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Power and Endurance: Polar Opposites or Willing Partners?

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ABSTRACT

Introduction. Peak neuromuscular power and endurance are distinct qualities of dynamic exercise performance. Dynamometry is used to assess peak neuromuscular power, often during performance across a single joint e.g., isotonic or isokinetic torque, while aptitude for endurance exercise may be inferred by measurement of critical power/speed or cardiopulmonary exercise testing to determine e.g., gas exchange threshold (GET), maximum oxygen uptake ($\dot{V}O_2max$) and exercise economy. Specificity is a critical component of any training program, but oversimplification of the specificity principle has contributed to the view that training adaptations to increase peak neuromuscular power or the ability to endure high power outputs are mutually exclusive, due to: (i) differences in the types of motor units recruited and their patterns of activation; and (ii) induction of distinct, antagonistic molecular signaling pathways in response to resistance and endurance exercise training (the "interference effect"). **Methods, Results and Conclusion.** This review explores evidence for reciprocation between peak neuromuscular power and endurance performance in sport, aging and among general and clinical populations. We also review the molecular events that mediate peak neuromuscular power and endurance training adaptations and their interactions. Finally, we describe the musculo-cardio-pulmonary exercise test (mCPET) to demonstrate that peak neuromuscular power and aerobic mediators of endurance performance are less polar opposites and more willing partners.

Key Words: CONCURRENT TRAINING, CARDIOPULMONARY EXERCISE TESTING, MCPET, INTERFERENCE EFFECT, PHYSIOLOGICAL RESILIENCE, AGING

INTRODUCTION

Skeletal muscle is a highly plastic tissue that exhibits large adaptations in terms of size, force-generation and metabolism to different exercise training stimuli. Peak neuromuscular power and the ability to endure high power outputs are distinct qualities of dynamic exercise performance. The power-duration model (stylized in Fig. 1A) provides a framework for the contributions of peak neuromuscular power (x-axis) and endurance (y-axis) to peak performance of a specific exercise task. Peak neuromuscular power can be readily assessed by dynamometry, often using isolated movements across a single joint e.g., isotonic or isokinetic torque, while aptitude for endurance exercise performance can be measured using ramp-incremental, constant power or all-out cardiopulmonary exercise testing to determine e.g., gas exchange threshold (GET), critical power (CP) or critical speed (CS), maximum oxygen uptake ($\dot{V}O_2$max) and economy. The associations of these discrete laboratory-based measures of task-specific peak neuromuscular power and endurance ability with exercise performance are well described (1-5).

The principle of specificity is a critical component of any training program that aims to bring about physiological adaptations to enhance performance of explicit exercise tasks. We argue that the specificity principle has contributed to an oversimplified view of the mediators of exercise performance, and that the interplay between peak neuromuscular power and endurance ability in determining exercise performance is more nuanced. Specifically, a strong focus in the exercise science literature on qualities of physiology and molecular signaling that associate with event-specific performance and training adaptations (Fig. 1A) have contributed to the view that adaptations to increase peak neuromuscular power and endurance exercise performance are mutually exclusive, mediated through: (i) differences in the types of motor units recruited and their patterns of activation; and (ii) antagonism among muscle molecular signaling pathways moderating adaptations in peak neuromuscular power when endurance and resistance training is conducted concurrently (the “interference effect” (6)). Here we will explore the evidence that concurrent training, defined as performing both endurance- and resistance-type exercises during a training program, results in interference of performance adaptations. For this review, we focus on the concept of acute peak power-generating, dynamic, task-specific movements (peak power) in comparison to the ability to maintain some fraction of that peak neuromuscular power chronically over time (endurance). This focus is because power has strong applicability to physical function, activities of daily living and sports performance. Nevertheless, many studies that assess resistance exercise training outcomes use strength-based measures of neuromuscular performance e.g., isometric force or torque, 1 repetition maximum (1-RM). We recognize that force/torque and power are distinct quantities of neuromuscular performance, but for simplicity here we refer to “peak neuromuscular power” when discussing outcomes of resistance-type exercise training that may also modify strength.

The two-parameter power-duration model may also contribute to a mutually exclusive view of peak neuromuscular power and endurance ability, where the CP/CS parameter (the asymptote of the power-duration relationship and the greatest power output for which $\dot{V}O_2$ and blood lactate stabilize) is strongly positively associated with physiological variables that support aerobic metabolism, while the W’ parameter (the curvature constant of the power-duration relationship) is positively associated with variables that support high peak neuromuscular power . Many studies on healthy young participants found no association between CP and W’. However, it was not until these variables were investigated across the spectrum of biological function (i.e., from young to old, and from health to chronic disease) that a relationship was revealed (Fig. 1B; (14)). The finding of an association between CP and W' across a wide range of biological function challenges the dogma that a high peak neuromuscular power and the ability to sustain high power outputs for a long duration are polar opposite characteristics of exercise performance. This association between peak neuromuscular power and endurance ability warrants renewed scrutiny.

While optimizing event-specific performance relies on highly task-specific training programs to obtain the marginal gains required to excel in elite sports competition (performance of which that may necessitate combined qualities spanning the power-duration relationship), this degree of specificity does not translate well to exercise performance in a general population where concurrent adaptions in peak neuromuscular power and endurance ability may provide reciprocal benefits for promoting health. Indeed, current physical activity guidelines emphasize the requirement for concurrent resistance and endurance activity to gain the multiple health benefits that are strongly associated with both peak neuromuscular power and aerobic capacity – both key components for promoting a healthy lifespan, or "healthspan". This review explores evidence for reciprocation between peak neuromuscular power and endurance performance, and the molecular events that mediate training adaptation, in sport, in age-related decline and rehabilitation, and among general and clinical populations. We also describe the musculo-cardio-pulmonary exercise test (mCPET) to demonstrate that peak neuromuscular power and aerobic mediators of endurance performance are indeed more willing partners than polar opposites.

The “Interference Effect”

Seminal work from Hickson (1980) established the concept that endurance training interferes with peak neuromuscular power gains in response to resistance training in healthy, but training-naïve, human skeletal muscle (6). This provocative and potential deleterious “interference effect” of endurance training on resistance training-induced adaptations has been extensively studied (16).

Long-term adaptations to resistance or endurance training are distinct and characterized by a substantial increase in skeletal muscle hypertrophy or oxidative capacity, respectively (17). The most extensively studied pathway in the context of adaptations to resistance training involve activation of protein kinase B (PKB/Akt) and the mammalian target of rapamycin complex 1 (mTORC1) (17). Key pathways in endurance training adaptation are the activation of AMP-activated protein kinase (AMPK) leading to greater expression and transcription activity of peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α). Atherton et al. (2005) proposed a molecular explanation for the interference effect thought to occur after concurrent exercise, which could lead to blunted long-term resistance training adaptations (18). High- or low-frequency electrical stimulation of muscle mimicking a single bout of resistance and endurance exercise, respectively, activated the Akt-mTORC1 pathway (resistance) or the AMPK-PGC-1α axis (endurance) (18). Low-frequency stimulation also activated tuberous sclerosis complex 2 (TSC2), a negative regulator of mTORC1, leading to a reduction in signaling through downstream effectors of mTORC1 (18). This inhibitory effect on mTORC1 signaling by endurance exercise-induced AMPK activation has served as a mechanistic explanation for potentially impaired adaptation to resistance training when combined with endurance training.

Despite these mechanistic data, the *in vivo* response to voluntary endurance and resistance exercise is more complex and inferring interference in molecular signaling might be oversimplified from the acute rat muscle stimulation model data. Although endurance and resistance exercise modalities elicit very distinct long-term adaptations in skeletal muscle, they acutely induce remarkably similar signals, including hormones, mechanical stress, alterations in intracellular calcium levels, heat stress, PO_2 and others (19). For example, catecholamine, cortisol and growth factor concentrations are each elevated after an acute bout of both resistance and endurance exercise (20). Similarly, increased mechanical stress, intracellular calcium concentrations and heat stress are observed with both resistance and endurance training paradigms (19). Therefore, it is not surprising that an acute bout of either resistance or endurance exercise both increase the phosphorylation of AMPK and mTORC1 (21).

This overlap in signaling pathways likely contributes to the substantial similarities that can occur in the acute transcriptional response to both resistance and endurance exercise modalities (Fig. 2) (19, 22). In fact, approximately 60% of the upregulated genes 3 hours after an acute bout of endurance exercise in untrained individuals are also elevated in response to resistance exercise (22). A direct comparison of the muscle transcriptome responses between acute resistance versus endurance exercise in recreationally active men suggests a larger, more diverse, transcriptomic response after resistance exercise (23). However, adding endurance to resistance exercise may accentuate the resistance exercise transcriptome (24); nevertheless 'omic studies directly comparing and combining these training modalities are scarce (25).

