.09
	Endurance-Strength	4.81±0.54	+18; 1.63	-3; 0.28			
CMJ-H (cm)	Strength-Endurance	32.26±3.20	-4; 0.45	-7; 0.72	-1; 0.13		*p* = 0.326, ES = 0.63
	Endurance-Strength	32.50±2.68	+2; 0.27	-1; 0.15	+3; 0.32		
CMJ-P (W)	Strength-Endurance	2.17±0.57	-2; 0.07	-1; 0.04	±0; 0.00		***p* = 0.007**, ES = 1.40
	Endurance-Strength	2.19±0.93	+4; 0.09	-6; 0.14	+2; 0.05		
CMJ-F (N)	Strength-Endurance	1.34±0.35	-4; 0.17	+1; 0.03	-2; 0.09		***p* = 0.033**, ES = 1.26
	Endurance-Strength	1.32±0.34	+2; 0.09	-11; 0.44	-1; 0.03		
RPE (score)	Strength-Endurance	7±1	+100; 7.00	+143; 10.00	+29; 2.00		***p* < 0.001**, ES = 2.05
	Endurance-Strength	8±2	+113; 4.50	+88; 3.50	±0; 0.00		

WBC = White blood cells; GRAN = Granulocytes; LYM = Lymphocytes; MONO = Monocytes; GLR = Granulocyte-Lymphocyte-ratio; SII = Systemic-inflammation-index; LA = Lactate: GLU = Glucose; CMJ-H = Counter-movement jump height; CMJ-P = Counter-movement jump power; Counter-movement jump force; RPE = Rating of perceived exertion; ES = Effect size, ∆% = delta change.

4.2.1 Immune responses

Findings indicated significant time*order interactions for LYM (p = 0.006), MONO (p = 0.035), GLR (p = 0.002), and SII (p = 0.029). For LYM, the post-hoc analysis indicated significantly larger PRE-to-POST increases (Δ+39%) in strength-endurance compared to endurance-strength (Δ-21%). In terms of MONO, the strength-endurance order induced larger PRE-to-POST (Δ+53%) increases compared to endurance-strength (Δ+6%). Regarding GLR and SII, findings indicated significantly larger PRE-to-POST increases for endurance-strength (Δ+127% and Δ+107%, respectively), compared to strength-endurance (Δ+40% and Δ+39%, respectively). No significant differences were observed at all other time points for all parameters. Specifically, similar changes were observed from PRE-to-POST6H. At POST22H, all parameters tended to return to the PRE values, irrespective of the exercise order. A graphical representation of these results can be found in Figure 9, 10, and 11.

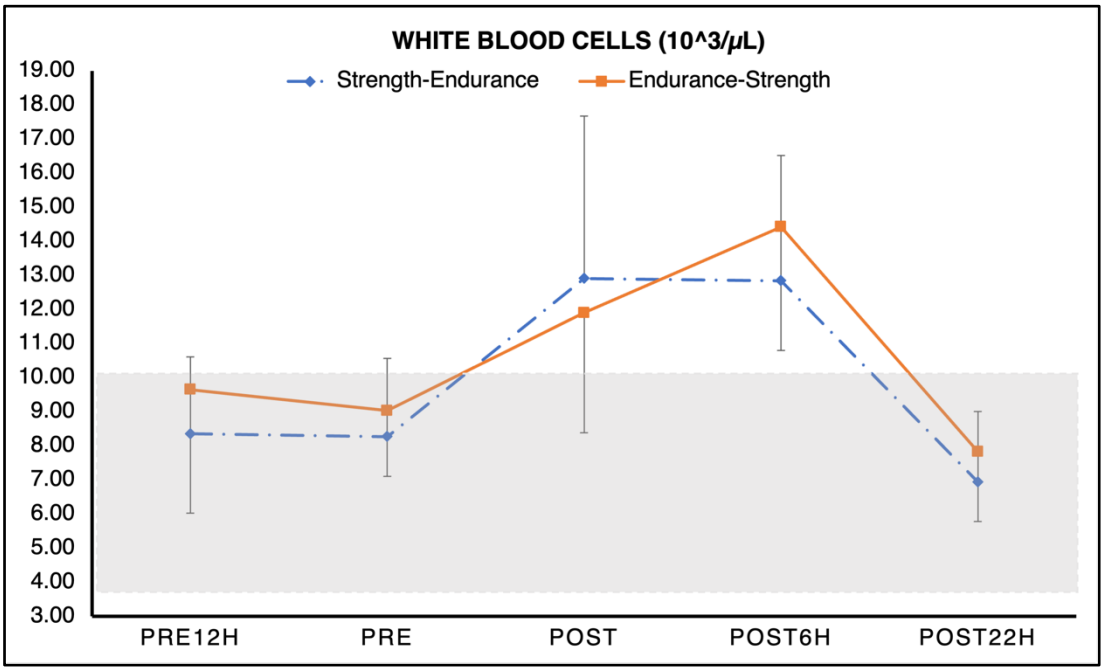

***Figure 9**. Means and standard deviation for white blood cells measured at PRE12H, PRE, POST, POST6H, and POST22H. The grey zone marks lower and upper reference values provided by the manufacturer (Medonic M32 series). ***:** stands for significant difference between the two exercise orders.*

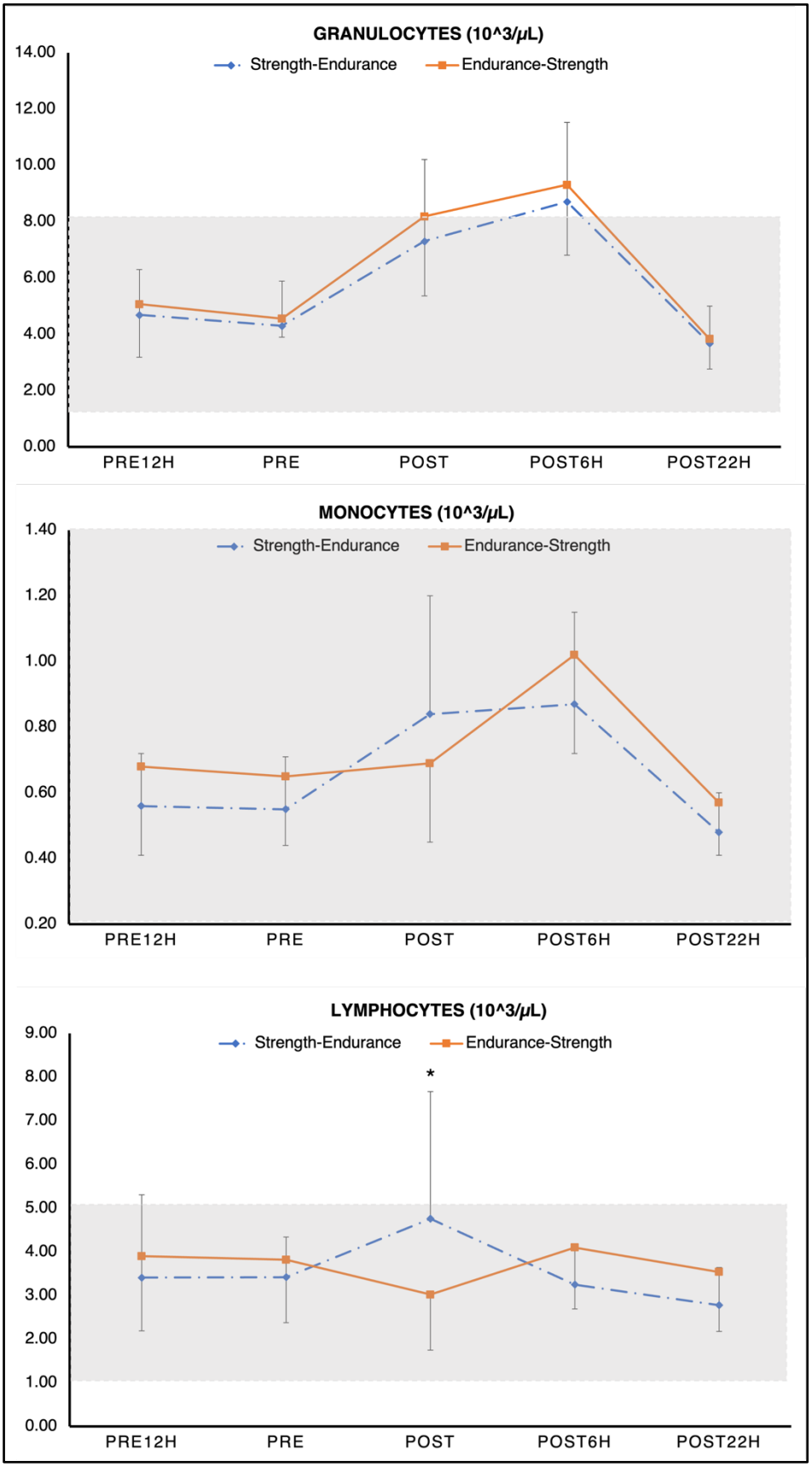

***Figure 10**. Means and standard deviation for granulocytes, monocytes, and lymphocytes, measured at PRE12H, PRE, POST, POST6H, and POST22H. The grey zone marks lower and upper reference values provided by the manufacturer (Medonic M32 series). ***:** stands for significant difference between the two exercise orders.*

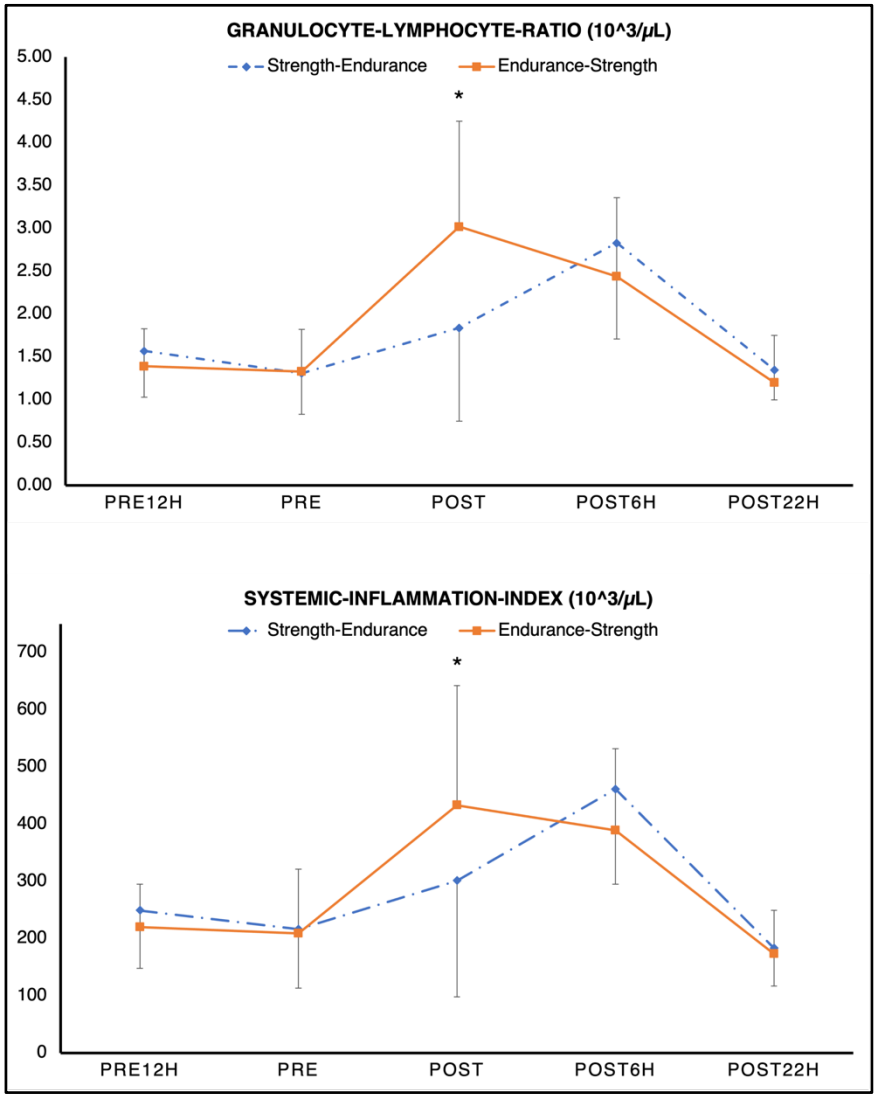

***Figure 11**. Means and standard deviation for the granulocytes-lymphocytes-ratio and systemic-inflammation-index calculated at PRE12H, PRE, POST, POST6H, and POST22H. ***:** stands for significant difference between the two exercise orders.*

4.2.2 Metabolic responses

Our findings indicated significant time*order interactions for blood glucose ($p < 0.01$) and lactate ($p = 0.018$). Results showed significantly larger PRE-to-MID increases in blood glucose and lactate following the endurance exercise (as part of the endurance-strength order, Δ+18% and Δ+621%, respectively) compared to the strength exercise (as part of the strength-endurance order, Δ-6% and Δ+351%, respectively). From PRE-to-POST, changes in blood glucose were significantly larger for the strength-endurance order (Δ+18%), compared to the endurance-strength order (Δ-3%). A graphical representation of these results can be found in Figure 12.

