Exercise induced muscle damage: mechanisms, assessment and nutritional factors to accelerate recovery

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Exercise-Induced Muscle Damage

- Overload and Progression – Principles of training that are required to generate physiological adaptation.
- Post-exercise soreness
- Associated with inflammatory response
  - Different from trauma induced inflammation
  - Induced via mechanical and metabolic stress of exercise
- Normal response to the adaptation process

Exercise-Induced Muscle Damage

- Result of mechanical and metabolic stress with activated muscle fibers.
- Mechanical stress – muscle lengthening under tension (more dominant effect) – leading to muscle protein damage.
- Metabolic stress – metabolic deficiencies that can lead to greater vulnerability to mechanical loading.

Post-Workout (Recovery Phase)

- Cascade of chemical events that changes chemical milieu:
- Increase in reactive oxygen species and inflammatory molecules – act as part of a signaling system initiating the recovery processes.
- Increase in both cell and vascular permeability leading to an increase in proteolytic enzymes and proinflammatory immune cells.
- Post-exercise chemical response accompanied by intramuscular edema, which is responsible for nociceptor activation and subsequent soreness

Muscle Disruption, Damage, and Repair

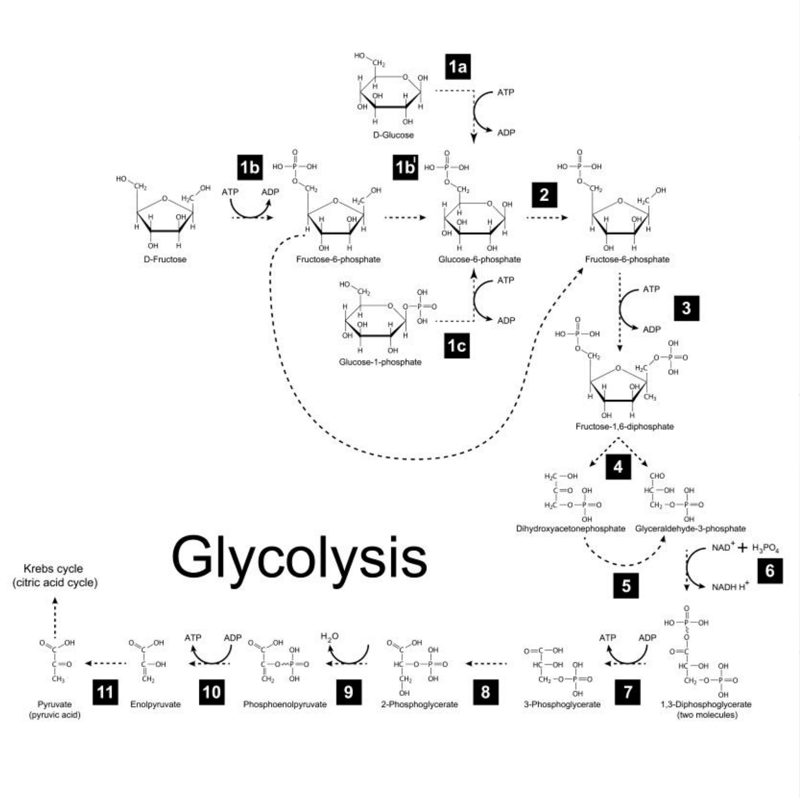
RESTING

Post-Eccentric Damage Exercise

Definition of Recovery

- From a performance perspective - a return to baseline performance measures. – <u>simplest of interpretations.</u>
- Use of quantifiable physical activities
  - Number of repetitions performed
  - Jump power
  - Cycling performance
  - Peak Torque Isokinetic testing
  - Fatigue index

Definition of Recovery



- A return of metabolic fuels to their pre-exercise levels.
  - Endurance athlete – muscle glycogen levels returning to pre-exercise levels!
- Biochemical Profile
  - Muscle damage and inflammatory markers
    - CPK, Mg, LDH, IL-6, CRP
  - Endocrine markers
    - Testosterone/cortisol

Methods Used to Examine Recovery (Protocols Creating Muscle Damage)

- A damage protocol:
- Heavy emphasis on eccentric muscle contractions:
  - Downhill running
  - Force generated by muscle lengthening – involves recruitment of fewer motor units, requires less energy and oxygen compared to concentric and isometric contractions.
- **Results in a cascade of events resulting in myofibrillar damage, degradation of structural proteins, membrane damage, and destruction of excitation contraction coupling – leading to accumulation of calcium ions in the cytoplasm, attraction of inflammatory markers to site of damage and a temporary disruption of muscle regeneration.**

Resistance Exercise Protocol to Cause Muscle Damage

Gonzalez et al., 2014; Hoffman et al., 2010; Jajtner et al., 2014 Townsend et al., 2013

LOWER BODY PROTOCOL

- Day 1:

Squats	4 x 8 – 10 @ 80% 1RM
Dead Lifts	4 x 8 – 10 @ 80% 1RM
Barbell Lunge	4 x 8 – 10 @ 80% 1RM

90 sec of rest between each set

Day 2 (24h):

Squats	4 x 8 – 10 @ 80% 1RM

90 sec of rest between each set

- Day 3 (48H):