Although similar signals are induced with resistance and endurance exercise in isolation, the magnitude of change can differ substantially and depend upon; for instance, the intensity, duration and rest period between contraction cycles (between set in resistance exercise or intervals in high intensity interval training). The transcriptional response to an acute exercise bout differs in untrained and trained muscle (22, 26). The acute stress response observed in untrained muscle is lessened after training, suggesting that the response becomes more specific as training progresses (26). It remains unclear how this training specificity is brought about (19). Furthermore, it appears that the interference effect may become more pronounced as training progresses (27). Differences in muscle damage induced by either resistance or endurance exercise may elicit distinct adaptive responses independent of the acute perturbation and activation of mTORC1 and AMPK. Moreover, potential overtraining or residual fatigue from previous training sessions may affect the adaptive response if both exercise paradigms are combined with insufficient rest between training sessions. It is noteworthy that the transcriptional and protein data are based on bulk analysis and do not take the multicellular complexity of muscle tissue into consideration. For example, tissue-resident type 2 innate lymphoid cells provide an important contribution to endurance training adaptation via the secretion of interleukin 13 (IL-13) (28). The contribution of tissue-resident mononucleated cells to resistance or endurance training adaptation, and the potential synergy or interference during concurrent training, remains unknown. Therefore, it remains elusive how training specificity is brought about and whether, and how, molecular signaling pathways induced by resistance and endurance exercise interfere with adaptive processes.

Current State of the Concurrent Training Literature

In 2016, Murach and Bagley were among the first to critically appraise the concurrent training literature, focusing on understanding the effects of endurance training on muscle mass strength, and explosive peak neuromuscular power adaptations to resistance training in humans (29). The conclusions from their analysis at that time were that there was no evidence in the literature to support the interference effect of endurance training on hypertrophic adaptations to resistance training, at least in untrained individuals. In fact, in most instances, the opposite was observed: concurrent training tended to augment whole muscle hypertrophy relative to resistance training alone. The evidence that endurance training interfered with strength adaptations was also generally lacking in a general population. Conversely, there was an emerging consensus that endurance-type training may impair explosive peak neuromuscular power. Schumann et al. (30) revisited this topic in 2022 and arrived at very similar conclusions. They added that a lack of an interference effect on muscle hypertrophy and strength gain was independent of the type of endurance training, frequency of concurrent training, training status (untrained vs. trained), and age. They also evaluated whether concurrent training differentially affected muscle fiber size relative to resistance training (31). The cellular data generally agreed with the whole muscle findings, although a modest attenuation of slow-twitch hypertrophy may occur when running is the endurance mode in the concurrent training design (31). The latter point has potentially meaningful consequences for elite athletic performance and program design for sport-specific training. There is an increasingly accepted understanding that explosive peak neuromuscular power adaptations are more susceptible to an interference effect in humans that train concurrently, but that endurance training does not impair strength or hypertrophy adaptations to resistance training (29, 32). These findings reflect a deeper and more nuanced understanding of the interrelated nature of endurance and resistance training adaptations, rather than being viewed as distinct qualities of exercise performance.

Pre-clinical models provide additional insights on concurrent training that compliment and expand upon what is known about simultaneous exercise training adaptations in humans. In mice, a high-volume combined endurance and resistance exercise approach was developed that replicates aspects of human concurrent training (33). This approach, called progressive weighted wheel running (PoWeR), induces skeletal muscle and muscle fiber hypertrophy concomitant with a faster-to-slower fiber type transition and cardiac adaptations that are consistent with a concurrently trained phenotype (33-35). Integrated analysis of the skeletal muscle DNA methylome with the global proteome after 8 weeks of the PoWeR intervention revealed widespread regulation of general protein translation (i.e. muscle hypertrophy) and mitochondrial machinery protein translation (i.e. muscle endurance capacity) that coincided with increased muscle torque production and fatigue resistance (36). These findings highlight the capacity for coordinated molecular synergy in response to a combined training stimulus in skeletal muscle that promotes a phenotype suitable for both peak neuromuscular power and endurance exercise performance. In both humans and rodents, more information on the interactions among types of training (e.g. resistance-type or endurance-type training with high-intensity interval training involving running, cycling, or rowing), proximity of endurance and resistance exercise in the training scheme, exercise order, biological sex, diet, and training status will further inform our understanding of how concurrent training affects neuromuscular adaptations.

The Benefits of Resistance Training for Endurance Performance and "Physiological Resilience"

In contrast to the evidence that increases in peak neuromuscular power may be negatively affected by concurrent endurance and resistance exercise training, meta-analyses show that adaptation in $\dot{V}O_2$max does not seem to be impaired by concurrent training (16, 38). In fact, it has been recognized for decades that resistance training has almost exclusively positive benefits for endurance performance regardless of training status (16, 39-42). Since $\dot{V}O_2$max is not the only determinant of endurance exercise performance, the question arises of whether resistance training might influence aerobic adaptations supporting endurance performance. Generally, three main determinants for endurance performance are recognized: 1) $\dot{V}O_2$max; 2) the intensity demarcators GET and CP; and 3) economy, which determines the $\dot{V}O_2$ required for a given submaximal speed or power (3, 43, 44). Evidence suggests that some of these parameters are not stable over time and that, for instance, after 2 hours of heavy intensity cycling, CP declined by an average of 10% (4). However, there was substantial variation among athletes, with declines in CP ranging from <1% to 32% following 2 hours of cycling, but with no effect after 80 minutes or less (4, 45-47). Therefore, the capacity to resist fatigue and sustain speed or power output throughout an endurance performance, and/or retain the neuromuscular 'reserve' for an end-sprint, might eventually differentiate the gold medalist from the other athletes with similar $\dot{V}O_2$max, critical power and economy. This phenomena, termed "physiological resilience"(4) or "durability" (48), has been proposed as a fourth determinant for endurance exercise performance. Therefore, while concurrent exercise might not cause interference with adaptations of $\dot{V}O_2$max, the resistance training component might even be a benefit for other determinants of endurance performance and physiological resilience.

In the past decades, several studies investigated the effects of concurrent endurance and resistance training on exercise economy in athletes. Meta-analyses including high-level middle- and long-distance athletes demonstrated a substantial beneficial effect of additional resistance training on exercise economy (42, 49). Studies included in the analysis involved 2-3 resistance training sessions per week in addition to 6-9 endurance training sessions. Resistance exercise was often combined with plyometric and/or sprint exercises (49). These training paradigms led to improvements in peak neuromuscular power in addition to enhanced running economy (49), although this required a minimum of 24 training sessions. Therefore, it appears that a training regime in which approximately 25% of the total sessions consist of resistance training is advantageous for endurance performance.

The effects of concurrent training on physiological resilience have also been investigated in well-trained male cross-country skiers, in whom the addition of resistance training to their regular training program did not further improve $\dot{V}O_2max$ or double-poling performance when assessed in a rested state (50). However, when time to intolerance was tested after prolonged submaximal exercise, only the group with the additional resistance training showed significant improvement, consistent with the notion of increased physiological resilience following concurrent training. Similar results were observed in well-trained cyclists and female duathletes. Only those performing additional resistance exercise increased running distance and power output assessed on a cycle ergometer during a 5-min all-out test following 1.5 hours of submaximal running or 3 hours of submaximal cycling, respectively (51, 52). Furthermore, the resistance-trained group reported a lower rate of perceived exertion towards the end of the submaximal exercise (50, 52). These data suggest that in addition to the benefits observed on running economy, resistance training might also improve physiological resilience, making it a highly effective strategy to improve endurance performance in well-trained athletes.

Practical Considerations for Concurrent Training in Sport

While there is strong evidence that the addition of resistance training enhances individual endurance performance e.g., (53), it remains unclear how athletes should balance resistance and endurance training to optimize performance gains in shorter sports events that also demand high peak neuromuscular power, such as 2,000 m rowing. Rowing performance is highly correlated with both $\dot{V}O_2max$ and thigh muscle volume, implying that improvements in both traits are needed for high-level rowing performance. It appears that concurrent training does not impair strength development in untrained and moderately trained individuals (27, 56). However, the interference effect becomes evident in trained individuals, suggesting that training specificity becomes increasingly important as fitness progresses towards that required for elite performance. A closer examination of the interference effects of concurrent training on strength development in athletes reveals that interference primarily occurs when resistance and endurance exercise are performed within the same session, but not when performed in separate sessions (56). Of note, in untrained or moderately trained individuals, maximal strength is not impaired when both modalities are performed within the same session (56). Regarding the optimal timing between resistance and endurance training, a recovery of at least 6 hours has been proposed (57). If it is not possible to separate the two training sessions, resistance preceding endurance exercise is more beneficial for strength gains (58-60). By performing resistance prior to endurance exercise, the quality and quantity of the resistance exercise are not compromised by residual fatigue from a preceding endurance training session, thereby favoring optimal training adaptations (60). Conversely, to increase aerobic parameters such as $\dot{V}O_2max$, the sequence of exercise mode does not affect the outcome.