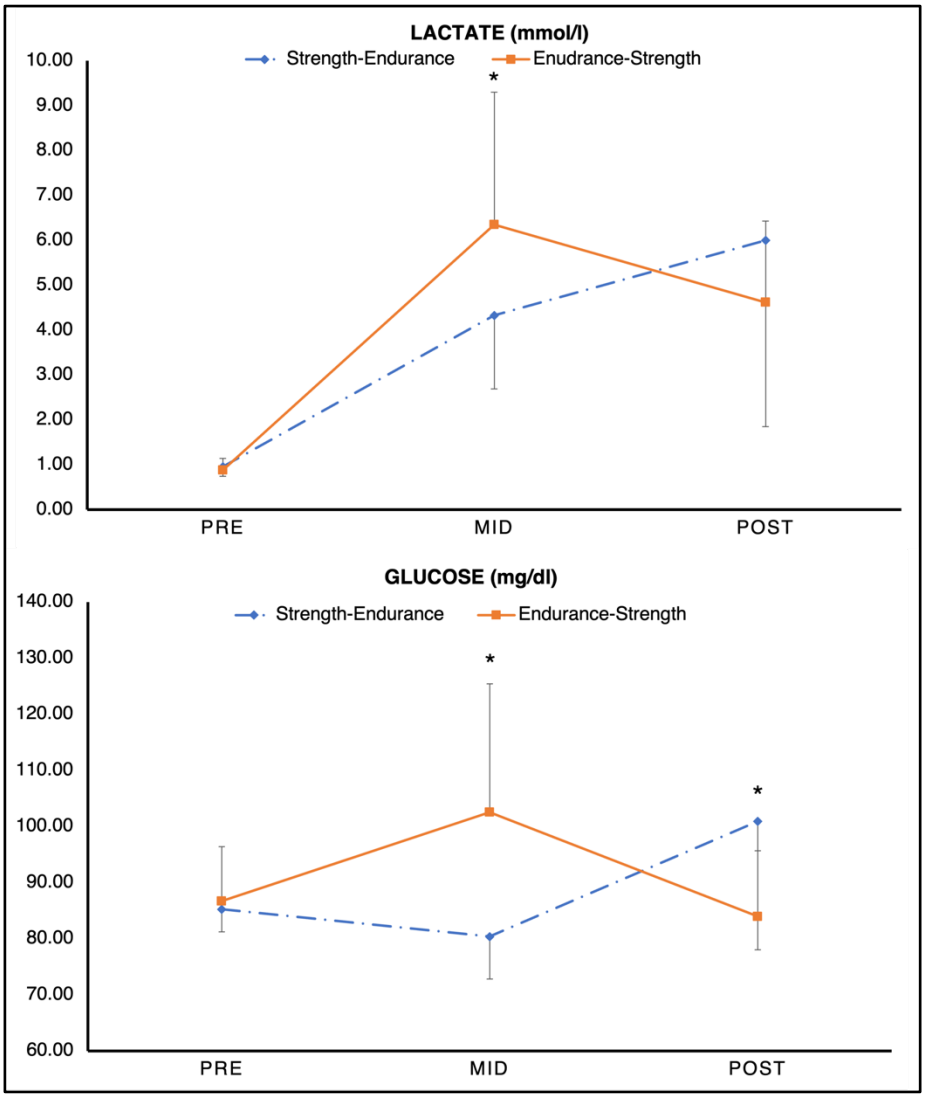

***Figure 12**. Means and standard deviation for blood lactate and blood glucose measured at PRE, MID, and POST. *: stands for significant difference between the two exercise orders.*

4.2.3 Physical fitness and Rating of perceived exertion

For physical fitness a significant time*order interaction was observed for CMJ-power ($p < 0.01$) and force ($p = 0.033$) with significantly larger PRE-to-MID performance increases for the endurance-strength order (Δ+4% and Δ+2%, respectively), compared to the strength-endurance order (Δ-2% and Δ-4%). Regarding RPE, there was a significant time*order interaction ($p < 0.01$) with larger PRE-to-MID values following the endurance exercise (as part of the endurance-strength order, Δ+113%), compared to the strength exercise (as part of the strength-endurance order, Δ+100%). Additionally, RPE values were significantly larger from PRE-to-POST following the strength-endurance

order (Δ+143%), compared to endurance-strength (Δ+88%). A graphical representation of these results can be found in Figure 13.

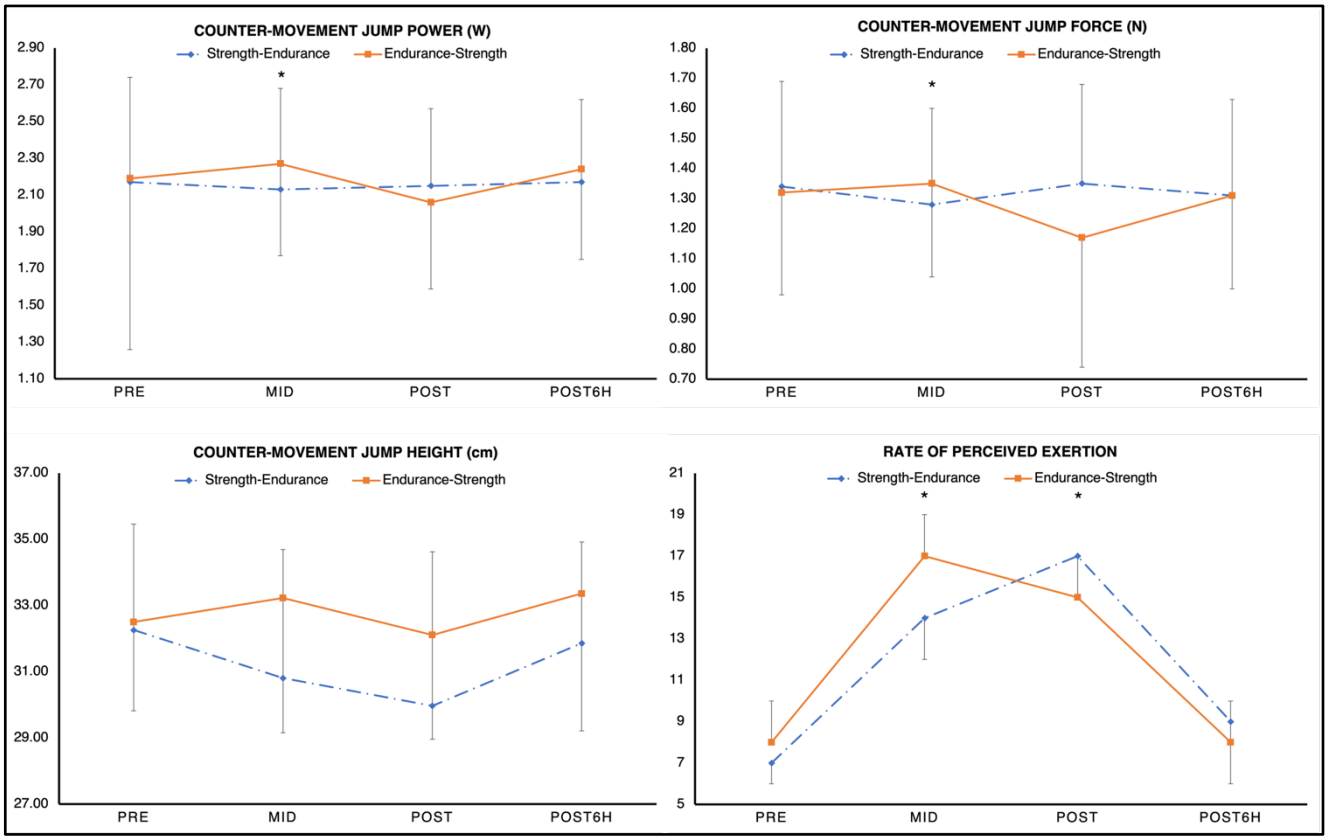

Figure 13**. Means and standard deviation for counter-movement jump height, power, force, and rate of perceived exertion measured at PRE, MID, POST, and POST6H. ***: stands for significant difference between the two exercise orders.

5 Discussion

The main objective of this thesis was to explore the impact of CT exercise order (i.e., power/strength-endurance versus endurance-power/strength) on acute (< 15min) and delayed (≥ 6 hours) immunological stress responses (i.e., WBC, LYM, GRAN, MONO, GLR, and SII) in male and female youth judo athletes. Additionally, this thesis aimed to investigate the effects of CT exercise order on other variables, such as muscular fitness (i.e., CMJ height, force, power), metabolic responses (i.e., blood lactate and glucose), and RPE in the same population. Based on previous literature, it was hypothesised that the order of exercise in CT would influence immune cell counts (i.e., WBC, LYM, GRAN, MONO) in both male and female youth judo athletes [40, 41]. Furthermore, it was hypothesised that the order of exercise in CT would affect measures of muscular fitness, metabolic responses, and RPE in this specific population [40, 41].

5.1 Hypothesis 1

5.1.1 Study 1

The main findings of study 1[1] indicated that CT induced acute (≤ 15 min) and delayed (≥ 6 hours) order-dependent immune cell count alterations in youth male judo athletes. In general, the power-endurance order induced higher increases in WBC compared to the endurance-power order. Additionally, there was an order-dependent effect observed for GRAN, MONO, LYM, GLR, and SII.

This study represents the first investigation into the acute effects of CT on immunological stress responses in youth male judo athletes, comparing the impact of two different exercise orders. As a result, there is a scarcity of comparative literature available in this specific area. Generally, physical exercise that involves repetitive muscle contraction acutely stimulates the activity of the central nervous system and causes systemic

[1] Parts of study 1 were previously published in the European Journal of Applied Physiology. For more details refer to section 11 (i.e., List of Publications). **Markov, A.,** et al., *Acute effects of concurrent muscle power and sport-specific endurance exercises on markers of immunological stress response and measures of muscular fitness in highly trained youth male athletes.* European Journal of Applied Physiology, 2023: p. 1-12

substrate metabolism [145]. This would lead to alterations in immune cell activity and function and would also stimulate the release of glucocorticoid hormones (e.g., cortisol), catecholamines (e.g., adrenaline), cytokines (e.g., Interleukin-6), and WBC into peripheral circulation [145, 155]. The increase in WBC appears to be due to demarginating from the blood vessel walls and to the release of cells from organic storage (e.g., liver, lung, thymus gland, bone marrow, lymph nodes, and skeletal muscle) [156]. The magnitude and time course of exercise-induced leukocytosis, and thus any alteration within circulating immune cell counts, is dependent on numerous factors, including age, duration and intensity, and type of exercise employed [5, 13, 23]. Previous studies reported acute leukocytosis after strength [157, 158], endurance [24, 159-161], and concurrent strength and endurance exercises [14], in trained [14, 24, 160, 161] and recreationally active [157-159] adults. Although a direct comparison to most of the forenamed studies is difficult, the findings of study 1 generally corroborate with the literature since both exercise orders resulted in acute (≤ 15 min) and delayed (≥ 6 hours) immune cell count alterations (e.g., WBC, LYM, GRAN) in male youth judo athletes. However, it seems that the magnitude of acute and delayed immune cell count alterations to CT is exercise order-dependent with particularly higher increases in WBC following the power-endurance order compared to the endurance-power order (Figure 4).