Squats	4 x 8 – 10 @ 80% 1RM

90 sec of rest between each set

Split squat can be substituted for barbell lunge

Resistance Exercise Protocol to Cause Muscle Damage

Hoffman et al., 2022

UPPER BODY PROTOCOL

- Day 1:

Bench Press	6 x 8 – 10 @ 80% 1RM	60 sec of rest between each set
Incline Bench Press	6 x 8 – 10 @ 80% 1RM	

- Day 2 (24h):

Bench Press	6 x 8 – 10 @ 80% 1RM	60 sec of rest between each set

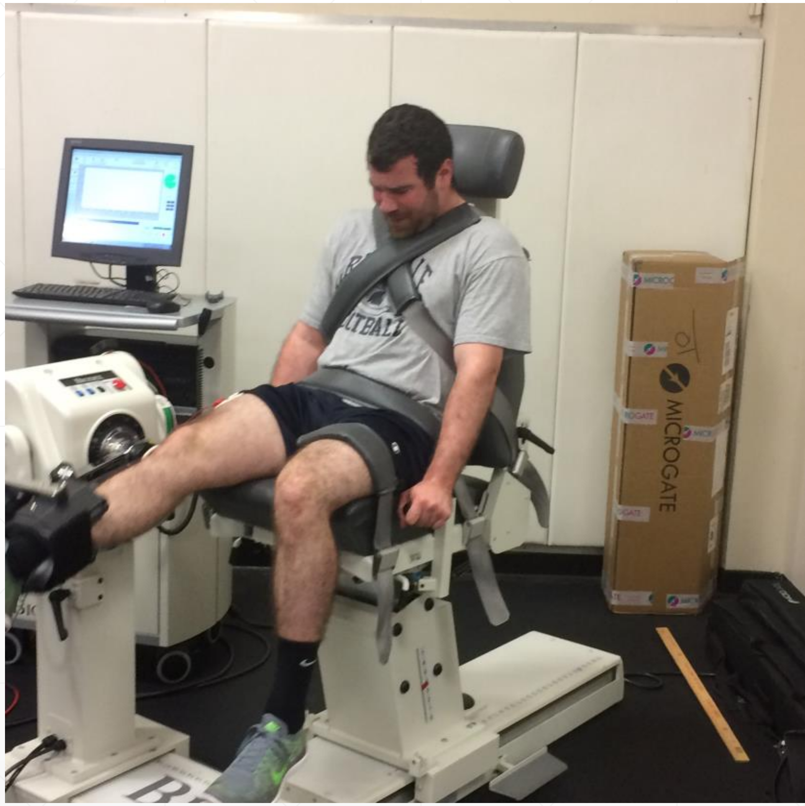
- Day 3 (48H):

Bench Press	6 x 8 – 10 @ 80% 1RM	60 sec of rest between each set

Resistance Exercise Protocol to Cause Muscle Damage

High volume isokinetic assessment protocol:

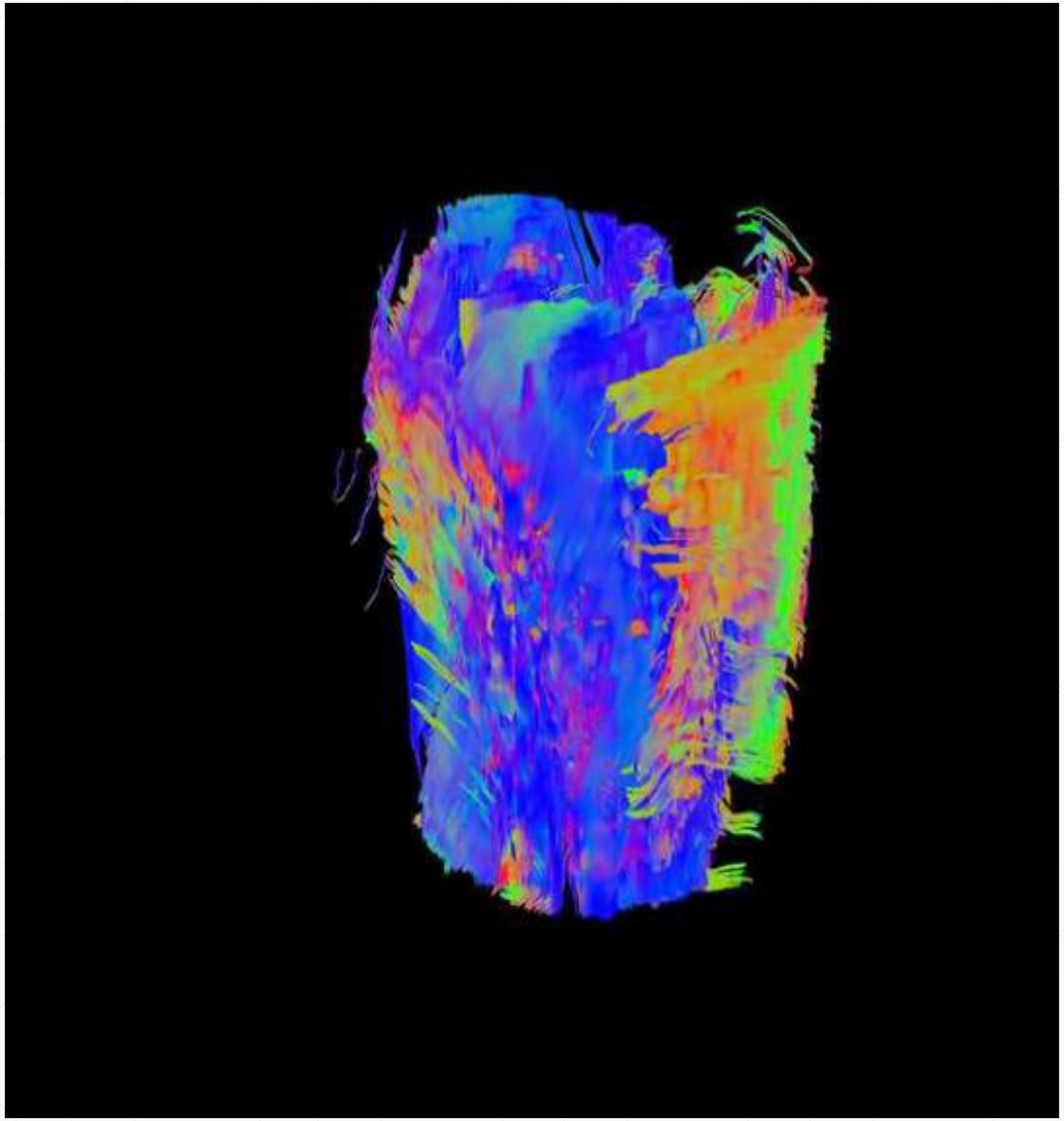
- 8 x 10 knee extension (concentric/eccentric) contractions @ 60°·sec^{-1}
- (1 x 3 reps) of isometric, slow (60°·sec^{-1}) and fast (240°·sec^{-1})