Given the high training loads in athletes performing concurrent training, optimal training intensity is crucial for enhancing recovery and adaptive processes. Greater increases in peak neuromuscular power are typically associated with resistance exercise to repetition failure (60, 61). However, a recent meta-analysis provides evidence that exercise to repetition failure is not a prerequisite for optimal increases in peak neuromuscular power and hypertrophy (62). Izquierdo-Gabarren et al. (63) investigated the effects of resistance exercise performed to repetition failure and non-failure in well-trained rowers on peak neuromuscular power and 20-min all-out rowing performance. For 8 weeks, resistance exercises to repetition failure or non-failure were performed in addition to their regular training program, which consisted of nearly 8 hours of aerobic exercise per week (63). While the resistance exercises were performed at the same percentage of repetition maximum (1RM), the non-failure half completed as many repetitions compared to the group that went to repetition failure. Despite the lower training volume, the non-failure group exhibited a greater increase in peak neuromuscular power, and had greater improvements in rowing performance compared to the group that trained to repetition failure (63). These findings are in line with the results from Held et al. (64), that exercise to 10% velocity loss induced greater 1RM gains in well-trained rowers compared to exercise to repetition failure - although it was noted that the velocity loss of the repetition failure group was not measured. Nevertheless, the 10% velocity loss approach resulted in lower overall stress and faster recovery after 24 and 48 hours post-exercise (64).

In summary, in untrained or moderately trained individuals, concurrent resistance and endurance exercise can be performed without an impairment in peak neuromuscular power and endurance performance gains. This is true whether the two exercise modalities are performed in separate sessions or within the same session. Furthermore, adding resistance exercise to endurance training does not impair the increase in $\dot{V}O_2max$ and can even enhance endurance performance in athletes (65). The gains in endurance performance from resistance training are primarily attributed to increases in economy (when assessed in running) and greater physiological resilience with the addition of resistance exercise. The most robust interference with concurrent training occurs in the development of explosive peak neuromuscular power. Although data on 'power' athletes are limited, the inclusion of endurance training in these elite athletes might be detrimental for the optimization of explosive peak neuromuscular power. Finally, for athletes requiring both high endurance and peak neuromuscular power, such as 2,000 m rowers, the implementation of resistance and endurance training is inevitable. There are additional considerations for specific performance requirements of team sports such as soccer that are reviewed elsewhere (66). Accordingly, several aspects should be considered when designing training programs to optimize peak neuromuscular power and endurance adaptations. The two exercise modalities should be performed in separate sessions, with a recovery period of at least 6 hours, preferably even 24 hours (57). If performed within the same session, much of the available evidence supports that resistance exercise should precede endurance exercise to ensure high training quality to elicit the desired adaptive response. Also, resistance exercise should not be performed to repetition failure to mitigate stress and enhance recovery.

Physiological Basis for Parallel Loss of Skeletal Muscle Strength and Endurance with Aging

Another way to approach the question of whether muscle strength and endurance are disconnected is to consider how these properties of muscle are affected with aging. Skeletal muscle alterations with aging are well-known and contribute to both impaired mobility and exacerbated health outcomes that include death. Whereas reductions in skeletal muscle peak neuromuscular power and endurance with aging are well-established, most often they are treated as independent problems rather than arising from common biological processes. Studies in a rat model of aging, the Fisher 344 x Brown Norway F1-hybrid (F344BN) rat, revealed that losses of muscle mass, contractile performance and aerobic capacity showed a similar decline with an accelerating trajectory in advanced age, suggesting that there may be common biological aging mechanisms driving the phenomena (67). If true, this would suggest that therapeutic strategies targeting the biology underlying aging muscle deterioration may provide a more effective approach than targeting peak neuromuscular power and endurance ability individually.

Similar Trajectory of Declines in Skeletal Muscle Mass, Contractility, and Aerobic Capacity with Aging

Previous studies characterized changes in mass, contractility and metabolic function of hindlimb muscles in three age groups of the F344BN rat model (Fig. 3): (i) young adult skeletally mature rats [8-9 months of age]; (ii) older aged rats [28-30 months of age]; and (iii) very old rats [35-36 months of age]. Using survival curves for the F344BN rat compared to that of humans (70), these ages equate to approximately 20 years, 60 years, and 80+ years of age in humans, respectively. The rationale for selecting these ages is that they represent an early stage when skeletal muscles manifest relatively mild alterations in mass and function (old age: ~60 years) and spans the subsequent accelerating phase of skeletal muscle impairment that precipitates the most clinically meaningful alterations in mobility and health outcomes in advanced age (very old: 80+ years). In Fig. 3A, we show the mass of major distal hindlimb muscles of the rat that span extremes of muscle fiber type composition featuring distinct phenotypes and functions (slow oxidative/postural maintenance: the soleus; mixed fast twitch/locomotion: gastrocnemius and plantaris). Note that all three muscles exhibit a modest degree of atrophy in old age that becomes much more severe in very old age. Further, the trajectory of muscle mass decline between the fast twitch gastrocnemius and the slow oxidative soleus are remarkably similar between old and very old age (Fig. 3B), contrasting with the widely held view that slow oxidative muscles are better protected with aging.

The same animals were examined using a hindlimb pump-perfusion approach (Fig. 3C), which involved catheterizing the femoral artery and vein to create an extracorporeal circuit where the experimenter can control blood flow, and thus convective oxygen delivery, to the contracting muscles while measuring hindlimb $\dot{V}O_2$ from the product of femoral blood flow and femoral arterial-venous O_2 concentration difference. The Achilles tendon with a portion of the calcaneus was severed and connected to a force transducer, and the sciatic nerve was cut in the avascular space between the biceps femoris to provide a means of electrically stimulating isometric tetanic contractions of the distal hindlimb muscles. Using this model, during a 4-min contraction bout, we observed parallel declines in peak muscle force (Fig. 3D), $\dot{V}O_2$max (Fig. 3E), and lactate efflux (a proxy measure of muscle glycolytic flux) (Fig. 3F) with increasing age (67, 68), mirroring observations in older humans (see *The Interaction of Power and Endurance Assessed by the Musculo-Cardio-Pulmonary Exercise Test (mCPET)*, and Fig. 4B, below). Furthermore, there was a strong correlation in the rate model between muscle lactate efflux and $\dot{V}O_2max$ (Fig. 3G), supporting the hypothesis that a common biology links declines in these contrasting metabolic processes with aging.

It is important to point out that in contrast to the parallel declines in muscle mass and both glycolytic and oxidative metabolic capacities that occur with aging, disuse is associated with an increase in glycolytic capacity whilst muscle mass and oxidative metabolic capacity decline (71). Human data here are sparse, with one group reporting negligible changes in muscle glycolytic and oxidative metabolism in the tibialis anterior muscle in septuagenarians (72) (muscle mass was not reported). Since the tibialis anterior does not exhibit a decline in oxidative capacity with aging, and contrasts with changes observed in the vastus lateralis (73), additional studies are needed. In this respect, outcomes from large longitudinal human cohort studies such as the Baltimore Longitudinal Study of Aging (BLSA) and Study of Muscle, Mobility and Aging (SOMMA) should be able to contribute to addressing future questions of whether muscle mass, and glycolytic and oxidative metabolic capacities decline in parallel with aging in humans.

What Biological Processes Might Link Declines in Skeletal Muscle Mass, Contractility, and Metabolic Responses with Aging?

An obvious choice for a mechanism that could explain parallel declines in skeletal muscle mass, contractility and metabolic processes with aging concerns the mitochondrion. Not only are mitochondria the primary site of $\dot{V}O_2$ during muscle contractions through their role in generating ATP for cross-bridge cycling and ion pumps, but they are also implicated in driving aging biology through activation of proteolytic, inflammatory, and cell death pathways (74). It is important to also note that mitochondria are enriched on both sides of the neuromuscular junction (pre-synaptic motoneuron terminals and the subsynaptic domain of the muscle fiber) and are likely involved in degeneration of the neuromuscular junction leading to denervation (75). It is also relevant to point out that denervation does not only contribute to atrophy and impaired contractility, but also mitochondrial dysfunction and depletion of mitochondria in skeletal muscle (76-78). Consistent with an important role for mitochondria in driving aging muscle biology, experimental models that perturb mitochondrial biology in skeletal muscle can phenocopy various aspects of aging muscle. For example, reducing the autophagic removal of dysfunctional mitochondria (mitophagy) by knockout of Park2 (encodes Parkin), or double knockout of both Park2 and Pink1, causes skeletal muscle contractile impairment, compromised mitochondrial respiratory function, and denervation of muscle fibers (79, 80). Consistent with this point, mice in which the neuromuscular junction is destabilized, consequent to reduced Muscle Specific Kinase (MuSK) activation, exhibit lower grip strength and muscle mass, as well as decreased muscle respiratory capacity (76, 81). Conversely, therapeutic targeting of mitochondria rescues muscle aging phenotypes. For example, overexpressing Park2 to promote mitophagy in aging mice increases muscle mass, contractility, and mitochondrial content (82). Similarly, in the superoxide dismutase 1 (SOD1) knockout model of precocious muscle aging (a phenocopy of denervation-related phenotypes) , muscular overexpression of the H_2O_2 scavenger peroxiredoxin 3 ameliorates losses in muscle mass, specific force and muscle respiratory function (84). In view of the evidence that genetic interventions targeting mitochondria can attenuate aging muscle phenotypes, including muscle atrophy and weakness, further study is warranted to establish whether exercise interventions targeting muscle mitochondria might also serve a similar purpose for human aging.