GRAN represents the largest component of total WBC (up to 60%) in healthy young adults [182]. GRAN mature within bone marrow [5] and increase several folds during and after exercise [13, 23, 158, 183]. Unlike LYM, GRAN are made of myeloid stem cells and are responsible for the innate immune response. They partly circulate throughout the peripheral system while adhering to the endothelial surface. Exercise-induced hemodynamics, such as increased blood flow and shear stress, can lead to demarginating of GRAN from the blood vessel walls. This process results in an acute increase in the number of circulating cells [156]. Previous studies showed that the general trend of post-exercise GRAN kinetics is a continuous increase, which begins during exercise but can last up to six hours, depending on the nature of the exercise applied [183-186]. Therefore, our results are consistent with the existing literature, as

GRAN gradually increased regardless of the applied exercise order. However, we found a significantly higher delayed (i.e., PRE-to-POST6H) increase in GRAN following the power-endurance order (Δ160%) compared to the endurance-power order (Δ94%). Cortisol and catecholamines play a key role in activating the immune system and particularly, GRAN release from the bone marrow [187]. Previous studies have suggested that the release of cortisol and catecholamines is intensity-dependent [188, 189]. Although, hormone levels were not measured in our study, it is noteworthy that RPE was significantly higher following the sport-specific endurance exercise compared to the muscle power exercise. This finding suggests that the former exercise induced greater physiological stress compared to the latter. Consequently, it seems that the sport-specific endurance exercise was the main driver of the observed immune responses, while in the endurance-power order, the applied power exercise may have partially attenuated the delayed increase in GRAN.

Like GRAN, MONO are part of the innate immune system, made up of myeloid stem cells, and mature within the bone marrow. A recent review by James Tidball [136] reported that MONO and their direct descendants, the macrophages, form the majority of intramuscular leucocytes while being rapidly activated in response to increased and/or sustained muscle contraction. Meanwhile, MONO make up to 8% of total WBC within the bloodstream [182] and travel through the peripheral system. From here, MONO immigrate to skeletal muscles, which are filled with a high concentration of cytokines, including the tumour-necrosis-factor-α and interferon-γ. These two specific cytokines are released from other immune cells such as natural killer cells and are key for macrophage activation. In this context, skeletal muscle macrophages are generally separated into M1-and M2-macrophages [136, 190, 191]. This process directly links the inflammatory process with muscle regeneration [136] and highlights the importance of MONO in the context of exercise. However, it should be noted that MONO were measured indirectly. The device used for blood analysis within both conducted studies does not measure MONO directly but estimates the number of middle-sized-cells based on the number of LYM and GRAN. Of note, middle-sized-cells are primarily

made of MONO. Despite the indirect measurement of MONO, the results are still of great importance given the critical role of MONO in muscle repair and growth [137]. Our findings indicated significant acute differences (≤ 15 min) between the two exercise orders, with a markedly higher increase in MONO from PRE-to-POST following the power-endurance order (Δ69%), compared to the endurance-power order (Δ15%). No statistically significant difference was found in MONO levels from PRE-to-POST6H. However, Figure 5, illustrates a notable and potentially meaningful difference in the increase of MONO between the power-endurance order (Δ91%) and the endurance-power order (Δ45%). From PRE-to-POST22H, no difference in MONO levels was observed, with values approaching the baseline levels, regardless of the exercise order. A study by Smith et al. [192] investigated immune cell kinetics following two bouts of downhill running in active young adults aged 20 years. The authors found a significant increase in MONO immediately after exercise, which returned to baseline one-hour post-exercise. Interestingly, they also reported a second significant increase in MONO levels five hours post-exercise. With respect to the endurance-power order, these findings suggest that the time point at which MONO were elevated may have been missed. Since there were no immune blood analyses between PRE and POST (i.e., MID) and between POST and POST6H, this may be a potential explanation for the observed results. Therefore, future studies should consider taking more time points of measurement to further investigate MONO kinetics following exercise.

LYM, which constitute approximately 40% of the total WBC count in the bloodstream [182], are derived from lymphoid stem cells within the bone marrow and play a critical role in the adaptive immune system. During and immediately after exercise, adrenergic stimulation can cause LYM to detach from blood vessel walls and enter circulation, leading to lymphocytosis [149]. However, shortly after exercise (≤ 30 min), LYM levels often fall back and can even drop below baseline values. Several attempts have been previously proposed to explain this rapid decrease, including the shift of LYM to peripheral tissues to increase immune surveillance [149, 193, 194]. The magnitude of lymphocytosis and lymphocytopenia is generally proportional to the duration and intensity

of exercise applied [5, 149]. Regarding the current study, LYM increased only in the power-endurance order from PRE-to-POST but then decreased from POST towards POST6H. For the endurance-power order, LYM decreased from PRE-to-POST, before slightly increasing towards POST6H. Therefore, we would report an acute but not delayed difference in LYM between the two exercise orders. Acute lymphocytosis was expected following both exercise orders, considering the equal overall exercise workload. However, this highlights the impact of exercise order on the kinetic of LYM responses. Like reported for MONO, it should be noted that cell kinetics were not measured between the power and sport-specific endurance protocol (i.e., MID). As such, it could be assumed that the time point at which LYM were elevated within the endurance-power order was missed.

The application of GLR and SII in the field of exercise science is still limited, but from a clinical perspective, they are well-established markers of diseases [176] and death [195, 196]. For example, Fois et al. [195] revealed that SII on admission was an independent predictor of in-hospital mortality in COVID-19 patients. However, previous studies showed moderate-to-high correlations of GLR and SII with other well-established inflammatory markers, such as the C-reactive protein and Interleukin-6 [197-199]. A recent review by Walzik et al [200] suggested that GLR and SII could be feasible tools to assess exercise-induced strain and indicators of recovery processes. Most studies that have measured GLR and SII in an exercise setting have focused on the effects of endurance exercises on these markers. For instance, Wahl et al. [161] compared different recovery strategies following high-intensity or sprint interval cycling and their effects on immune cell kinetics in male cyclists/triathletes aged 25 years. The authors reported that GLR and SII increased significantly up to 3 hours post-exercise, irrespective of the type of exercise performed. In a separate study, Bessa et al. [14] examined the effects of CT on biomarkers of injury and inflammation in elite cyclists aged 28 years and reported a significant increase in GLR that lasted 3 hours before dropping significantly below baseline 12 hours post-exercise. In our results, there were significant time*order interaction effects for GLR and SII. Following the endurance-

power order, GLR and SII increased by one-fold immediately post-exercise and remained elevated after 6 hours. In contrast, in the power-endurance order, both parameters did not change significantly from PRE-to-POST but rose towards POST6H to a similar level compared to endurance-power. In general, GLR (SII) values typically increase when GRAN (and platelets) are high while LYM are low [200]. Our results seem reasonable given the elevated LYM following the power-endurance order but not the endurance-power order.

5.1.2 Study 2

The main findings of study 2 show that CT resulted in acute (≤ 15 min) but not delayed (≥ 6 hours) order-dependent alterations in immune cell count in female youth judo athletes. Specifically, the results demonstrated an order effect for LYM, MONO, GLR, and SII, while WBC and GRAN did not show any order-dependent effects at all time points.

The current study indicated that concurrent strength and sport-specific endurance exercises produced similar changes in WBC and GRAN cell counts from PRE-to-POST and PRE-to-POST6H in healthy youth female judo athletes, regardless of the exercise-order employed. In the strength-endurance order, there was an increase in WBC and GRAN from PRE-to-POST (Δ56% and 70%, respectively), and from PRE-to-POST6H (Δ55% and 103%, respectively). Similarly, in the endurance-strength order, WBC and GRAN increased from PRE-to-POST (Δ32% and 80%, respectively), and PRE-to-POST6H (Δ60% and 104%, respectively). However, from PRE-to-POS22H, both markers decreased slightly below the baseline values (up to Δ-16%). In fact, our current findings are partly different from those found in study 1. In study 1, we observed an acute (≤ 15 min) and delayed (≥ 6 hours) order-dependent effect for WBC and GRAN. However, study 2 differed significantly from study 1 in several ways. Firstly, it had relatively a smaller sample size and included only female participants. Secondly, the strength exercise used in the current study aimed to induce muscle hypertrophy effects (i.e., 4 sets to volitional failure at 70 to 80% of one-repetition maximum), whereas the

exercise conducted in study 1 aimed to develop muscle power (i.e., 4 sets of 8 repetitions performed with maximal velocity at 30 to 40% of one-repetition maximum). These differences in study design and participant characteristics may have contributed to the divergent results. Therefore, making a direct comparison between the two investigations may not be justified. However, it is assumed that the different exercises applied (i.e., power versus strength) and/or sex differences (males [study 1] vs females [study 2]) likely account for the distinct results between these two studies [136, 137].

For MONO, we found a significant time*order interaction. Following the strength-endurance order, the results showed an increase from PRE-to-POST (Δ53%) and PRE-to-POST6H (Δ58%). In contrast, following the endurance-strength order, MONO increased marginally from PRE-to-POST (Δ6%) but markedly from PRE-to-POST6H (Δ57%). Meanwhile, MONO went below baseline from PRE-to-POST22H following both the strength-endurance order and the endurance-strength order (Δ-13% and Δ-12%, respectively). This indicates that there was an immediate increase in the inflammatory response following the strength-endurance order, and this heightened level was maintained up to 6 hours post-exercise. On the other hand, the acute inflammatory response after the endurance-strength order was minor initially but showed a significant increase after 6 hours. These results differ from those seen in study 1, probably because of the different exercises applied and the variation in participants' characteristics (males [study 1] vs females [study 2]). In fact, studies which directly compared MONO responses to strength-, power- and/or endurance exercises are yet missing. Nonetheless, based on the available literature it is likely that MONO responses to exercise are not only intensity and/or duration-dependent, but also exercise-type-dependent (e.g., strength, power, endurance) [13, 23, 201]. Collectively, the findings suggest that the strength-endurance order elicits a greater immediate inflammatory response and immune activation compared to the endurance-strength order. However, in the delayed period (POST6H), comparable high levels of inflammatory response were

observed for both exercise orders. Furthermore, from PRE-to-POST22H, there was a decrease in MONO levels, reaching slightly below baseline values for both exercise orders.

LYM showed a significant increase of approximately one-third (Δ39%) from PRE-to-POST in the strength-endurance order compared to a slight decrease (Δ21%) within the endurance-strength order. One possible explanation for the increase in LYM after the strength-endurance order is that it reflects a mobilization of immune cells from lymphoid tissues into the bloodstream [193, 194]. However, it should be noted that the decrease in LYM immediately after the endurance-strength order could reflect an increased demand for immune cells in peripheral tissues. As a result, LYM may temporarily leave the bloodstream and migrate to these tissues to perform their immune functions, leading to a transient decrease in circulating LYM [149, 193, 194]. However, LYM exhibited a negative trend from PRE-to-POST6H following the strength-endurance order, while such a pattern was not observed in the endurance-strength order. Specifically, albeit not statistically significant, LYM increased slightly from POST-to-POST6H following the endurance-strength order compared to the strength-endurance order. It needs to be mentioned that LYM kinetics were not measured between the strength and sport-specific endurance protocol (i.e., MID). As such, given that the changes in LYM are typically transient in nature, it could be that the time point at which LYM were elevated within the endurance-strength order was missed. Further, POST22H values of LYM were slightly lower compared to those registered at PRE following both exercise orders. This could be explained by the fact that LYM have left the bloodstream and migrated to peripheral tissues to increase immune surveillance [149, 193, 194], leading to a transient decrease in circulating LYM. This phenomenon was not observed in study 1, which strengthens the assumption that strength exercise (i.e., study 2) compared to power exercise (i.e., study 1) is associated with greater immune activation and inflammatory responses. Compared to power exercises, the application of strength exercises within a CT setting could have extended the transient timeframe during which LYM leaves the bloodstream to the affected tissues due to increasing demands for immune

surveillance and tissue repair. In this context, it would have been interesting to differentiate between the two subpopulations in future research. Currently, T-cell responses to exercise are relatively well-established, while studies related to B-cell kinetics following exercise are still rare. Nonetheless, recent literature indicates that the duration and intensity of exercise, among others, are likely important moderators for T- and B-cell responses [145]. The current study lacks supportive literature, making any conclusion rather preliminary. Therefore, it would be valuable to conduct more comprehensive investigations into the kinetics of the two main LYM subpopulations in response to CT in the future.