METHODS FOR ASSESSING EXERCISE-INDUCED MUSCLE DAMAGE

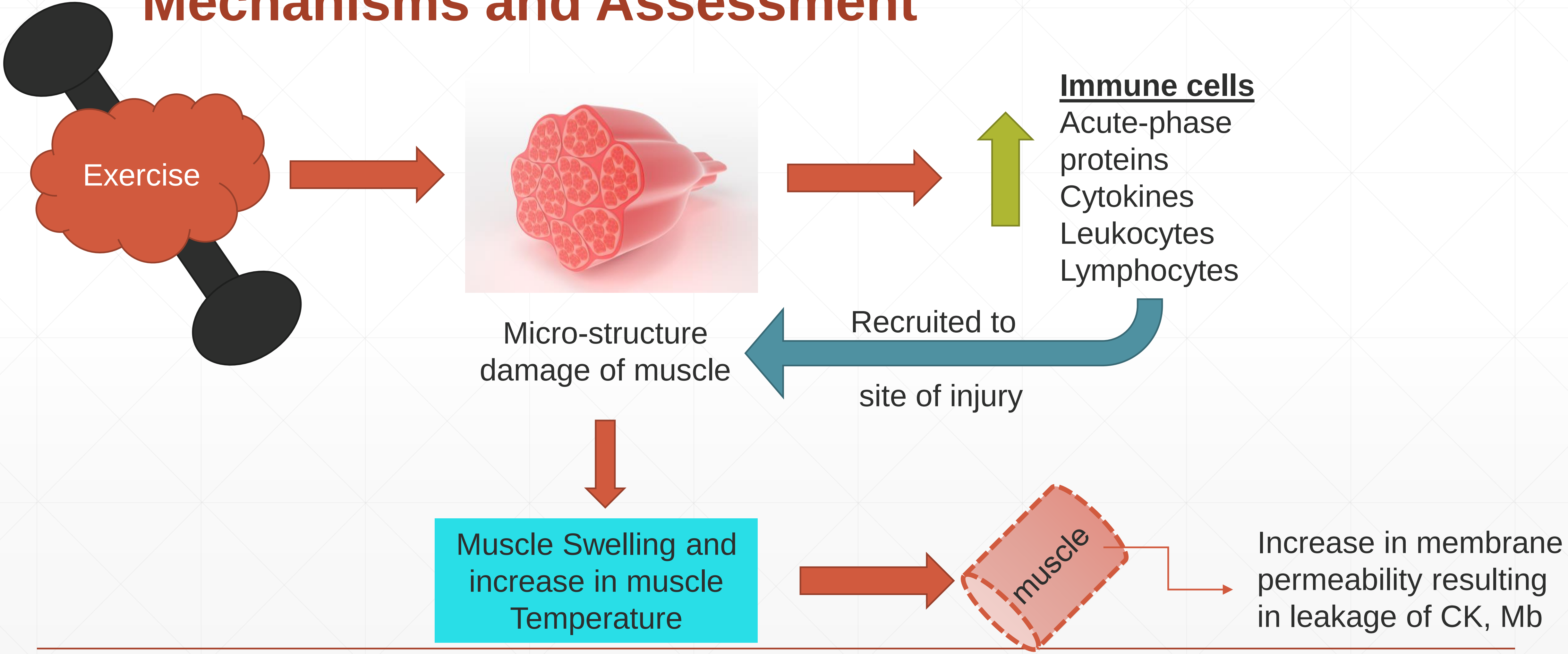
Parameter	Invasive	Non-invasive
Mechanical muscle damage	Muscle biopsy	- **MRI (T1, T2), MRI-DTI** - **Ultrasound** - **Electromyography**
Inflammation	- Muscle proteins (creatine kinase & myoglobin) - Muscle biopsy - Pro- & anti-inflammatory cytokines (e.g., IL-6, IL-8, TNF-α) - White blood cells (e.g., neutrophils, macrophages) - C-creative protein - Lactate dehydrogenase	- **Edema** - **Swelling**
Muscle soreness		- **VAS** - **Borg RPE scale** - **McGill Pain Questionnaire** - **Stretching protocol**
Performance & related measures		- **Vertical jump** - **Muscle strength using maximal voluntary contraction and/or 1-Repetition maximum** - **Economy/efficiency**
Range of motion		- **Goniometer** - **Joint movement**
Muscle regeneration	Muscle biopsy	- **MRI (T1, T2), MRI-DTI** - **Ultrasound**