Endurance Training Promotes Strength with Aging

Resistance training is the most prescribed exercise modality for aging muscle. However, the central role that mitochondria appears to play in loss of muscle mass, contractility and aerobic function suggests that the benefits of endurance training (which is typically prescribed to improve muscle metabolic responses and reduce fatigue rather than to improve muscle strength or peak power) may be underappreciated as a treatment strategy for aging muscle. Consistent with this idea, there is some evidence that older individuals who partake in long-term endurance training can have superior muscle strength to non-exercisers (85, 86). Similarly, swimming exercise in c. Elegans fosters a better maintenance of mobility and less mitochondrial fragmentation with aging (87). A recent study from The Molecular Transducers of Physical Activity Consortium (MoTrPAC) found that endurance training in rats yielded profound remodeling of proteins involved in diverse aspects of mitochondrial biology in multiple tissues (skeletal muscle, heart, liver, etc.), providing insights to the pleiotropic systemic mechanisms by which endurance training may confer benefits to aging muscle. It is also worth pointing out that resistance training in elderly men and women produces skeletal muscle adaptations most often associated with endurance training, including increased mitochondrial enzyme activity and increased muscle capillarization (90). Thus, there is considerable discordance between the basic theory informing selection of therapeutic approaches for targeting aging muscle and the observed outcomes of different training strategies. This discordance speaks to the fundamental biology linking changes in muscle size, strength, power with endurance exercise capacity in aging, and should be used to inform more effective exercise prescription.

Clinical and Translational Perspectives

The preceding evidence demonstrates the proposition that peak neuromuscular power and endurance ability are independent qualities of exercise performance is an oversimplification. On an individual level, the greatest $\dot{V}O_2$ achievable for endurance exercise is moderated by the muscle mass that can be activated, prior to reaching the task-specific maximum rate of oxygen transport and utilization ($\dot{V}O_2$max). For example, the ~5-10% greater $\dot{V}O_2$max observed in running than in cycling is typically explained by a greater volume of active muscle mass in running (91). Such an effect of active muscle mass on $\dot{V}O_2$max was nicely demonstrated by McPhee et al. , who showed that the major correlate of task-specific $\dot{V}O_2$max during one-legged cycling in untrained individuals was quadriceps muscle volume, and that under these conditions $\dot{V}O_2$max was not associated with muscle fiber type expression, muscle mitochondrial enzyme activity, height, body mass or body mass index (BMI). When the same participants performed two-legged cycling, $\dot{V}O_2$max increased, but did not double, implying that, in their population (n=71; 18-39 years old), two-legged $\dot{V}O_2$max was limited by convective or diffusive O_2 transport to the active musculature. Approximately doubling the active muscle volume available for oxygen utilization by comparing one- to two-legged cycling elicited only a 52% increase in $\dot{V}O_2$, on average. However, the proposed individual specificity in the reciprocation between peak neuromuscular power and endurance may explain how some participants were able to nearly double $\dot{V}O_2$max between one- and two-legged cycling (1:2 leg $\dot{V}O_2$ ratio of 0.58) while others barely increased at all (1:2 leg $\dot{V}O_2$ ratio of 0.96). Extra- and intra-muscular physiology and biomechanics will influence the ability to access an oxidative metabolic reserve when additional muscle volume is activated during progressive exercise, including but not limited to convective and diffusive O_2 transport, muscle mitochondrial enzyme activity, peak muscle power, muscle-afferent mediated feedback inhibition of spinal and/or cortical motor excitability, muscle mechanics (e.g. pedaling cadence) and symptoms, among others.

The typical method that attempts to account for the role of available muscle mass on $\dot{V}O_2max$ is to normalize to body mass. However, when normalizing $\dot{V}O_2max$ to body mass, a strong association of $\dot{V}O_2max$ with both sex and age remains (93), revealing the weaknesses in this normalization approach to appropriately account for wide ranges in body composition and available neuromuscular power. Normalizing $\dot{V}O_2max$ to muscle volume, fat free mass or leg lean mass greatly reduces observed differences between sexes but large differences in normalized $\dot{V}O_2max$ across age remain (93, 94). Normalizing $\dot{V}O_2max$ to peak isokinetic muscle power, however, reduces residual differences in $\dot{V}O_2max$ among males and females ranging 20 to 80 years old to zero (93), suggesting that available neuromuscular power provides an perhaps the best context identified to date to understand the relative aerobic capacity of an individual. These findings highlight that peak neuromuscular power is a significant mediator of $\dot{V}O_2max$, and suggest that available neuromuscular power can constrain $\dot{V}O_2max$, especially in an individual in whom the O_2 transport system is relatively more adapted than the available peak neuromuscular power.

The Interaction of Power and Endurance Assessed by the Musculo-Cardio-Pulmonary Exercise Test (mCPET)

The current gold-standard technique for evaluating the role of peak neuromuscular power and neuromuscular fatigue on endurance exercise performance uses isometric quadriceps maximum voluntary contractions coupled with evoked twitches (which can be deployed at the motor cortex, spinal cord, motor nerve or muscle surface). This allows a detailed sampling of the central and peripheral components of neuromuscular function. However, the results do not have the specificity to determine whether neuromuscular performance and fatigue are limiting to the mode or the contractile velocity of a complex whole body exercise task such as cycling. In addition, in most labs, evoked twitches cannot be implemented at the immediate point of exercise limitation; and as such, interpretation of results is complicated by the very fast recovery kinetics of neuromuscular function (95, 96). Overall, this approach is currently limited to research settings.

The musculo-cardio-pulmonary exercise test (mCPET) was developed with the aim of overcoming these limitations and providing an independent assessment of neuromuscular, cardiovascular and pulmonary systems prior to and during a cycling ramp-incremental exercise test to intolerance (46, 95). It was designed for use in cycle ergometry such that it does not affect the measurement of gas exchange, ventilation or cardiovascular function assessed during traditional CPET in a clinical setting. mCPET quantifies maximum voluntary isokinetic power (Piso) at baseline (before exercise, in the fresh state) and at the instant of ramp-incremental peak, which provides insight on the role neuromuscular performance and fatigue in determining exercise performance. mCPET is therefore the first integrated exercise test to assess each of the three physiological systems represented in "Wasserman's Gears" (neuromuscular, cardiovascular, pulmonary) independently during a single exercise test.

mCPET methods are depicted in Fig. 4A (46, 95, 98). Cycling Piso is measured at baseline and the limit of tolerance using ~5 crank revolutions (~4 seconds), performed with maximal effort, and constrained to a fixed cadence of, typically, 70 or 80 rpm (the fixed rpm is chosen to reflect the approximate average spontaneous cycling cadence encountered in clinical exercise testing). At baseline, the three consecutive isokinetic crank revolutions that result in the greatest mean power provide a highly reliable measure of the maximum performance of the neuromuscular system to produce power at the crank during cycling (CV=7%; ICC=0.97; (95)). Repeating the same ~4 second maximal effort Piso measurement at the tolerable limit of ramp-incremental exercise allows measurement of the decline in neuromuscular performance between baseline and peak exercise. These measurements are made possible by the ability to: (1) instantaneously switch cycling mode between standard (hyperbolic) control and isokinetic control during ramp-incremental exercise; (2) maintain isokinetic control at a target cadence within a tolerance of ±2 rpm; coupled with (3) high frequency measurements of crank torque and velocity. mCPET provides several new variables that evaluate neuromuscular and endurance exercise performance, which also reveal interactions between peak neuromuscular power and endurance exercise capacity.

The first variable provided by mCPET is the baseline isokinetic power (baseline Piso; watts) (Fig. 4A-B), which measures the maximum performance of the neuromuscular system to produce power at the crank during cycling in the fresh state. Baseline Piso is positively associated with leg lean mass (r^2=0.276; p=0.030), isometric (r^2=0.560; p=0.002) and isokinetic (r^2=0.323; p=0.011) maximal voluntary contractions using knee extensor dynamometry , but is specific to the cycling task that is also used to evaluate $\dot{V}O_2$max. These correlations are not anticipated to explain all the variance between gross muscle morphology or single-joint neuromuscular performance and a high-degree-of-freedom movement such as cycling, but rather they are provided to develop construct validity to the baseline Piso variable measured in mCPET. As such, baseline Piso is expected to be greater in strength-, power- or sprint-trained individuals, and lower in elderly or chronic disease conditions where muscle mass and peak torque are reduced. Unsurprisingly, baseline Piso is lower in older individuals than in young (Fig. 5A), and even lower in chronic disease states that affect muscle mass and function, such as chronic obstructive pulmonary disease (COPD) (Fig. 5A) (98, 100, 102). However, baseline Piso is also strongly associated with $\dot{V}O_2max$ across a wide range of aerobic function (r^2=0.598; $p<0.0001$; pooled data from 6 studies containing 55 healthy participants) (46, 47, 95, 98, 100, 101). These relationships simply remind us that a large muscle mass and high capacity to generate peak neuromuscular power is needed to generate high rates of oxygen uptake – hence peak neuromuscular power and endurance exercise capacity are strong and willing partners.