GLR and SII are established markers of disease [176] and their high correlations with other commonly used inflammatory markers in sports science (e.g., C-reactive-protein, Interleukin-6) [197-199] makes their calculation relevant for assessing exercise-induced strain. However, the sport and exercise science literature on the use of GLR and SII in CT is scarce. Previous studies have shown that CT generally induces GLR increases lasting for up to 3 hours [14]. In the current study, we found significant time*order interaction effects for GLR and SII. Both markers increased by more than one-fold from PRE-to-POST in the endurance-strength order (Δ127% and 107% for GLR and SII, respectively), while the strength-endurance order induced significantly lower increases (Δ40% and 39% for GLR and SII, respectively). However, from a delayed perspective (i.e., PRE-to-POST6H), the strength-endurance order induced greater GLR increases compared to the endurance-strength order (Δ116% and 83%, respectively). The same trend was observed for the SII, showing a greater increase following the strength-endurance order from PRE to POST6H compared to the endurance-strength order (Δ113% and 86%, respectively). It is important to note that the GLR and SII differences between the two exercise orders at POST6H did not reach statistical significance. These results suggest that there is an acute and temporary larger increase in the inflammatory response in the body following the endurance-strength order. However, the pattern tends to be different from a delayed perspective, as there are slightly greater signs of inflammation following the strength-endurance order compared to the

endurance-strength order at POST6H. Furthermore, at POST22H, both markers of inflammation returned to baseline values, indicating that the body is recovering from the exercise-induced stress and supporting the transient nature of these changes.

5.1.3 Interim conclusion

Generally, the results of both studies supported the first hypothesis, showing exercise order-dependent effects on immune cell counts (i.e., WBC, LYM, GRAN, MONO) and indirect markers of inflammation (i.e., GLR, SII) in healthy youth male and female judo athletes. Specifically, the main findings of study 1 showed that the power-endurance order resulted in higher acute (≤ 15 minutes) and delayed (≥ 6 hours) immunological stress responses compared to the endurance-power order. In study 2, the results indicated acute (≤ 15 minutes) but not delayed (≥ 6 hours) order-dependent changes in immune cell count in female youth judo athletes. More specifically, the strength-endurance order led to slightly higher acute immunological activation compared to the endurance-strength order. Of note, at POST22H, all markers of immune response returned (or were close to) baseline values, indicating a successful recovery from the exercise-induced immune stress reaction in both sexes.

5.2 Hypothesis 2

5.2.1 Study 1

The secondary aim of this thesis was to examine the effect of CT exercise order on CMJ performance, metabolic responses, and RPE. For CMJ-force, there was a significant difference between exercise orders from PRE-to-POST, with a larger reduction observed following the endurance-power order (Δ5%). Further, from PRE-to-MID, there was a significant difference between exercise orders (Δ4%), showing a larger decrease in CMJ-power following the power-endurance order. Regarding RPE, there was a significant time*order interaction with larger PRE-to-MID values following the endurance exercise (as part of the endurance-power order, Δ+157%), compared to the power exercise (as part of the power-endurance order, Δ+29%). Additionally, there was a significant increase in RPE from PRE-to-POST, with the power-endurance order showing a

larger increase (Δ157%) compared to the endurance-power order (Δ57%). However, by POST6H, CMJ-force, CMJ-power, as well as RPE, had returned to baseline levels. Moreover, findings indicated larger increases in blood glucose and lactate from PRE-to-MID following the endurance exercise (as part of the endurance-power order) compared to the power exercise (as part of the power-endurance order). However, from PRE-to-POST, changes in blood glucose and lactate were larger for the power-endurance order compared to the endurance-power order.

Based on the literature, it is highly recommended to report aspects of internal and external load to give the most accurate feedback about the experienced effort [202-207]. Bessa et al. [14] investigated the effects of CT on markers of muscle damage and inflammation in elite male cyclists aged 28 years. They showed an inverse relationship between GLR and upper-body muscle strength. More specifically, the authors revealed that GLR significantly increased 3 hours post-CT while muscle strength significantly decreased. However, both values returned to baseline levels following 48 hours. In the present study, CMJ-force significantly decreased from PRE-to-POST and CMJ-power significantly increased from PRE-to-MID following the endurance-power order. CMJ-height, on the other hand, did not exhibit a clear fluctuation throughout the two CT orders. Meanwhile, subjective RPE showed substantial changes throughout the two exercise orders. In fact, there was a significantly larger increase in RPE from PRE-to-POST for the power-endurance order (Δ+157%) compared to the endurance-power order (Δ+57%). This finding aligns with the conclusion drawn from the immune markers, indicating that the power-endurance order induced greater acute physiological stress. Further, RPE values returned to baseline 6 hours post-exercise, suggesting that both exercise orders were indeed physiologically demanding but that the endurance exercise was the main driver for the observed increases in RPE throughout both exercise orders. This is supported by the results obtained from metabolic responses. Following the endurance-power order, blood lactate values increased several folds from PRE-to-MID (Δ+947) before returning toward baseline from PRE-to-POST (Δ+280). Meanwhile, following the power-endurance order, PRE-to-MID change in blood lactate was rather

marginal (Δ+52). However, from PRE-to-POST, a notable increase (Δ+814%) in blood lactate concentration was observed. This would mean that the endurance exercise was the main driver of blood lactate concentration. Typically, changes in blood lactate concentrations are directly linked to exercise intensity and duration [208]. Historically, blood lactate was believed to be a biochemical waste product that being responsible for exercise-induced fatigue and tissue damage [209]. However, current evidence indicates that blood lactate is far more than a simple waste product. In fact, it serves as an important source of fuel while being a metabolic signal with important regulating functions [209].

A very similar pattern was observed for blood glucose with significantly greater concentration at MID following the endurance-power order (Δ18%) and at POST following the power-endurance order (Δ17%). This reflects the greater mobilization of stored glycogen in the liver (i.e., glycogenolysis) and an increased rate of glucose production by the liver (i.e., gluconeogenesis) following the endurance exercise when the demand for glucose is higher. There is evidence that plasma glucose supplies up to 50% of the total oxidative energy production and up to 100% of total carbohydrates oxidised during submaximal exercise [210]. Glucose utilisation is mostly dictated by diet, training experience, exercise intensity and duration, the type of exercise applied as well as the number and type of activated muscle fibres within the working muscle [210, 211].

It should be mentioned though, that blood lactate and glucose were measured at PRE, MID, and POST only, but not at POST6H and/or POST22H. Overall, it is important to highlight that our findings revealed a discrepancy between immunological, perceived exertion, and physical responses following both exercise order conditions. Specifically, the immunological responses suggested the necessity for an extended recovery period (≥ 6 hours) to restore immunological homeostasis (Figure 4). In contrast, the perceived exertion and physical responses indicated that athletes felt prepared for another session as early as 6 hours post-exercise (Figure 8). These contrasting findings suggest that measures of internal load, such as immune markers, may differ from measures of

external load. Therefore, practitioners need to recognize these differences and consider them when designing training programs. However, it is crucial to note that further research is needed to validate these findings and provide more comprehensive insights.

5.2.2 Study 2

The findings of the second study pointed toward a significant order effect for CMJ-power and CMJ-force from PRE-to-MID. Particularly, while CMJ-power decreased immediately after the strength exercise (as part of the strength-endurance order, Δ2%), it increased significantly after the endurance exercise (as part of the endurance-strength order, Δ4%). This aligns with the results observed for CMJ-force. More specifically, CMJ-force significantly decreased immediately after the strength exercise (as part of the strength-endurance order, Δ4%) and then increased after the endurance exercise (as part of the endurance-strength order, Δ2%). Hence, it is reasonable to propose that the enhancement in CMJ-power and CMJ-force following the endurance exercise can be attributed to the phenomenon of post-activation performance enhancement [212]. In a recently published systematic review with meta-analysis by Markov and colleagues [42], the acute effects of endurance exercise on muscle strength and power in trained individuals were investigated. The review reported that endurance exercises performed at higher intensities and/or longer durations (up to 15 minutes) acutely reduce measures of muscle strength, but not power. However, despite the high intensity, the intermittent nature of the endurance task conducted in the present study did not seem to induce excessive fatigue to the extent that would diminish subsequent strength and power performances. From PRE-to-POST and PRE-to-POST6H, no significant differences between the two exercise orders were noted for CMJ-power and CMJ-force.

In terms of RPE, like the results of study 1, the endurance exercise (irrespective of the applied exercise order) was perceived to be more strenuous compared to the strength exercise. Compared to study 1, it is evident that the strength exercise implemented in study 2 was considerably more taxing than the power exercise employed in study 1.

Despite that, the RPE values recorded from PRE-to-MID were still significantly higher (Δ113%) following the endurance-strength order compared to the strength-endurance order (Δ100%). Meanwhile, from PRE-to-POST, significantly larger values of RPE following the strength-endurance order (Δ143%) compared to the endurance-strength order (Δ88%) were observed. This indicates that the endurance exercise was the most demanding task. From PRE-to-POST6H, no significant RPE differences were observed. Although RPE values tended to return toward baseline levels after 6 hours following both exercise orders, it is noteworthy that athletes who executed the strength-endurance order reported slightly higher but statistically non-significant RPE values (Δ29%) compared to the those who performed the endurance-strength order (Δ0%).

Regarding metabolic responses, results indicated significant time*order interactions for blood lactate and glucose. Specifically, we observed larger increases in blood glucose and lactate from PRE-to-MID following the endurance exercise (as part of the endurance-strength order, Δ+18% and Δ+621%, respectively) compared to the strength exercise (as part of the strength-endurance order, Δ-6% and Δ+351%, respectively). Additionally, when comparing PRE-to-POST changes, the strength-endurance order generated greater alterations in blood glucose and lactate (Δ+18% and Δ+525%, respectively) compared to the endurance-strength order (Δ-3% and Δ+425%, respectively). Consistent with the findings from study 1, it is evident that the endurance task remains the most significant contributor to the observed metabolic responses.

5.2.3 Interim conclusion

Taken together, the results of both studies highlight order-dependent acute (< 15min) alterations in measures of muscular fitness, perceived exertion, and metabolic responses in youth male and female judo athletes. These greater responses seem to be mainly attributable to the endurance exercise employed.