MRI: magnetic resonance imaging; DTI: Diffusion tensor imaging; IL: interleukin; TNF: tumor necrosis factor; VAS: visual analog scale; RPE: rating of perceived exertion



- **MRI-DTI of skeletal muscle.** Image showing a posterior view of the thigh muscle fibers using 3-Tesla magnetic resonance imaging (MRI) scan with the color-coded measure of mean diffusivity (MD). Diffusion-tensor imaging (DTI) assessment is dependent on cell membranes and other structures constraining water diffusion. Water movement can be evaluated by determining the three orthogonal directions of water diffusion, called eigenvectors, and their intensities - eigenvalues. From the three eigenvalues ($\lambda 1$, $\lambda 2$, and $\lambda 3$), parameters such as fractional anisotropy (FA) and mean diffusivity (MD) can be calculated to evaluate the character of water diffusion in a voxel. These measures have been shown to provide information about the integrity of skeletal muscle. FA and direction map with per voxel color-coded vector values.

Inflammatory Response to Exercise: Mechanisms and Assessment

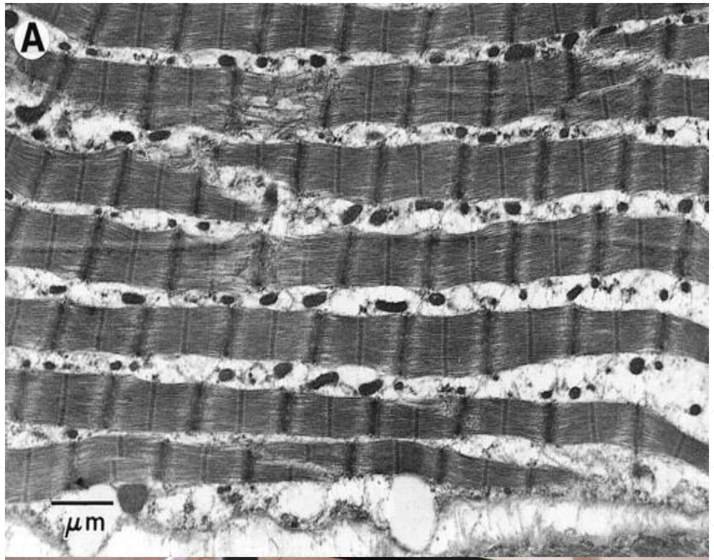


Inflammatory Response to Exercise

- The inflammatory response appears to have two phases, which include activation of both anti- and pro-inflammatory mediators, having antagonistic roles.
- Upon initial tissue insult from the exercise stimulus, pro-inflammatory cytokines are activated.
  - Cytokines such as IL-6, IL-8 and TNF-α are activated.
- The anti-inflammatory markers inhibit the expression of pro-inflammatory cytokines, thus controlling the magnitude of the inflammatory process.

Exercise induced muscle damage and immune /inflammatory response – role of TNF-α

- TNF-α involved in signaling the migration of neutrophils and macrophages to **<u>site of damage to initiate the breakdown</u>** of tissue (Peterson et al., 2006).
- TNF-α involved in mediating the initial **<u>decline in contractile performance</u>** following damage (Li and Reid, 2001)
- TNF-α **<u>impairs protein synthesis</u>** by delaying or inhibiting translation initiation, decreasing mRNA translational efficiency
- **Attenuating TNF-α may reduce skeletal muscle breakdown and enhance recovery**.