A second variable measured by mCPET is the aerobic power index (API; % of baseline Piso) (Fig. 4A-C). This is calculated as the percentage of baseline Piso that is supported by aerobic metabolism at peak aerobic power in the ramp-incremental exercise test (98). API has strong validity because it uses the same degrees of freedom, range of motion and exercise mode for both its numerator and denominator. In so doing, API provides the first truly dimensionless clinical assessment of the relative capacity the oxygen transport and utilization systems in the context of the available peak neuromuscular power. API is independent of sex, age, height, weight or BMI (all $r^2<0.1$; $p>0.189$). The similar API between young (26±6 years; n=42) and older individuals (65±9 years; n=12) demonstrates that a lower available baseline Piso in the elderly is accompanied by a parallel reduction in aerobic power (Fig. 5B); again emphasizing the importance of available peak neuromuscular power to maintain endurance exercise capacity during aging. Available published data also show that API is lower in COPD patients than age-matched controls (Fig. 5B). This means that, despite overt muscle weakness in COPD (lower baseline Piso; Fig. 5A), the impairment in oxygen transport and utilization is greater than the impairment muscle power. Low API is a reasonable expectation in a group of individuals characterized by expiratory flow limitation and exertional dyspnea; the low API quantifies the degree to which COPD patients are (un)able to ventilate their available peak neuromuscular power. As such, in COPD, unlike in health, API is negatively associated with the percent predicted of forced expiratory volume in 1 second (FEV_1 %predicted) (r^2=0.293; p=0.002) (100). API might therefore be considered a more apposite index of relative aerobic capacity than $\dot{V}O_2$max normalized for body mass, lean muscle mass or predicted $\dot{V}O_2$max based on sex, height and/or weight.

A third variable measured by mCPET is power reserve (PR; % of baseline Piso) (Fig. 4A-C). PR describes the capacity to acutely increase isokinetic power at the limit of tolerance and represents the percentage of baseline Piso that can be achieved above peak ramp power by a ~4 second maximal isokinetic effort at the limit of tolerance. The data in Fig. 4A, taken from , show typical mean values from healthy young individuals where PR is a small fraction of baseline Piso and represents a negligible ability to increase muscle power above that required by the ramp-incremental test. The zero or negligible PR at ramp peak is evidence that the participant is unable to increase neuromuscular performance above that required by the ramp-incremental test and hence neuromuscular limitation explains their endurance exercise intolerance. However, in some tasks, and in some individuals, a large PR is observed. Tasks that engender contribution from central fatigue, such as prolonged ramp- or constant-power exercise, result in exercise limitation at $\dot{V}O_2$max with a large PR (47). Such cases demonstrate that neuromuscular performance does not consistently constrain exercise tolerance in ramp-incremental exercise, even in healthy individuals. The presence of a PR means that $\dot{V}O_2$max can be reached with an untapped reserve in the ability for an acute increase power output. In athletes where a capacity to sprint for the line may be beneficial, a large PR could confer a performance advantage. However, more commonly, a large PR reflects a cardiovascular or pulmonary, as opposed to neuromuscular, limitation to $\dot{V}O_2$max. For example, PR is more than double in COPD compared with age-matched controls (Fig. 4B and 5C).

mCPET also measures the fatigue index (FI, % of baseline Piso). FI is the decline in neuromuscular performance at the limit of tolerance, calculated by FI = Piso – API – PR (Fig. 4A-C). FI describes the decline in maximal voluntary neuromuscular performance i.e., combined central and peripheral neuromuscular function , at peak ramp-incremental exercise. Despite wide variability in FI, on average, FI appears to be similar across age, sex and health status at ~50% (Fig. 5D). This is conceptually similar to observations in studies that measure the decline in muscle potentiated twitch force following the limit of cycling tolerance, where afferent feedback from fatiguing muscle is suggested to confine peripheral muscle fatigue to a maximum limit of ~35-40% (103). This is despite a difference in methods used to assess neuromuscular performance fatigability (voluntary efforts using mCPET vs. volition-independent methods). The mCPET data appear to suggest that sensory inputs also contribute to constraining neuromuscular performance to a particular limit, because the ~50% FI in mCPET is measured using a voluntary effort.

However, because peak aerobic power is highly variable, FI can be also usefully expressed as a percentage decline in neuromuscular performance per watt of peak aerobic power achieved in the ramp-incremental test (%/W; Fig. 5E). This reveals a greater FI per watt of peak aerobic power in COPD patients compared with young or age matched controls, which is consistent with the greater cycling-induced decline in twitch force (fatigability) in COPD muscle compared with controls (104).

Overall, mCPET demonstrates that maximum voluntary isokinetic muscle power is a key mediator of endurance exercise performance in a healthy population across the spectrum of age, sex and body habitus. mCPET improves the specificity of clinical exercise testing to identify deficits peak neuromuscular power at baseline, performance fatiguability and the presence of a power reserve on an individual basis and can identify whether neuromuscular performance limits aerobic capacity.

CONCLUSIONS

Since the initial proposition of an interference effect between endurance- and resistance-type exercise training there is now strong evidence to support that resistance training does not interfere with endurance training adaptations in athletes, untrained healthy individuals, elderly or clinical populations. While there may be some interference of concurrent training in the development of muscle explosive force supporting power-type events, parallel activation of molecular pathways in muscle to produce endurance adaptations (e.g., AMPK-PGC-1α axis) and strength adaptations (Akt-mTORC1 pathway) are seen during concurrent training. Separating resistance and endurance training by 6-24 hours and avoiding repetition failure in resistance training might optimize strength and power adaptations for sports performance; however, this training specificity appears to be unnecessary for a general population where interference is not observed. The parallel loss of muscle mass and aerobic capacity in aging, that accelerates at very old age, supports the idea that a common biology may link the loss of power and endurance in the elderly. It is suggested that mitochondrial function in the motor neuron and skeletal muscle may be the common factor underlying this parallel loss, such that overexpression of e.g., Park2 to promote mitophagy in aging mice, results in greater muscle mass, contractility, and mitochondrial content in older age. These preclinical data are reflected in human studies where use of the musculo-cardio-pulmonary exercise test (mCPET) provides a single integrated means of assessing muscle power, performance fatigability and endurance capacities as well as identifying individuals in whom the neuromuscular system limits peak aerobic power. mCPET responses reveal a parallel loss in muscle power and aerobic capacity with age, emphasizing that peak neuromuscular power and endurance exercise capacity are less polar opposites and more willing partners.

Disclosures

Carrie Ferguson is supported by a grant from NIH (R01HL166850; 5UH3HL155798). She is involved in contracted clinical research with United Therapeutics, Genentech, Regeneron, Respira Therapeutics and Mezzion. She reports consulting fees from Respira Therapeutics. She is a visiting Associate Professor at the University of Leeds, UK. Kevin Murach is supported by NIH R00 AG063994 and R01 AG080047. Russell Hepple is supported by grants from NIH (R21AR084591, R01AG059416, and R01AG076490). Harry Rossiter is supported by grants from NIH (R01HL151452, R01HL166850, R01HL153460, P50HD098593, R01DK122767), Tobacco Related Disease Research Program (T31IP1666) and Department of Defense / USAMRAA (HT9425-24-1-0249). He reports consulting fees from the NIH RECOVER-ENERGIZE working group (1OT2HL156812), and is involved in contracted clinical research with Astellas, GlaxoSmithKline, Genentech, Intervene Immune, Mezzion, Regeneron, Respira, Roche, and United Therapeutics. He is a visiting Professor at the University of Leeds, UK and University of

Pavia, Italy. Harry Rossiter and Carrie Ferguson report a pending patent application filed by The Lundquist Institute, titled "Testing System to Diagnose Neuromuscular Deconditioning and Pathologic Conditions". The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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FIGURE LEGENDS

Fig. 1. A) The schematic power-duration relationship across the continuum of sports performance and key training adaptations that contribute during different events. Although exercise is often dichotomized into endurance-type or resistance-type, there is a large reciprocation between these modalities in terms of power output, intensity or duration. Example distances e.g., for running, are for illustrative purposes to depict their relative position on the power-duration curve. Examples of the relative position of training intensity are illustrated: MICT, moderate-intensity continuous training. HIIT, high-intensity interval training. SIT, sprint-interval training. 1RM, one repetition maximum. Reproduced with permission (19). **B)** The association between critical power (CP; the asymptote of the power-duration relationship) and W' (the curvature constant of the power-duration relationship) in young healthy individuals (aged 18-33 yr; n=60; filled circles), older healthy individuals (58-73 yr; n=10; open triangles), chronic heart failure patients (56-76 yr; n=15;filled squares) and chronic obstructive pulmonary disease patients (51-76 yr; n=27; open diamonds). While correlation between W' and CP within individual sub-populations are weak or absent, investigating the relationship across a wide range or aerobic function reveals a significant association. Regression equation is CP (W) = 9.84 * W' (kJ) + 31.5 (r^2=0.589, $p<0.0001$). Modified from (14).