6 Limitations and Future Research Perspectives

This study has some limitations that warrant discussion. First, cell kinetics were measured at PRE12H, PRE, POST, POST6H, and POST22H but not in between the power/strength and sport-specific endurance protocol (i.e., MID) or in between POST and POST6H or between POST6H and POST22H. Additional blood measures would have helped to provide a better overview of the effects of the applied CT order on the selected markers of the immunological stress response. However, because of the athletes' congested training schedule besides the COVID-19 restrictions, it was not possible to collect additional blood samples. Furthermore, blood samples required immediate analyses. This would have led to experimental delays, due to the short time frame between the power/strength- and endurance exercises. Second, contrasting endurance and/or power/strength exercise alone with endurance-power/strength and power/strength-endurance would have led to a more comprehensive comparison. Third, there was one power/strength exercise, only. To be in line with real-world scenarios, including several exercises may be more suitable when investigating combined power/strength and endurance sessions. Nonetheless, the applied procedure is common practice and was agreed upon in consultation with the coaching staff. Fourth, studies that investigated the effects of power exercises and/or CT order on WBC count alterations are yet missing. Accordingly, any comparison made between the two current studies with other studies should be interpreted with caution. Fifth, much of the discussed content assumes that GRAN, LYM, and MONO reflect on certain successor cells and their respective function within highly complex immunological mechanisms. In fact, the measured parameters should primarily be seen as precursor cells of those which are the actual biological players. For instance, LYM should be separated into T- and B-cells while GRAN are made of neutrophils, basophils, and eosinophils. Further, MONO were obtained due to an estimation but not the actual cell count while GLR and SII reflect indirect markers of inflammation. Finally, in Figures 4, 5, 9, and 10, we have provided the upper and lower reference values for WBC, LYM, GRAN, and MONO to offer general guidance regarding the acceptable lower and upper bounds. These values were taken with reference to the manufacturer (i.e., Medonic M32 series) and are

in line with those represented in the exercise physiology literature [213]. Still, caution is needed when interpreting these results since reference values for youth (athletes) from both sexes are yet missing. Generally, there is a need for more studies considering youth athletes of both sexes. Such studies should consider measures of muscular fitness and the underlying physiological events. Specifically, upcoming studies should explore the effects of different CT settings on acute, delayed but also chronic immune system responses. In this context, investigators should strive for diagnostically conclusive markers (e.g., T/B-cells, neutrophils, M1/2-macrophages, dendritic cells, interleukin-6, tumour-necrosis-factor-α, interferon-γ) and a more comprehensive analysis of cell variances. This could strengthen our understanding of the complexity of inflammatory processes in response to exercise.

7 General Conclusion

The main findings of this thesis indicated order-dependent effects on the immune responses, supporting the first hypothesis. Specifically, the main results of study 1 showed greater immunological stress responses, both from acute (≤ 15 min) and delayed (≥ 6 hours) perspectives, after the power-endurance order compared to the endurance-power order in male youth judo athletes. Regarding study 2, the results indicated acute but not delayed order-dependent changes in immune responses. Overall, like in male participants, the strength-endurance order resulted in higher acute immunological activation compared to the endurance-strength order in youth female judo athletes. It is important to note though, that in both studies, all markers of immune system response returned to baseline (or at least very close to it) after 22 hours, indicating that recovery from the exercise-induced immune stress response was achieved successfully. With respect to metabolic responses, physical fitness, and perceived exertion, the results of both studies showed order-dependent acute (≤ 15 min) alterations. These alterations are mainly guided by the endurance exercise. As mainly established in study 1, the findings suggest that measures of internal load, such as immune markers, may differ from measures of external load, pointing towards a divergence between immunological, perceived, and physical responses following both CT orders. Therefore, practitioners need to recognize these differences and consider them when designing training programs.

8 References

1. Gleeson, M., *Immune function in sport and exercise.* Journal of applied physiology, 2007. **103**(2): p. 693-699.
2. Kraemer, W.J., et al., *Growth hormone (s), testosterone, insulin-like growth factors, and cortisol: roles and integration for cellular development and growth with exercise.* Frontiers in endocrinology, 2020. **11**: p. 33.
3. Gleeson, M., et al., *The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease.* Nature reviews immunology, 2011. **11**(9): p. 607-615.
4. Walsh, N.P., *Recommendations to maintain immune health in athletes.* European journal of sport science, 2018. **18**(6): p. 820-831.
5. Walsh, N.P., et al., *Position statement part one: immune function and exercise.* 2011.
6. Nieman, D.C. and L.M. Wentz, *The compelling link between physical activity and the body's defense system.* Journal of sport and health science, 2019. **8**(3): p. 201-217.
7. Krüger, K., F.-C. Mooren, and C. Pilat, *The immunomodulatory effects of physical activity.* Current pharmaceutical design, 2016. **22**(24): p. 3730-3748.
8. Campbell, J.P. and J.E. Turner, *Debunking the myth of exercise-induced immune suppression: redefining the impact of exercise on immunological health across the lifespan.* Frontiers in immunology, 2018. **9**: p. 648.
9. Opdenakker, G., W.E. Fibbe, and J. Van Damme, *The molecular basis of leukocytosis.* Immunology today, 1998. **19**(4): p. 182-189.
10. Paulsen, G., et al., *Leucocytes, cytokines and satellite cells: what role do they play in muscle damage and regeneration following eccentric exercise?* Exercise immunology review, 2012. **18**.
11. Bruunsgaard, H., et al., *Exercise-induced increase in serum interleukin-6 in humans is related to muscle damage.* The Journal of physiology, 1997. **499**(3): p. 833-841.
12. Ghanbari-Niaki, A., M. Saghebjoo, and M. Hedayati, *A single session of circuit-resistance exercise effects on human peripheral blood lymphocyte ABCA1 expression and plasma HDL-C level.* Regulatory peptides, 2011. **166**(1-3): p. 42-47.
13. Schlagheck, M.L., et al., *Cellular immune response to acute exercise: Comparison of endurance and resistance exercise.* European journal of haematology, 2020. **105**(1): p. 75-84.
14. Bessa, A.L., et al., *Exercise intensity and recovery: biomarkers of injury, inflammation, and oxidative stress.* The Journal of Strength & Conditioning Research, 2016. **30**(2): p. 311-319.

15. da Silva, L.S., et al., *Training protocols and specific performance in judo athletes: A systematic review.* The Journal of Strength & Conditioning Research, 2022.

16. Ghahramani, M.H., H. Agha-Alinejhad, and M. Molanouri Shamsi, *Effect of Different Concurrent Training Protocols on Muscle Strength, Serum Testosterone and Cortisol Level in Young Wrestlers.* Journal of Applied Health Studies in Sport Physiology, 2022. **9**(1): p. 1-11.

17. Navickaitė, A. and G. Thomas, *Strength and Conditioning Considerations for Kyokushin Karate Athletes.* Strength & Conditioning Journal, 2022: p. 10.1519.

18. Ruddock, A., et al., *High-intensity conditioning for combat athletes: practical recommendations.* Applied Sciences, 2021. **11**(22): p. 10658.

19. Seipp, D., et al., *Concurrent training in team sports: A systematic review.* International Journal of Sports Science & Coaching, 2022: p. 17479541221099846.

20. Hickson, R.C., *Interference of strength development by simultaneously training for strength and endurance.* Eur J Appl Physiol Occup Physiol, 1980. **45**(2-3): p. 255-63.

21. Petré, H., et al., *Development of maximal dynamic strength during concurrent resistance and endurance training in untrained, moderately trained, and trained individuals: a systematic review and meta-analysis.* Sports Medicine, 2021. **51**(5): p. 991-1010.

22. Senna, G.W., et al., *Higher muscle damage triggered by shorter inter-set rest periods in volume-equated resistance exercise.* Frontiers in physiology, 2022: p. 225.

23. Natale, V.M., et al., *Effects of three different types of exercise on blood leukocyte count during and following exercise.* Sao Paulo Medical Journal, 2003. **121**: p. 09-14.

24. Nielsen, H., et al., *Lymphocyte, NK and LAK cell responses to maximal exercise.* International journal of sports medicine, 1996. **17**(01): p. 60-65.

25. DiFiori, J.P., et al., *Overuse injuries and burnout in youth sports: a position statement from the American Medical Society for Sports Medicine.* British journal of sports medicine, 2014. **48**(4): p. 287-288.

26. Moreira, A., et al., *Does exercise increase the risk of upper respiratory tract infections?* British Medical Bulletin, 2009. **90**(1): p. 111-131.

27. Fabricant, P.D., et al., *Youth sports specialization and musculoskeletal injury: a systematic review of the literature.* The Physician and sportsmedicine, 2016. **44**(3): p. 257-262.

28. Roberts, W.O., *Overuse injuries and burnout in youth sports*. 2014, LWW. p. 1-2.

29. Freitas, C.G., et al., *Monitoring salivary immunoglobulin a responses to official and simulated matches in elite young soccer players.* Journal of human kinetics, 2016. **53**: p. 107.

30. Moraes, H., et al., *SIgA response and incidence of upper respiratory tract infections during intensified training in youth basketball players.* Biology of sport, 2017. **34**(1): p. 49.

31. Puta, C., et al., *Standardized assessment of resistance training-induced subjective symptoms and objective signs of immunological stress responses in young athletes.* Frontiers in physiology, 2018. **9**: p. 698.

32. Costello, J.T., F. Bieuzen, and C.M. Bleakley, *Where are all the female participants in Sports and Exercise Medicine research?* European journal of sport science, 2014. **14**(8): p. 847-851.

33. Patel, R., et al., *The underrepresentation of females in studies assessing the impact of high-dose exercise on cardiovascular outcomes: a scoping review.* Sports Medicine-Open, 2021. **7**(1): p. 1-10.

34. Lew, L.A., et al., *Examination of Sex-Specific Participant Inclusion in Exercise Physiology Endothelial Function Research: A Systematic Review.* Frontiers in Sports and Active Living, 2022. **4**.

35. Landen, S., et al., *Physiological and molecular sex differences in human skeletal muscle in response to exercise training.* The Journal of Physiology, 2021.

36. Fyfe, J.J., D.J. Bishop, and N.K. Stepto, *Interference between concurrent resistance and endurance exercise: molecular bases and the role of individual training variables.* Sports Med, 2014. **44**(6): p. 743-62.

37. Fyfe, J.J. and J.P. Loenneke, *Interpreting Adaptation to Concurrent Compared with Single-Mode Exercise Training: Some Methodological Considerations.* Sports Med, 2018. **48**(2): p. 289-297.

38. Ihalainen, J.K., et al., *Resistance training status modifies inflammatory response to explosive and hypertrophic resistance exercise bouts.* Journal of physiology and biochemistry, 2017. **73**(4): p. 595-604.

39. Coffey, V.G. and J.A. Hawley, *Concurrent exercise training: do opposites distract?* The Journal of physiology, 2017. **595**(9): p. 2883-2896.

40. Schumann, M., et al., *Acute neuromuscular and endocrine responses and recovery to single-session combined endurance and strength loadings:"order effect" in untrained young men.* The Journal of Strength & Conditioning Research, 2013. **27**(2): p. 421-433.

41. Taipale, R.S., et al., *Acute neuromuscular and metabolic responses to combined strength and endurance loadings: the "order effect" in recreationally endurance trained runners.* Journal of sports sciences, 2014. **32**(12): p. 1155-1164.

42. Markov, A., et al., *Acute Effects of Aerobic Exercise on Muscle Strength and Power in Trained Male Individuals: A Systematic Review with Meta-analysis.* Sports Medicine, 2021: p. 1-14.

43. Markov, A., L. Hauser, and H. Chaabene, *Effects of Concurrent Strength and Endurance Training on Measures of Physical Fitness in Healthy Middle-Aged and Older Adults: A Systematic Review with Meta-Analysis.* Sports Medicine, 2022: p. 1-19.

44. Craig, B.W., et al., *The effects of running, weightlifting and a combination of both on growth hormone release.* The Journal of Strength & Conditioning Research, 1991. **5**(4): p. 198-203.

45. Atherton, P.J., et al., *Selective activation of AMPK-PGC-1α or PKB-TSC2-mTOR signaling can explain specific adaptive responses to endurance or resistance training-like electrical muscle stimulation.* The FASEB journal, 2005. **19**(7): p. 1-23.

46. Coffey, V.G. and J.A. Hawley, *The molecular bases of training adaptation.* Sports medicine, 2007. **37**: p. 737-763.

47. Baar, K., *Training for endurance and strength: lessons from cell signaling.* Medicine and science in sports and exercise, 2006. **38**(11): p. 1939.