Muscle Damage Markers

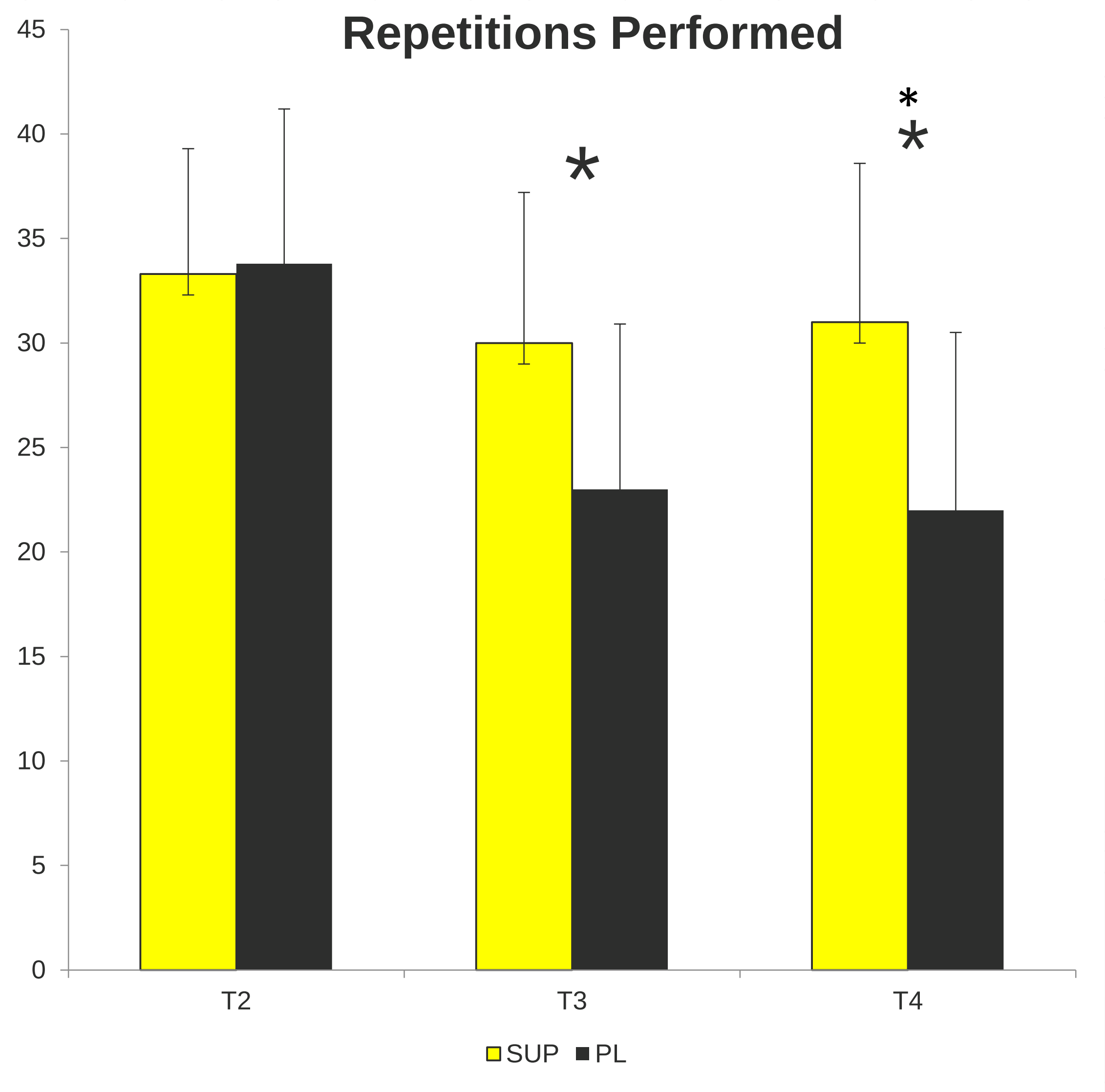
- One of the more well-known and important blood markers of muscle damage and indicator of muscle membrane permeability is creatine kinase (CK) and myoglobin (Mb).
- The magnitude of increase reflects the extent of muscle damage and cellular necrosis.
- Both CK and Mb are normally found in skeletal muscle tissue, and when muscle integrity is disrupted, as occurs during damaging exercise, these molecules leak into the circulation.
- Timing of appearance differ.
- Since Mb is a smaller molecule, its elevation is generally seen immediately after repeated eccentric contractions, whereas CK is a larger molecule and therefore takes longer (24-48 hours) to leak out of the cell.
- Despite the different timeline regarding peak appearance in the circulation, changes in both CK and Mb similarly reflect the extent of muscle damage and are positively correlated to each other

Pain and Soreness related to Muscle Damage

- Muscle soreness is often characterized by stiffness, muscle sensitivity and local pain.
- Thought to be a consequence of micro-trauma to the muscle caused by the strain and breakdown of the sarcomere resulting in an inflammatory response that may heighten pain receptors, thus causing feelings of soreness
- Most of the research has focused on exercise in novice populations, which generally results in a heightened level of soreness, often referred to as delayed onset of muscle soreness or DOMS.
- This response likely differs from that seen following an intense exercise session in competitive athletes or even recreational individuals.
- Participants often experience less soreness following a repeated exercise compared to the first bout. This is generally referred to as the "*repeated bout affect*" (Nosaka et al. 2001).

Impact of Metabolic Stress from Intense Resistance Exercise

- Induced by concentric contractions, which may amplify muscle damage and inflammation produced by the eccentric contractions (Tee et al. 2007).
- This combination may also provide the appropriate stimulus to enhance tissue repair and adaptation.
- Several investigations have supported the role of metabolite accumulation for muscle growth by influencing muscle fiber recruitment, hormonal elevations, local myokine response and reactive oxygen species.
- A problem with trying to define the relationship between mechanical tension and metabolic stress is that these phenomena occur in tandem, confounding the possibility of differentiating the specific role of each effect.