Fig 2. Interference or additive effect of concurrent training. Resistance and endurance training elicit distinct adaptations. Resistance training primarily increases muscle mass, strength and power, while endurance training induces cardiovascular and neuromuscular adaptations that include increased cardiac output, peripheral blood flow and capillary density, increased substrate uptake, storage and utilization, and mitochondrial biogenesis in cardiac, respiratory and skeletal muscle. Despite distinct long-term adaptations of resistance and endurance training, the induced perturbations during an exercise bout, and the subsequent signaling pathways, express considerable overlap. It remains unclear how specificity is brought about. Therefore, it is also unclear whether, and how, the two training paradigms interfere at a molecular level. For endurance performance, resistance training has benefits for long-term adaptations, regardless of training status. There is no interference on the expected gain in $\dot{V}O_2$max in response to concurrent endurance and resistance training, which may even enhance economy (in running) and physiological resilience; each contributing to increased endurance performance. The effect of adding endurance training to resistance training for gains in strength/power performance is dependent on the training state. In untrained and moderately trained individuals, there is no negative effect of endurance training on muscle mass and strength gains, independent of whether the training is performed in the same or separate session. In well-trained individuals, there might be an impairment in strength development if the training is performed in the same session. The strongest potential interference effect is on the development of explosive force that can be impaired with the addition of endurance to resistance training.

Fig. 3. Aging studies in young adult (8-9 months old), old (28-30 months old) and very old (36 months old) male F344BN rats. **A)** The distal hindlimb muscles exhibited a progressive decline in mass with increasing age. **B)** Whereas muscle atrophy between young adult and old age was greater in glycolytic muscles (plantaris, gastrocnemius), between old age and very old age the rate of atrophy in slow oxidative muscle (soleus) was not different from glycolytic muscle (gastrocnemius); and the rate of atrophy in each was far more severe than between young adult

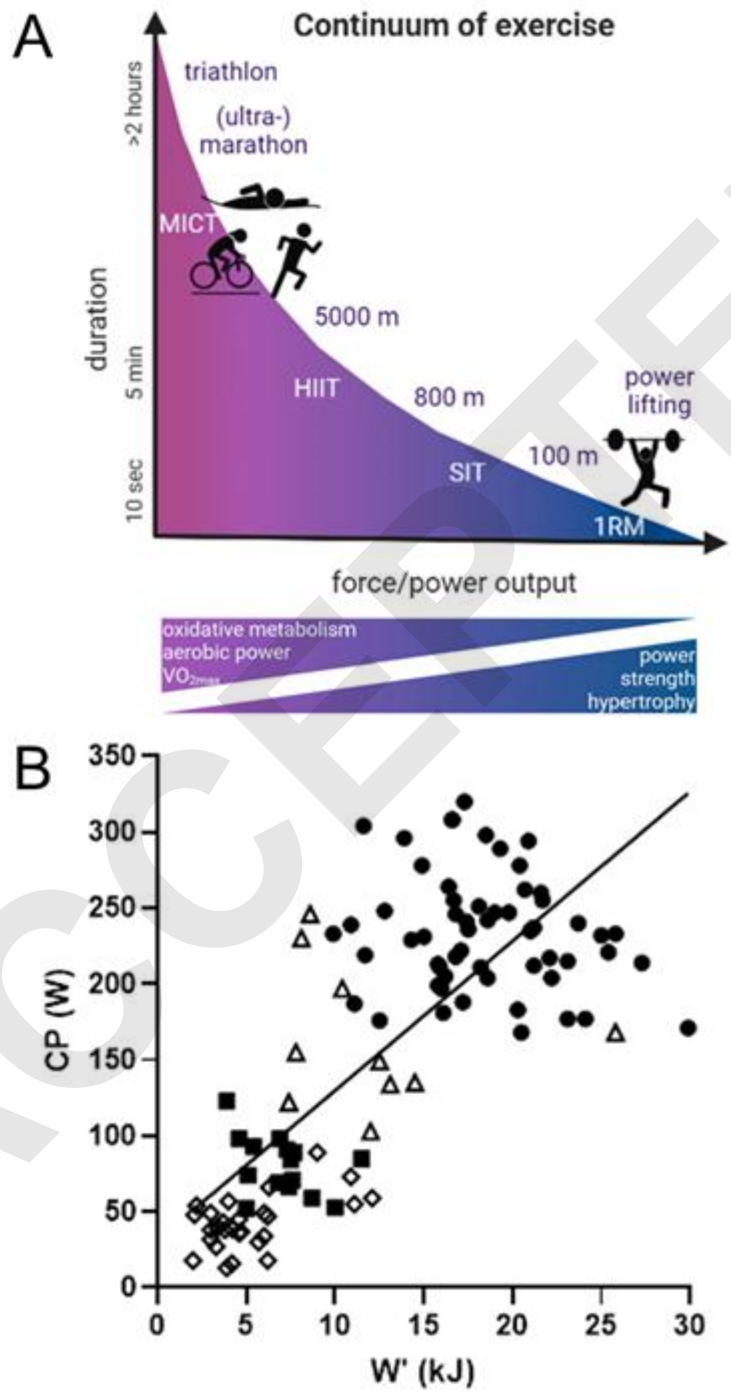
and old age. **C)** Model of the pump-perfused rat hindlimb preparation, to permit matching of skeletal muscle convective O_2 delivery between age groups during a 4-min isometric tetanic muscle contraction bout. Using this model, there were parallel declines with aging in skeletal muscle peak tetanic force **(D)**, VO_{2max} **(E)**, and lactate efflux **(F)**. Furthermore, there was a close relationship between the peak lactate efflux and $\dot{V}O_2max$ regardless of age **(G)**. Data taken and figures modified from (67, 68).

Fig. 4. A) The musculo-cardio-pulmonary exercise test (mCPET), using combined brief, maximal isokinetic efforts (filled square at baseline, open square at intolerance) combined with standard ramp-incremental exercise (solid line) to the limit of tolerance (filled circle). mCPET determines: maximal baseline isokinetic power (filled square) (Piso); aerobic power index (API); power reserve (PR); and fatigue index (FI). See text for details. Example data from healthy young adults (46). **B)** Mean differences in absolute (watts) mCPET variables among young healthy adults (n=42), older individuals age-matched to chronic obstructive pulmonary disease (COPD) (n=12) and COPD patients (n=31). **C)** Relative differences (% of basline Piso) in mCPET variables among the same groups as panel B. Note the reduction in API and increase in PR in the COPD group relative to the age-matched controls. Mean data for B and C are pooled from (47, 95, 98, 100-102).

Fig. 5. Differences among musculo-cardio-pulmonary exercise testing (mCPET) variables in young healthy adults (n=42), older individuals age-matched to chronic obstructive pulmonary disease (COPD) (n=12) and COPD patients (n=31). **A)** Maximal baseline isokinetic power (Piso) in watts; **B)** Aerobic power index (API) expressed as a percentage of baseline Piso. **C)** Power reserve (PR) expressed as a percentage of baseline Piso. **D)** Fatigue index (FI) expressed as a