48. Baar, K., *Using molecular biology to maximize concurrent training.* Sports Medicine, 2014. **44**(2): p. 117-125.

49. Murach, K.A. and J.R. Bagley, *Skeletal Muscle Hypertrophy with Concurrent Exercise Training: Contrary Evidence for an Interference Effect.* Sports Med, 2016. **46**(8): p. 1029-39.

50. Docherty, D. and B. Sporer, *A proposed model for examining the interference phenomenon between concurrent aerobic and strength training.* Sports medicine, 2000. **30**(6): p. 385-394.

51. Vechin, F.C., et al., *Interference Phenomenon with Concurrent Strength and High-Intensity Interval Training-Based Aerobic Training: An Updated Model.* Sports Medicine: p. 1-7.

52. Monserdà-Vilaró, A., et al., *Effects of Concurrent Resistance and Endurance Training Using Continuous or Intermittent Protocols on Muscle Hypertrophy: Systematic Review With Meta-Analysis.* The Journal of Strength & Conditioning Research, 2022: p. 10.1519.

53. Rose, A.J., et al., *Skeletal muscle eEF2 and 4EBP1 phosphorylation during endurance exercise is dependent on intensity and muscle fiber type.* Am J Physiol Regul Integr Comp Physiol, 2009. **296**(2): p. R326-33.

54. Chen, Z.P., et al., *AMPK signaling in contracting human skeletal muscle: acetyl-CoA carboxylase and NO synthase phosphorylation.* Am J Physiol Endocrinol Metab, 2000. **279**(5): p. E1202-6.

55. Wojtaszewski, J.F., et al., *Dissociation of AMPK activity and ACCbeta phosphorylation in human muscle during prolonged exercise.* Biochem Biophys Res Commun, 2002. **298**(3): p. 309-16.

56. Rønnestad, B.R., E.A. Hansen, and T. Raastad, *High volume of endurance training impairs adaptations to 12 weeks of strength training in well-trained endurance athletes.* Eur J Appl Physiol, 2012. **112**(4): p. 1457-66.

57. Jones, T.W., et al., *Performance and neuromuscular adaptations following differing ratios of concurrent strength and endurance training.* J Strength Cond Res, 2013. **27**(12): p. 3342-51.

58. Glowacki, S.P., et al., *Effects of resistance, endurance, and concurrent exercise on training outcomes in men.* Med Sci Sports Exerc, 2004. **36**(12): p. 2119-27.

59. Häkkinen, K., et al., *Neuromuscular adaptations during concurrent strength and endurance training versus strength training.* Eur J Appl Physiol, 2003. **89**(1): p. 42-52.

60. McCarthy, J.P., M.A. Pozniak, and J.C. Agre, *Neuromuscular adaptations to concurrent strength and endurance training.* Med Sci Sports Exerc, 2002. **34**(3): p. 511-9.

61. Kraemer, W.J., et al., *Compatibility of high-intensity strength and endurance training on hormonal and skeletal muscle adaptations.* Journal of applied physiology, 1995. **78**(3): p. 976-989.

62. Bell, G.J., et al., *Effect of concurrent strength and endurance training on skeletal muscle properties and hormone concentrations in humans.* Eur J Appl Physiol, 2000. **81**(5): p. 418-27.

63. Wilson, J.M., et al., *Concurrent Training: A Meta-Analysis Examining Interference of Aerobic and Resistance Exercises.* The Journal of Strength & Conditioning Research, 2012. **26**(8): p. 2293-2307.

64. Leveritt, M., et al., *Concurrent strength and endurance training.* Sports medicine, 1999. **28**(6): p. 413-427.

65. Gergley, J.C., *Comparison of Two Lower-Body Modes of Endurance Training on Lower-Body Strength Development While Concurrently Training.* The Journal of Strength & Conditioning Research, 2009. **23**(3): p. 979-987.

66. Silva, R.F., et al., *Concurrent training with different aerobic exercises.* Int J Sports Med, 2012. **33**(8): p. 627-34.

67. LEVERITT, M. and P.J. ABERNETHY, *Acute effects of high-intensity endurance exercise on subsequent resistance activity.* The Journal of Strength & Conditioning Research, 1999. **13**(1): p. 47-51.

68. Bentley, D.J., et al., *Muscle activation of the knee extensors following high intensity endurance exercise in cyclists.* European journal of applied physiology, 2000. **81**(4): p. 297-302.

69. Sporer, B.C. and H.A. Wenger, *Effects of aerobic exercise on strength performance following various periods of recovery.* The Journal of Strength & Conditioning Research, 2003. **17**(4): p. 638-644.

70. Tesch, P., *Skeletal muscle adaptations consequent to long-term heavy resistance exercise.* Medicine and science in sports and exercise, 1988. **20**(5 Suppl): p. S132-4.

71. Creer, A., et al., *Influence of muscle glycogen availability on ERK1/2 and Akt signaling after resistance exercise in human skeletal muscle.* Journal of applied physiology, 2005. **99**(3): p. 950-956.

72. Eddens, L., K. van Someren, and G. Howatson, *The Role of Intra-Session Exercise Sequence in the Interference Effect: A Systematic Review with Meta-Analysis.* Sports Med, 2018. **48**(1): p. 177-188.

73. Murlasits, Z., Z. Kneffel, and L. Thalib, *The physiological effects of concurrent strength and endurance training sequence: A systematic review and meta-analysis.* J Sports Sci, 2018. **36**(11): p. 1212-1219.

74. Jones, T.W., et al., *Signaling Responses After Varying Sequencing of Strength and Endurance Training in a Fed State.* Int J Sports Physiol Perform, 2016. **11**(7): p. 868-875.

75. Coffey, V.G., et al., *Effect of consecutive repeated sprint and resistance exercise bouts on acute adaptive responses in human skeletal muscle.* American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 2009. **297**(5): p. R1441-R1451.

76. Coffey, V.G., et al., *Consecutive bouts of diverse contractile activity alter acute responses in human skeletal muscle.* J Appl Physiol (1985), 2009. **106**(4): p. 1187-97.

77. Enoka, R.M. and J. Duchateau, *Translating fatigue to human performance.* Medicine and science in sports and exercise, 2016. **48**(11): p. 2228.

78. Noakes, T.D.O., *Fatigue is a brain-derived emotion that regulates the exercise behavior to ensure the protection of whole body homeostasis.* Frontiers in physiology, 2012. **3**: p. 82.

79. Pugh, J.K., et al., *Acute molecular responses to concurrent resistance and high-intensity interval exercise in untrained skeletal muscle.* Physiol Rep, 2015. **3**(4).

80. Bolster, D.R., et al., *AMP-activated protein kinase suppresses protein synthesis in rat skeletal muscle through down-regulated mammalian target of rapamycin (mTOR) signaling.* J Biol Chem, 2002. **277**(27): p. 23977-80.

81. Furrer, R., et al., *Attenuated increase in maximal force of rat medial gastrocnemius muscle after concurrent peak power and endurance training.* Biomed Res Int, 2013. **2013**: p. 935671.

82. Lundberg, T.R., R. Fernandez-Gonzalo, and P.A. Tesch, *Exercise-induced AMPK activation does not interfere with muscle hypertrophy in response to resistance training in men.* J Appl Physiol (1985), 2014. **116**(6): p. 611-20.

83. Wang, L., et al., *Resistance exercise enhances the molecular signaling of mitochondrial biogenesis induced by endurance exercise in human skeletal muscle.* J Appl Physiol (1985), 2011. **111**(5): p. 1335-44.

84. Lundberg, T.R., et al., *Aerobic exercise alters skeletal muscle molecular responses to resistance exercise.* Medicine & Science in Sports & Exercise, 2012. **44**(9): p. 1680-1688.

85. Lundberg, T.R., R. Fernandez-Gonzalo, and P.A. Tesch, *Exercise-induced AMPK activation does not interfere with muscle hypertrophy in response to resistance training in men.* Journal of applied physiology, 2014. **116**(6): p. 611-620.

86. Donges, C.E., et al., *Concurrent resistance and aerobic exercise stimulates both myofibrillar and mitochondrial protein synthesis in sedentary middle-aged men.* Journal of Applied Physiology, 2012. **112**(12): p. 1992-2001.

87. Camera, D.M., et al., *Early time course of Akt phosphorylation after endurance and resistance exercise.* Med Sci Sports Exerc, 2010. **42**(10): p. 1843-52.

88. Vissing, K., et al., *Differentiated mTOR but not AMPK signaling after strength vs endurance exercise in training-accustomed individuals.* Scand J Med Sci Sports, 2013. **23**(3): p. 355-66.

89. Wilkinson, S.B., et al., *Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle.* J Physiol, 2008. **586**(15): p. 3701-17.

90. Gäbler, M., et al., *The effects of concurrent strength and endurance training on physical fitness and athletic performance in youth: a systematic review and meta-analysis.* Frontiers in physiology, 2018. **9**: p. 1057.

91. Hansen, M., *Female hormones: do they influence muscle and tendon protein metabolism?* Proceedings of the Nutrition Society, 2018. **77**(1): p. 32-41.

92. Oxfeldt, M., et al., *Sex Hormones and Satellite Cell Regulation in Women.* Translational Sports Medicine, 2022. **2022**.

93. Oxfeldt, M., et al., *Molecular markers of skeletal muscle hypertrophy following 10 wk of resistance training in oral contraceptive users and nonusers.* Journal of Applied Physiology, 2020.

94. Del Coso, J. and A. Lucia, *Genetic Influence in Exercise Performance*. 2021, MDPI. p. 651.

95. Hall, E.C., et al., *The genetic association with injury risk in male academy soccer players depends on maturity status.* Scandinavian Journal of Medicine & Science in Sports, 2022. **32**(2): p. 338-350.

96. Varillas-Delgado, D., et al., *Genetics and sports performance: the present and future in the identification of talent for sports based on DNA testing.* European Journal of Applied Physiology, 2022. **122**(8): p. 1811-1830.

97. Chung, H.C., et al., *Do exercise-associated genes explain phenotypic variance in the three components of fitness? A systematic review & meta-analysis.* PLoS One, 2021. **16**(10): p. e0249501.

98. Pixabay. Available from: https://pixabay.com.

99. Schumann, M., et al., *Compatibility of Concurrent Aerobic and Strength Training for Skeletal Muscle Size and Function: An Updated Systematic Review and Meta-Analysis.* Sports Med, 2022. **52**(3): p. 601-612.

100. de Araújo Ruas, V.D., et al., *Effect of cycling exercise at different pedal cadences on subsequent muscle strength.* Journal of Exercise Science & Fitness, 2011. **9**(2): p. 93-99.

101. Schumann, M., et al., *The order effect of combined endurance and strength loadings on force and hormone responses: effects of prolonged training.* European journal of applied physiology, 2014. **114**(4): p. 867-880.

102. Boullosa, D.A., et al., *Concurrent fatigue and potentiation in endurance athletes.* International journal of sports physiology and performance, 2011. **6**(1): p. 82-93.

103. García-Pinillos, F., V.M. Soto-Hermoso, and P.A. Latorre-Román, *Acute effects of extended interval training on countermovement jump and handgrip strength performance in endurance athletes: postactivation potentiation.* The Journal of Strength & Conditioning Research, 2015. **29**(1): p. 11-21.

104. Latorre-Román, P.Á., et al., *Concurrent fatigue and postactivation potentiation during extended interval training in long-distance runners.* Motriz: Revista de Educação Física, 2014. **20**(4): p. 423-430.

105. Moberg, M., et al., *Exercise Induces Different Molecular Responses in Trained and Untrained Human Muscle.* Medicine & Science in Sports & Exercise, 2020. **52**(8): p. 1679-1690.

106. Fitts, R.H., *Cellular mechanisms of muscle fatigue.* Physiological reviews, 1994. **74**(1): p. 49-94.

107. Gandevia, S.C., *Spinal and supraspinal factors in human muscle fatigue.* Physiological reviews, 2001.

108. Baar, K., *Using nutrition and molecular biology to maximize concurrent training.* Sports Sci Exch, 2014. **136**: p. 1-5.