Hoffman et al., 2010

Eur J Appl Physiol (2017) 117:1287–1298
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ORIGINAL ARTICLE

Comparison of the recovery response from high-intensity and high-volume resistance exercise in trained men

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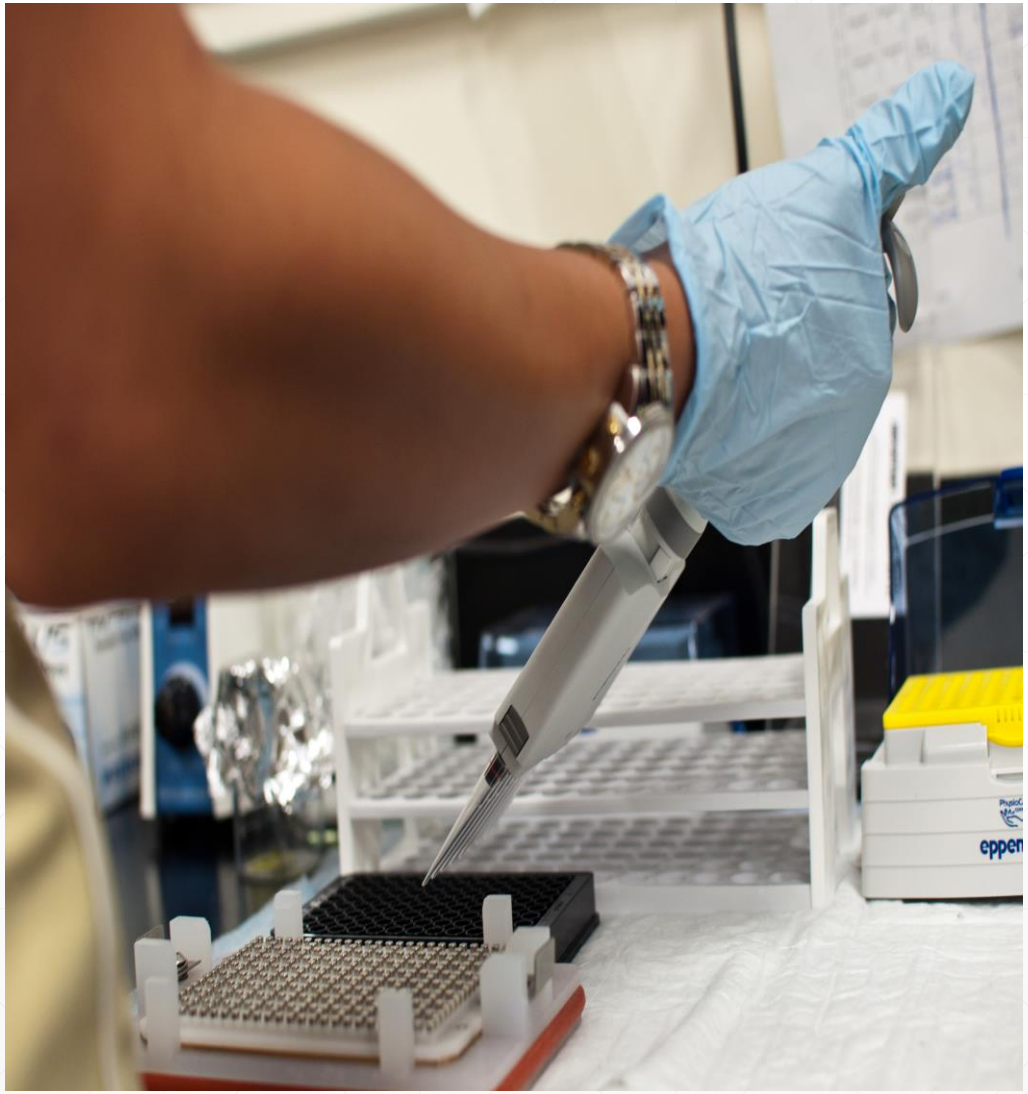
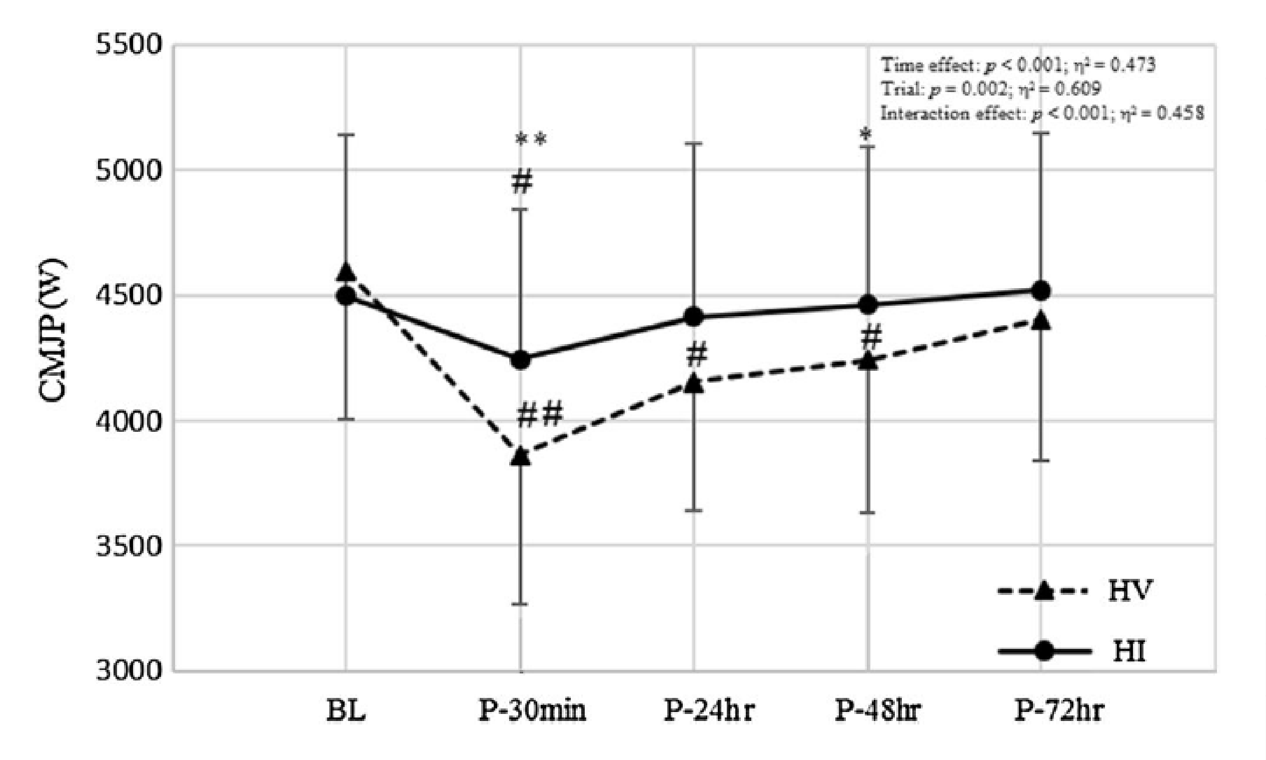
- 12 Experienced Resistance Trained Men counterbalanced, randomized design (7 days between training sessions)
- HI 8 sets x 3 reps (90% 1RM)
- HV 8 sets x 10 reps (70% 1RM)
- Measures:
  - CMJ on force plate
  - Isometric mid-thigh pull
  - Isokinetic and isometric torque measures at slow and fast speeds
  - Ultrasound measures
  - Muscle damage markers
  - Inflammatory and endocrine markers
  - Soreness questionnaires