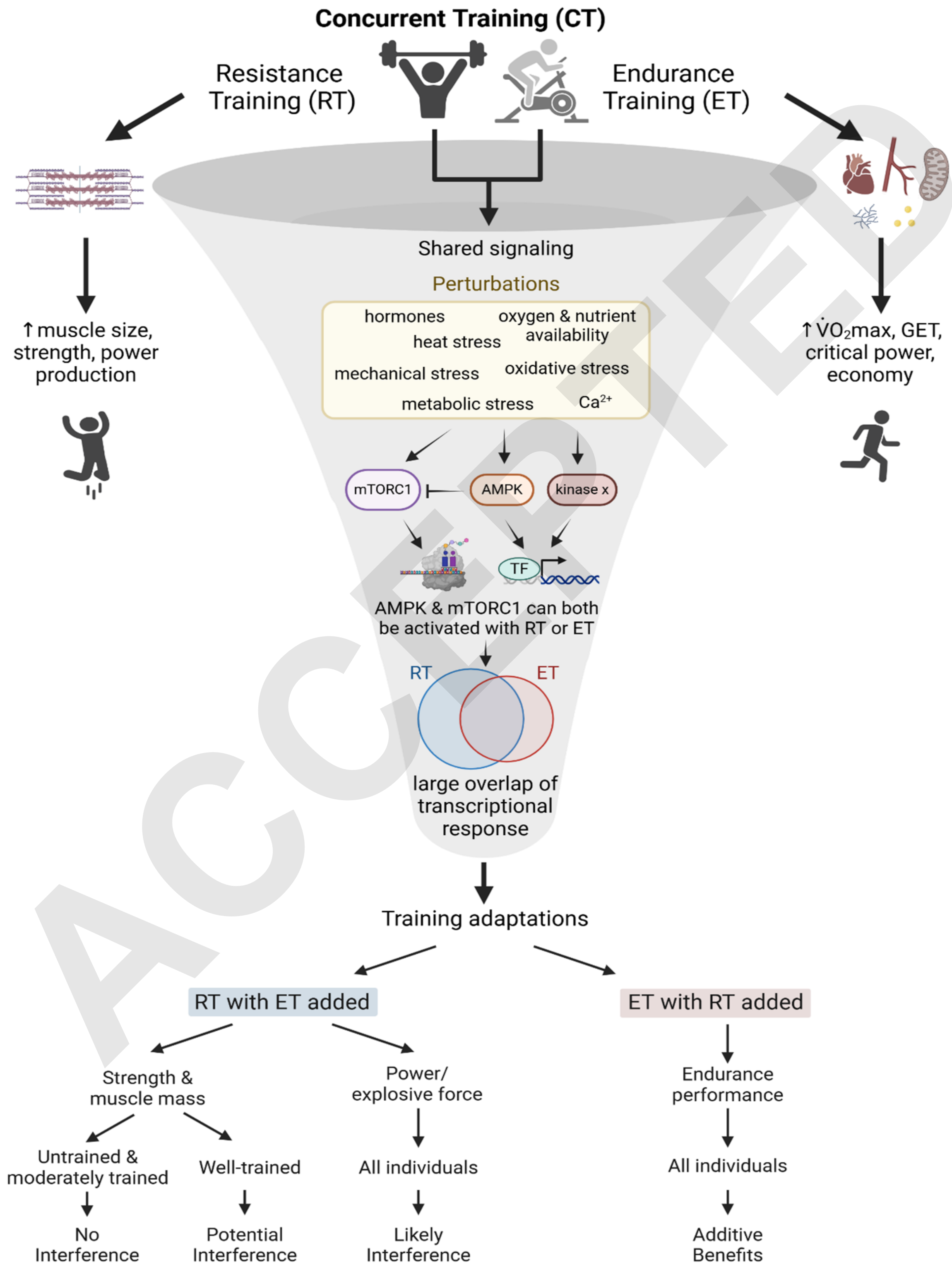
percentage of baseline Piso; **E)** Fatigue index (FI) expressed as a percentage decline in baseline Piso per watt of aerobic power achieved during ramp incremental exercise. ns not significant; * $p<0.05$; ** $p<0.01$; **** $p<0.0001$. Comparisons are by repeated measures ANOVA with Dunnet's *post hoc* test, where older individuals age-matched to COPD are the reference group. Data are pooled from .

Figure 1



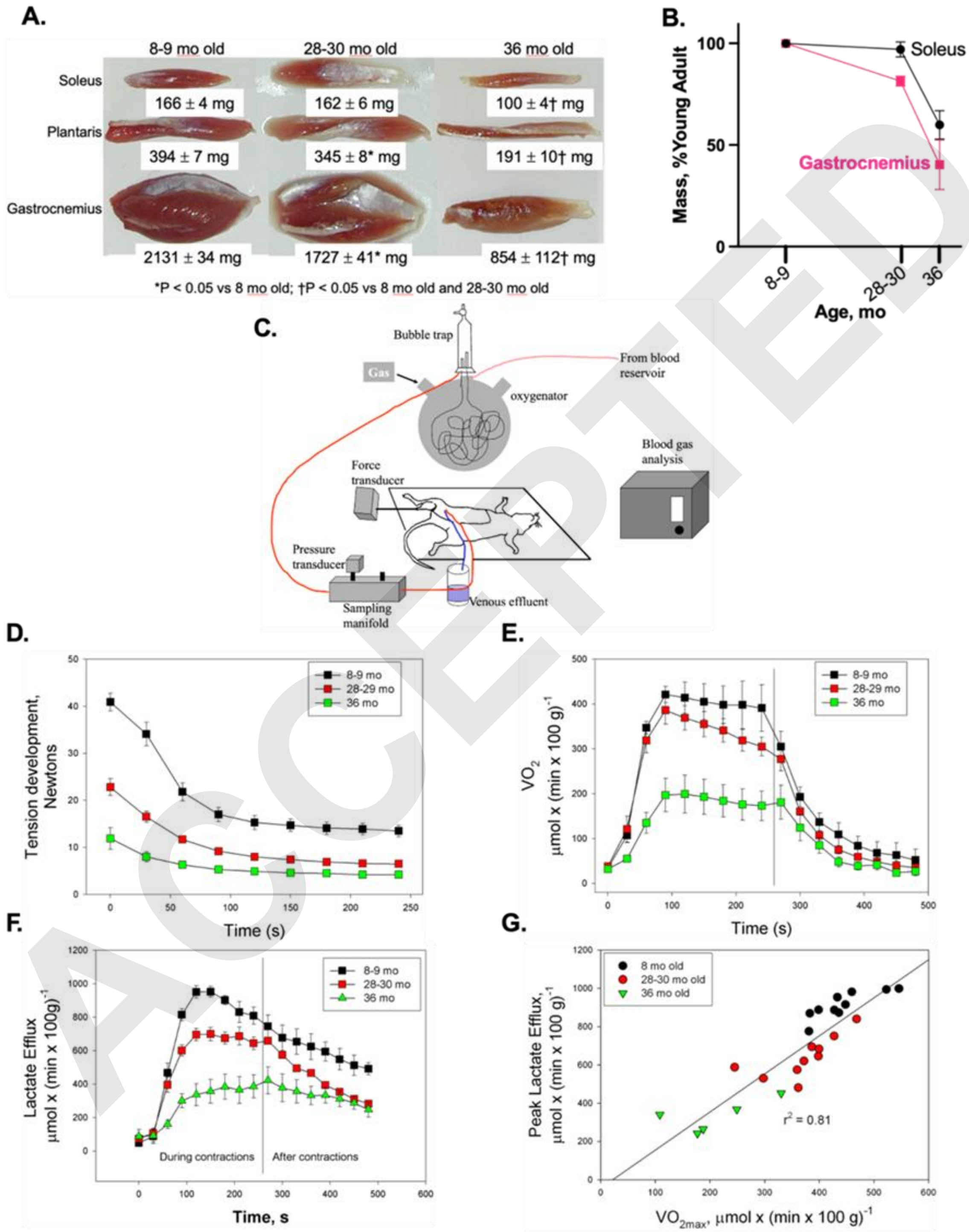
A
Continuum of exercise
triathlon
(ultra-)
marathon
MICT
5000 m
HIIT
800 m
power
lifting
100 m
SIT
1RM
>2 hours
5 min
10 sec
duration
force/power output
oxidative metabolism
aerobic power
VO_{2max}
power
strength
hypertrophy
B
CP (W)
W' (kJ)
0
50
100
150
200
250
300
350
5
10
15
20
25
30