109. Burniston, J.G., M. Towler, and H. Wackerhage, *Signal transduction and adaptation to exercise: background and methods.* Molecular Exercise Physiology: An Introduction, 2014: p. 52.

110. Cuthbertson, D.J., et al., *Anabolic signaling and protein synthesis in human skeletal muscle after dynamic shortening or lengthening exercise.* Am J Physiol Endocrinol Metab, 2006. **290**(4): p. E731-8.

111. Rennie, M.J., *Control of muscle protein synthesis as a result of contractile activity and amino acid availability: implications for protein requirements.* Int J Sport Nutr Exerc Metab, 2001. **11 Suppl**: p. S170-6.

112. Wu, Z., et al., *Mechanisms controlling mitochondrial biogenesis and respiration through the thermogenic coactivator PGC-1.* Cell, 1999. **98**(1): p. 115-124.

113. Bolster, D.R., et al., *Immediate response of mammalian target of rapamycin (mTOR)-mediated signalling following acute resistance exercise in rat skeletal muscle.* J Physiol, 2003. **553**(Pt 1): p. 213-20.

114. Bodine, S.C., et al., *Akt/mTOR pathway is a crucial regulator of skeletal muscle hypertrophy and can prevent muscle atrophy in vivo.* Nat Cell Biol, 2001. **3**(11): p. 1014-9.

115. Karlsson, H.K., et al., *Branched-chain amino acids increase p70S6k phosphorylation in human skeletal muscle after resistance exercise.* Am J Physiol Endocrinol Metab, 2004. **287**(1): p. E1-7.

116. Baar, K., *Training for endurance and strength: lessons from cell signaling.* Med Sci Sports Exerc, 2006. **38**(11): p. 1939-44.

117. Carling, D., et al., *AMP-activated protein kinase: new regulation, new roles?* Biochem J, 2012. **445**(1): p. 11-27.

118. Baar, K., et al., *Adaptations of skeletal muscle to exercise: rapid increase in the transcriptional coactivator PGC-1.* Faseb j, 2002. **16**(14): p. 1879-86.

119. Kang, C. and L. Li Ji, *Role of PGC-1α signaling in skeletal muscle health and disease.* Ann N Y Acad Sci, 2012. **1271**(1): p. 110-7.

120. Ying, F., et al., *Muscle fiber-type conversion in the transgenic pigs with overexpression of PGC1alpha gene in muscle.* Biochem Biophys Res Commun, 2016. **480**(4): p. 669-674.

121. Lin, J., et al., *Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres.* Nature, 2002. **418**(6899): p. 797-801.

122. de Souza, E.O., et al., *Molecular adaptations to concurrent training.* Int J Sports Med, 2013. **34**(3): p. 207-13.

123. Fyfe, J.J., et al., *Concurrent exercise incorporating high-intensity interval or continuous training modulates mTORC1 signaling and microRNA expression in human skeletal muscle.* Am J Physiol Regul Integr Comp Physiol, 2016. **310**(11): p. R1297-311.

124. Souza, E.O., et al., *Early adaptations to six weeks of non-periodized and periodized strength training regimens in recreational males.* J Sports Sci Med, 2014. **13**(3): p. 604-9.

125. Apro, W., et al., *Resistance exercise-induced S6K1 kinase activity is not inhibited in human skeletal muscle despite prior activation of AMPK by high-intensity interval cycling.* Am J Physiol Endocrinol Metab, 2015. **308**(6): p. E470-81.

126. Apro, W., et al., *Resistance exercise induced mTORC1 signaling is not impaired by subsequent endurance exercise in human skeletal muscle.* Am J Physiol Endocrinol Metab, 2013. **305**(1): p. E22-32.

127. Aguiar, A.F., et al., *A single set of exhaustive exercise before resistance training improves muscular performance in young men.* Eur J Appl Physiol, 2015. **115**(7): p. 1589-99.

128. Kazior, Z., et al., *Endurance Exercise Enhances the Effect of Strength Training on Muscle Fiber Size and Protein Expression of Akt and mTOR.* PLoS One, 2016. **11**(2): p. e0149082.

129. Psilander, N., et al., *Adding strength to endurance training does not enhance aerobic capacity in cyclists.* Scand J Med Sci Sports, 2015. **25**(4): p. e353-9.

130. Katzmarzyk, P., R. Malina, and G. Beunen, *The contribution of biological maturation to the strength and motor fitness of children.* Annals of human biology, 1997. **24**(6): p. 493-505.

131. Lloyd, R.S., et al., *Chronological age vs. biological maturation: implications for exercise programming in youth.* The Journal of Strength & Conditioning Research, 2014. **28**(5): p. 1454-1464.

132. Alves, A.R., et al., *Concurrent Training in Prepubescent Children: The Effects of 8 Weeks of Strength and Aerobic Training on Explosive Strength and V[Combining Dot Above]O2max.* J Strength Cond Res, 2016. **30**(7): p. 2019-32.

133. Alves, A.R., et al., *Does Intrasession Concurrent Strength and Aerobic Training Order Influence Training-Induced Explosive Strength and V[Combining Dot Above]O2max in Prepubescent Children?* J Strength Cond Res, 2016. **30**(12): p. 3267-3277.

134. Radovanovic, D., et al., *Oxidative stress biomarker response to concurrent strength and endurance training.* Gen Physiol Biophys, 2009. **28 Spec No**: p. 205-11.

135. Saini, J., et al., *Regenerative function of immune system: Modulation of muscle stem cells.* Ageing research reviews, 2016. **27**: p. 67-76.

136. Tidball, J.G., *Regulation of muscle growth and regeneration by the immune system.* Nature Reviews Immunology, 2017. **17**(3): p. 165-178.

137. Tidball, J.G. and S.A. Villalta, *Regulatory interactions between muscle and the immune system during muscle regeneration.* American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 2010. **298**(5): p. R1173-R1187.

138. Parkin, J. and B. Cohen, *An overview of the immune system.* The Lancet, 2001. **357**(9270): p. 1777-1789.

139. Blanco, J.L. and M.E. Garcia, *Immune response to fungal infections.* Veterinary immunology and immunopathology, 2008. **125**(1-2): p. 47-70.

140. Thangam, E.B., et al., *The role of histamine and histamine receptors in mast cell-mediated allergy and inflammation: the hunt for new therapeutic targets.* Frontiers in immunology, 2018. **9**: p. 1873.

141. Andersen, M.H., et al., *Cytotoxic T cells.* Journal of Investigative Dermatology, 2006. **126**(1): p. 32-41.

142. LeBien, T.W. and T.F. Tedder, *B lymphocytes: how they develop and function.* Blood, The Journal of the American Society of Hematology, 2008. **112**(5): p. 1570-1580.

143. Shephard, R.J., *Development of the discipline of exercise immunology.* Exerc Immunol Rev, 2010. **16**: p. 194-222.

144. Kakanis, M.W., et al., *The open window of susceptibility to infection after acute exercise in healthy young male elite athletes.* Exerc Immunol Rev, 2010. **16**: p. 119-37.

145. Valencia-Sánchez, S., et al., *Effects of Exercise upon Immunoregulation: Facts and a Modern View of its Molecular Mechanisms.* Advances in Neuroimmune Biology, 2019. **7**(3-4): p. 187-198.

146. Nieman, D.C., *Exercise, infection, and immunity.* International journal of sports medicine, 1994. **15**(S 3): p. S131-S141.

147. Pedersen, B.K. and H. Bruunsgaard, *How physical exercise influences the establishment of infections.* Sports Medicine, 1995. **19**(6): p. 393-400.

148. Fett, D., K. Trompeter, and P. Platen, *Back pain in elite sports: a cross-sectional study on 1114 athletes.* PloS one, 2017. **12**(6): p. e0180130.

149. Campbell, J.P. and J.E. Turner, *Debunking the Myth of Exercise-Induced Immune Suppression: Redefining the Impact of Exercise on Immunological Health Across the Lifespan.* Frontiers in Immunology, 2018. **9**.

150. Cox, A.J., et al., *Clinical and laboratory evaluation of upper respiratory symptoms in elite athletes.* Clinical Journal of Sport Medicine, 2008. **18**(5): p. 438-445.

151. Gleeson, M., et al., *Epstein-Barr virus reactivation and upper-respiratory illness in elite swimmers.* Medicine and science in sports and exercise, 2002. **34**(3): p. 411-417.

152. Trammell, R.A. and L.A. Toth, *Genetic susceptibility and resistance to influenza infection and disease in humans and mice.* Expert review of molecular diagnostics, 2008. **8**(4): p. 515-529.

153. Dorneles, G.P., et al., *Physical fitness modulates the expression of CD39 and CD73 on CD4+ CD25– and CD4+ CD25+ T cells following high intensity interval exercise.* Journal of Cellular Biochemistry, 2019. **120**(6): p. 10726-10736.

154. Alack, K., C. Pilat, and K. Krüger, *Current knowledge and new challenges in exercise immunology.* Dtsch Z Sportmed, 2019. **70**(10): p. 250-260.

155. Rosa-Neto, J.C., et al., *Immunometabolism-fit: How exercise and training can modify T cell and macrophage metabolism in health and disease.* Exerc Immunol Rev, 2022. **28**: p. 29-46.

156. Simpson, R.J., et al., *Exercise and the regulation of immune functions.* Progress in molecular biology and translational science, 2015. **135**: p. 355-380.

157. Ihalainen, J., et al., *Acute leukocyte, cytokine and adipocytokine responses to maximal and hypertrophic resistance exercise bouts.* European journal of applied physiology, 2014. **114**(12): p. 2607-2616.

158. Nieman, D., et al., *The acute immune response to exhaustive resistance exercise.* International journal of sports medicine, 1995. **16**(05): p. 322-328.

159. Shek, P.N., et al., *Strenuous exercise and immunological changes.* International journal of sports medicine, 1995. **16**(07): p. 466-474.

160. Vider, J., et al., *Acute immune response in respect to exercise-induced oxidative stress.* Pathophysiology, 2001. **7**(4): p. 263-270.

161. Wahl, P., et al., *Acute impact of recovery on the restoration of cellular immunological homeostasis.* International journal of sports medicine, 2020. **41**(01): p. 12-20.

162. Donges, C.E., et al., *Cytokine mRNA expression responses to resistance, aerobic, and concurrent exercise in sedentary middle-aged men.* Applied Physiology, Nutrition, and Metabolism, 2014. **39**(2): p. 130-137.

163. Inoue, D.S., et al., *Immunometabolic responses to concurrent training: the effects of exercise order in recreational weightlifters.* Journal of Strength and Conditioning Research, 2016. **30**(7): p. 1960-1967.

164. Stewart, L.K., et al., *The influence of exercise training on inflammatory cytokines and C-reactive protein.* Medicine & Science in Sports & Exercise, 2007. **39**(10): p. 1714-1719.

165. Ihalainen, J.K., et al., *Combined aerobic and resistance training decreases inflammation markers in healthy men.* Scandinavian journal of medicine & science in sports, 2018. **28**(1): p. 40-47.

166. Libardi, C.A., et al., *Effect of resistance, endurance, and concurrent training on TNF-alpha, IL-6, and CRP.* Med Sci Sports Exerc, 2012. **44**(1): p. 50-6.

167. Libardi, C.A., et al., *Effects of concurrent training on interleukin-6, tumour necrosis factor-alpha and C-reactive protein in middle-aged men.* Journal of sports sciences, 2011. **29**(14): p. 1573-1581.

168. McKay, A.K., et al., *Defining Training and Performance Caliber: A Participant Classification Framework.* International Journal of Sports Physiology and Performance, 2022. **1**(aop): p. 1-15.

169. MIRWALD, R.L., et al., *An assessment of maturity from anthropometric measurements.* Medicine & Science in Sports & Exercise, 2002. **34**(4): p. 689-694.