Changes in Counter Movement Jump Power



* Indicates a significant ($p \leq 0.01$) difference between trials; ** indicates a significant ($p \leq 0.001$) difference between the two trials; # indicates a significant ($p \leq 0.01$) difference from BL.

Bartolomei et al., 2017

Performance Measures

Table 1 Changes in performance measures

Assessment	Trial	BL	P-30 min	P-24 h	P-48 h	P-72 h	Time Effect		Trial		Interaction effects	
							p	η^2	p	η^2	η^2	η^2
ISOK60 (Nm)	HV	253.0 ± 56.1	$\boxed{187.9 \pm 53.5^{\dagger,\#}}$	$\boxed{201.8 \pm 56.1^{\dagger,\#}}$	210.0 ± 61.9	219.0 ± 60.2	0.000	0.566	0.022	0.394	$\boxed{0.008}$	0.302
	HI	243.1 ± 45.3	223.8 ± 58.0	232.6 ± 60.9	240.8 ± 56.5	237.0 ± 61.0						
ISOK180 (Nm)	HV	202.8 ± 44.5	161.3 ± 42.1	171.0 ± 42.0	169.9 ± 52.7	180.0 ± 50.7	0.000	0.530	0.040	0.330	0.944	0.187
	HI	213.2 ± 37.3	178.7 ± 40.5	181.7 ± 38.9	185.3 ± 41.59	194.4 ± 43.0						
MIVC* (Nm)	HV	343.5 ± 60.6	$\boxed{262.5 \pm 71.4^{\#}}$	293.1 ± 73.3	295.8 ± 74.4†	$\boxed{305.8 \pm 67.9^{\dagger\#}}$	0.000	0.473	0.017	0.418	$\boxed{0.003}$	0.473
	HI	338.7 ± 61.9	310.0 ± 64.8	332.1 ± 77.1	346.1 ± 78.4	353.2 ± 85.9						
IMTP (N)	HV	3670.3 ± 602.8	3379.7 ± 675.2	3489.9 ± 635.8	3498.8 ± 648.8	3580.1 ± 625.9	0.057	0.194	0.171	0.163	0.192	0.133
	HI	3695.2 ± 713.1	3656.1 ± 671.5	3705.9 ± 754.6	3620.7 ± 607.9	3676.5 ± 639						
IMTP pRFD20 (N s^{-1})	HV	8718.8 ± 2021.5	7232.5 ± 1756.5	7780.4 ± 1492.7	7727.9 ± 2017.8	7504.6 ± 1695.7	0.296	0.105	0.808	0.006	0.268	0.113
	HI	7938.3 ± 2084.7	7821.2 ± 1995.3	7702.1 ± 2182.1	7985.7 ± 3060.0	7955.0 ± 1820.7						
ISQ (N)	HV	2749.2 ± 403.2	2342.2 ± 428.4	2532.9 ± 381.2	2619.6 ± 349.6	2726.2 ± 388.7	0.000	0.686	0.479	0.051	$\boxed{0.073}$	0.216
	HI	2737.8 ± 417.3	2539.9 ± 388.9	2614.2 ± 402.9	2649.4 ± 404.8	2719.3 ± 395.2						
ISQ pRFD20 (N s^{-1})	HV	5195.0 ± 1249.7	4180.0 ± 1581.4	4451.4 ± 1611.2	4665.8 ± 1482.8	5084.2 ± 1807.6	0.051	0.231	0.565	0.034	0.602	0.057
	HI	5004.6 ± 1507.7	4783.3 ± 1344.7	4476.3 ± 1179.8	4885.0 ± 1556.2	5117.5 ± 1270.0						