Figure 2



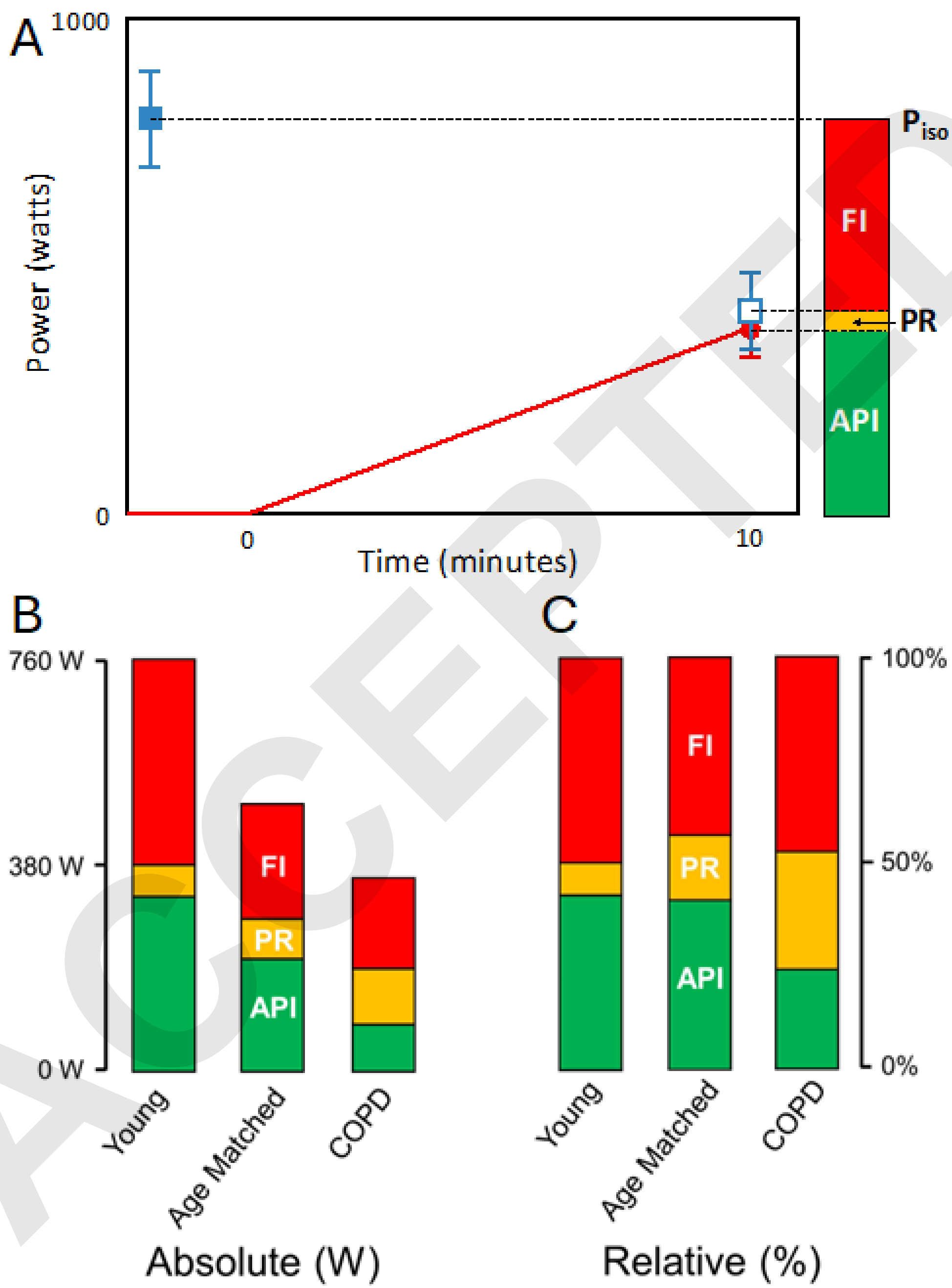
Concurrent Training (CT)
Resistance Training (RT)
Endurance Training (ET)
↑muscle size, strength, power production
↑$\dot{V}O_2$max, GET, critical power, economy
Shared signaling
Perturbations
hormones
heat stress
oxygen & nutrient availability
mechanical stress
oxidative stress
metabolic stress
Ca^{2+}
mTORC1
AMPK
kinase x
TF
AMPK & mTORC1 can both be activated with RT or ET
RT
ET
large overlap of transcriptional response
Training adaptations
RT with ET added
ET with RT added
Strength & muscle mass
Power/ explosive force
Endurance performance
Untrained & moderately trained
Well-trained
All individuals
All individuals
No Interference
Potential Interference
Likely Interference
Additive Benefits

Figure 3



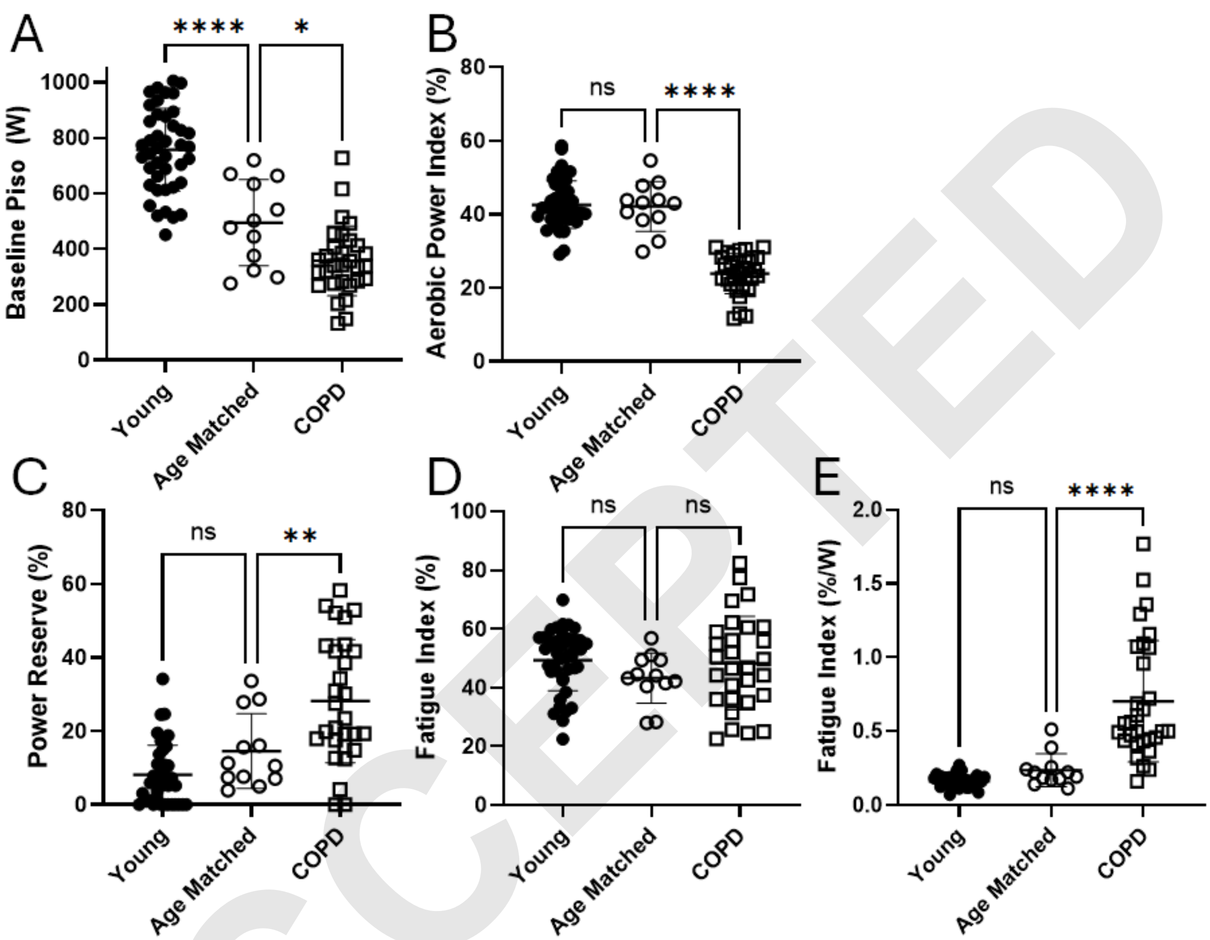
A.
8-9 mo old
28-30 mo old
36 mo old
Soleus
166 ± 4 mg
162 ± 6 mg
100 ± 4† mg
Plantaris
394 ± 7 mg
345 ± 8* mg
191 ± 10† mg
Gastrocnemius
2131 ± 34 mg
1727 ± 41* mg
854 ± 112† mg
*P < 0.05 vs 8 mo old; †P < 0.05 vs 8 mo old and 28-30 mo old
B.
Mass, %Young Adult
Soleus
Gastrocnemius
Age, mo
C.
Bubble trap
Gas
From blood reservoir
oxygenator
Blood gas analysis
Force transducer
Pressure transducer
Sampling manifold
Venous effluent
D.
Tension development, Newtons
Time (s)
8-9 mo
28-29 mo
36 mo
E.
VO2 μmol x (min x 100 g)-1
Time (s)
8-9 mo
28-29 mo
36 mo
F.
Lactate Efflux μmol x (min x 100g)-1
Time, s
8-9 mo
28-30 mo
36 mo
During contractions
After contractions
G.
Peak Lactate Efflux, μmol x (min x 100 g)-1
VO2max, μmol x (min x 100 g)-1
8 mo old
28-30 mo old
36 mo old
r2 = 0.81

Figure 4



A
1000
0
Power (watts)
0
10
Time (minutes)
P iso
FI
PR
API
B
760 W
380 W
0 W
FI
PR
API
Young
Age Matched
COPD
Absolute (W)
C
100%
50%
0%
FI
PR
API
Young
Age Matched
COPD
Relative (%)

Figure 5



A
****
*
Baseline Piso (W)
1000
800
600
400
200
0
Young
Age Matched
COPD
B
80
60
40
20
0
Aerobic Power Index (%)
ns
****
Young
Age Matched
COPD
C
80
60
40
20
0
Power Reserve (%)
ns
**
Young
Age Matched
COPD
D
100
80
60
40
20
0
Fatigue Index (%)
ns
ns
Young
Age Matched
COPD
E
2.0
1.5
1.0
0.5
0.0
Fatigue Index (%/W)
ns
****
Young
Age Matched
COPD