170. FIFA, *FIFA 11+.* https://www.f-marc.com/files/downloads/posters_generic/english.pdf.

171. Faigenbaum, A.D., et al., *Youth Resistance Training: Updated Position Statement Paper From the National Strength and Conditioning Association.* The Journal of Strength & Conditioning Research, 2009. **23**: p. S60-S79.

172. Burd, N.A., et al., *Muscle time under tension during resistance exercise stimulates differential muscle protein sub-fractional synthetic responses in men.* The Journal of physiology, 2012. **590**(2): p. 351-362.

173. Sterkowicz, S., A. Zuchowicz, and R. Kubica, *Levels of anaerobic and aerobic capacity indices and results for the special fitness test in judo competitors.* Journal of Human Kinetics, 1999. **2**(1): p. 115-135.

174. Franchini, E., et al., *Energy system contributions to the special judo fitness test.* International journal of sports physiology and performance, 2011. **6**(3): p. 334-343.

175. Steidten, T., et al., *Overnight Immune Regulation and Subjective Measures of Sleep: A Three Night Observational Study in Adolescent Track and Field Athletes.* Frontiers in sports and active living, 2021: p. 270.

176. Buonacera, A., et al., *Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases.* International Journal of Molecular Sciences, 2022. **23**(7): p. 3636.

177. Williams, N., *The Borg rating of perceived exertion (RPE) scale.* Occupational Medicine, 2017. **67**(5): p. 404-405.

178. St, L. and S. Wold, *Analysis of variance (ANOVA).* Chemometrics and intelligent laboratory systems, 1989. **6**(4): p. 259-272.

179. Ghasemi, A. and S. Zahediasl, *Normality tests for statistical analysis: a guide for non-statisticians.* International journal of endocrinology and metabolism, 2012. **10**(2): p. 486.

180. Field, A., *Discovering statistics using SPSS*. 2009: Sage publications.

181. Cohen, J., *Statistical Power Analysis for the Behavioral Sciences, no. 1.* Lwrence Earlbaum Associates Publishers, 1988.

182. Kverneland, A.H., et al., *Age and gender leucocytes variances and references values generated using the standardized ONE-Study protocol.* Cytometry part A, 2016. **89**(6): p. 543-564.

183. Nieman, D., et al., *Effects of long-endurance running on immune system parameters and lymphocyte function in experienced marathoners.* International journal of sports medicine, 1989. **10**(05): p. 317-323.

184. Ramel, A., K.-H. Wagner, and I. Elmadfa, *Acute impact of submaximal resistance exercise on immunological and hormonal parameters in young men.* Journal of Sports Science, 2003. **21**(12): p. 1001-1008.

185. Gabriel, H., A. Urhausen, and W. Kindermann, *Mobilization of circulating leucocyte and lymphocyte subpopulations during and after short, anaerobic exercise.* European journal of applied physiology and occupational physiology, 1992. **65**(2): p. 164-170.

186. Mayhew, D.L., J.P. Thyfault, and A.J. Koch, *Rest-interval length affects leukocyte levels during heavy resistance exercise.* The Journal of Strength & Conditioning Research, 2005. **19**(1): p. 16-22.

187. Peake, J.M., et al., *Recovery of the immune system after exercise.* Journal of Applied Physiology, 2017. **122**(5): p. 1077-1087.

188. Hill, E., et al., *Exercise and circulating cortisol levels: the intensity threshold effect.* Journal of endocrinological investigation, 2008. **31**(7): p. 587-591.

189. Kindermann, W., et al., *Catecholamines, growth hormone, cortisol, insulin, and sex hormones in anaerobic and aerobic exercise.* European journal of applied physiology and occupational physiology, 1982. **49**(3): p. 389-399.

190. Chazaud, B., *Inflammation and skeletal muscle regeneration: leave it to the macrophages!* Trends in immunology, 2020. **41**(6): p. 481-492.

191. Julier, Z., et al., *Promoting tissue regeneration by modulating the immune system.* Acta biomaterialia, 2017. **53**: p. 13-28.

192. Smith, L., et al., *Differential white cell count after two bouts of downhill running.* International journal of sports medicine, 1998. **19**(06): p. 432-437.

193. Krüger, K., et al., *Exercise-induced redistribution of T lymphocytes is regulated by adrenergic mechanisms.* Brain, behavior, and immunity, 2008. **22**(3): p. 324-338.

194. Kruger, K. and F. Mooren, *T cell homing and exercise.* Exerc Immunol Rev, 2007. **13**: p. 37-54.

195. Fois, A.G., et al., *The systemic inflammation index on admission predicts in-hospital mortality in COVID-19 patients.* Molecules, 2020. **25**(23): p. 5725.

196. Moisa, E., et al., *Dynamic changes of the neutrophil-to-lymphocyte ratio, systemic inflammation index, and derived neutrophil-to-lymphocyte ratio independently predict invasive mechanical ventilation need and death in critically ill COVID-19 patients.* Biomedicines, 2021. **9**(11): p. 1656.

197. Huang, Y., et al., *Relationship between monocytes to lymphocytes ratio and axial spondyloarthritis.* International immunopharmacology, 2018. **57**: p. 43-46.

198. Islas-Vazquez, L., et al., *IL-6, NLR, and SII markers and their relation with alterations in CD8+ T-lymphocyte subpopulations in patients treated for lung adenocarcinoma.* Biology, 2020. **9**(11): p. 376.

199. Zhu, Z., et al., *Clinical value of immune-inflammatory parameters to assess the severity of coronavirus disease 2019.* International Journal of Infectious Diseases, 2020. **95**: p. 332-339.

200. Walzik, D., et al., *Transferring clinically established immune inflammation markers into exercise physiology: focus on neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index.* European Journal of Applied Physiology, 2021. **121**(7): p. 1803-1814.

201. Freidenreich, D.J. and J.S. Volek, *The immune response to exercise: effects on cellular mobilization, immune function and muscle regeneration*, in *Nutrition and Enhanced Sports Performance*. 2013, Elsevier. p. 95-101.

202. Balsalobre-Fernández, C., C.M. Tejero-González, and J. del Campo-Vecino, *Relationships between training load, salivary cortisol responses and performance during season training in middle and long distance runners.* PloS one, 2014. **9**(8): p. e106066.

203. Halson, S.L., *Monitoring training load to understand fatigue in athletes.* Sports medicine, 2014. **44**(2): p. 139-147.

204. Cardinale, M. and M.H. Stone, *Is testosterone influencing explosive performance?* The Journal of Strength & Conditioning Research, 2006. **20**(1): p. 103-107.

205. García-Pinillos, F., et al., *Vertical Jumping as a Monitoring Tool in Endurance Runners: A Brief Review.* Journal of Human Kinetics, 2021. **80**(1): p. 297-308.

206. Impellizzeri, F.M., S.M. Marcora, and A.J. Coutts, *Internal and external training load: 15 years on.* International journal of sports physiology and performance, 2019. **14**(2): p. 270-273.

207. McLaren, S.J., et al., *The relationships between internal and external measures of training load and intensity in team sports: a meta-analysis.* Sports medicine, 2018. **48**(3): p. 641-658.

208. Beneke, R., R.M. Leithäuser, and O. Ochentel, *Blood lactate diagnostics in exercise testing and training.* Int J Sports Physiol Perform, 2011. **6**(1): p. 8-24.

209. Wahl, P., W. Bloch, and J. Mester, *Moderne Betrachtungsweisen des Laktats: Laktat ein uberschatztes und zugleich unterschatztes Molekul.* Schweizerische Zeitschrift fur Sportmedizin und Sporttraumatologie, 2009. **57**(3): p. 100.

210. Coggan, A.R., *Plasma glucose metabolism during exercise in humans.* Sports Medicine, 1991. **11**: p. 102-124.

211. Tsintzas, K. and C. Williams, *Human muscle glycogen metabolism during exercise. Effect of carbohydrate supplementation.* Sports Med, 1998. **25**(1): p. 7-23.

212. Prieske, O., et al., *Time to differentiate postactivation "potentiation" from "performance enhancement" in the strength and conditioning community.* Sports Medicine, 2020. **50**: p. 1559-1565.

213. Silverthorn, D.U., *Human physiology*. 2015: Jones & Bartlett Publishers.

9 List of Figures

10 List of Tables

11 List of Publications

1. **Markov, A.,** et al., *Acute effects of concurrent muscle power and sport-specific endurance exercises on markers of immunological stress response and measures of muscular fitness in highly trained youth male athletes.* European Journal of Applied Physiology, 2023: p. 1-12.
2. Arntz, F., **Markov, A**., et al., *Chronic Effects of Static Stretching Exercises on Muscle Strength and Power in Healthy Individuals Across the Lifespan: A Systematic Review with Multi-level Meta-analysis.* Sports Medicine, 2023. **53**(3): p. 723-745.
3. Bouguezzi, R., **Markov, A.,** et al., *Why Flexibility Deserves to Be Further Considered as a Standard Component of Physical Fitness: A Narrative Review of Existing Insights from Static Stretching Study Interventions.* Youth, 2023. **3**(1): p. 146-156.
4. **Markov, A.,** L. Hauser, and H. Chaabene, *Effects of Concurrent Strength and Endurance Training on Measures of Physical Fitness in Healthy Middle-Aged and Older Adults: A Systematic Review with Meta-Analysis.* Sports Med., 2022: p. 1-19.
5. **Markov, A**., Chaabene, H., Hauser, L., Behm, S., Bloch, W., Puta, C., Granacher, U. (2021). Acute Effects of Aerobic Exercise on Muscle Strength and Power in Trained Male Individuals: A Systematic Review with Meta-Aanalysis. *Sports Med.*
6. Bussweiler, J., **Markov, A**., Puta, C., Helm, N., Kappell, H., Granacher, U. (2021). Return to Performance: COVID-19 und die Herrausforderungen für das Training im Nachwuchsleistungssport. *Leistungssport*, 04/21.
7. Chaabene, H., **Markov, A**., Prieske, O., Hauser, L., Moran, J., Behrens, M., Negra, Y., Ramirez-Campillo, R., Koch, U., Mkouer, B. (2021). The Effects of Accentuated Eccentric versus Traditional Strength Training on Change of Direction Speed in Trained Males: A Systematic Review with Meta-Aanalysis. *Sports Medicine.*

8. Steidten, T., Baumbach, P., May, R., Gabriel, B., Herbsleb, M., **Markov, A**., Granacher, U., Kellmann, M., Bloch, W., Gabriel, H., Puta, C. (2021). Overnight Immune Regulation and Subjective Measures of Sleep: A Three Night Observational Study in Adolescent Track and Field Athletes. *Frontiers in Sports and Active Living*, 270.
9. Krohm, L., Krüger, T., **Markov, A**., Helm., Granacher, U. (2021). Systematische Analyse des konditionellen Anforderungsprofils im Olympischen Cross-Country Mountainbike. *Leistungssport*.
10. **Markov, A**., Hauser, L., Puta, C., Granacher, U. (2020). Concurrent Training: Effekte auf die Kardiorespiratorische Fitness, Neuromuskuläre Leistungsfähigkeit und Gesundheit von Erwachsenen. *Sportärztezeitung 03/20.*
11. Prieske, O., Chaabene, H., Gäbler, M., Herz., Helm, N., **Markov, A**., Granacher, U. (2020). Seasonal Changes in Anthropometry, Body Composition, and Physical Fitness and the Relationship with Sporting Success in Young Sub-Elite Judo Athletes: An Exploratory Study. *International Journal of Environmental Research and Public Health*, 17(19), 7169.
12. Kittel, R., Helm, N., **Markov, A**., Granacher, U. (2020). Rangeln und Raufen im Sportunterricht der Primarstufe: Spielerischer Kompetenzerwerb für den Bodenkampf. *Lehrhilfen.*
13. Helm, N., **Markov, A**., Kittel, R., Granacher, U. (2020). Die Bedeutung der Sportart Judo für den Sportunterricht der Primarstufe. *Lehrhilfen.*