ISOK60 isokinetic peak torque at 60°/s; *ISOK180* isokinetic peak torque at 180°/s; *MIVC* maximum voluntary contraction; *IMTP* isometric mid-thigh pull; *IMTP pRFD20* peak rate of force development at IMTP; *ISQ* isometric squat; *pRFD20* peak rate of force development at ISQ

† Indicates a significant ($p < 0.05$) difference between the two protocols at different time points (pairwise comparison)

\# Indicates a significant ($p \leq 0.01$) difference from BL. All data are reported as mean ± SD

Bartolomei et al., 2017

Ultrasound Measures

Table 2 Changes in ultrasound measures

Assessment	Trial	BL	P-30 min	P-24 h	P-48 h	P-72 h	Time effect p	Time effect η^2	Trial p	Trial η^2	Interaction effects p	Interaction effects η^2
CSA (cm^2)	HV	36.91 ± 8.2	41.09 ± 9.0†##	38.47 ± 9.3†#	38.49 ± 9.0†#	39.39 ± 7.8	0.001	0.469	0.000	0.803	0.032	0.294
	HI	36.34 ± 8.4	36.92 ± 8.4	36.66 ± 7.9	39.94 ± 8.1	36.8 ± 8.3						
MT (cm)	HV	2.21 ± 0.4	2.50 ± 0.4	2.36 ± 0.4	2.38 ± 0.4	2.39 ± 0.4	0.000	0.486	0.048	0.310	0.052	0.223
	HI	2.16 ± 0.4	2.27 ± 0.4	2.23 ± 38.9	2.26 ± 0.4	2.24 ± 0.3						
EI (a.u.)	HV	40.53 ± 8.6	47.91 ± 11.6##	39.62 ± 9.7	39.23 ± 9.6	40.51 ± 9.5	0.000	0.698	0.267	0.111	0.024	0.289
	HI	41.27 ± 8.8	43.32 ± 9.7	39.86 ± 8.4	39.96 ± 9.8	39.21 ± 8.2						

CSA cross-sectional area, *MT* muscle thickness, *EI* echo intensity

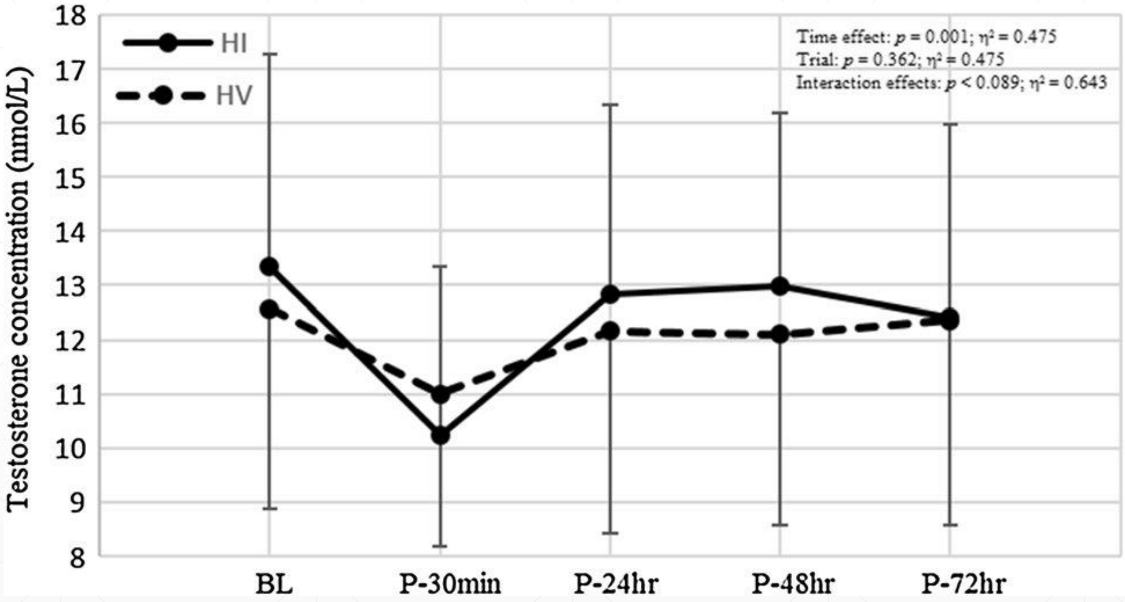
†Indicates a significant ($p < 0.05$) difference between the two protocols (pairwise comparison)

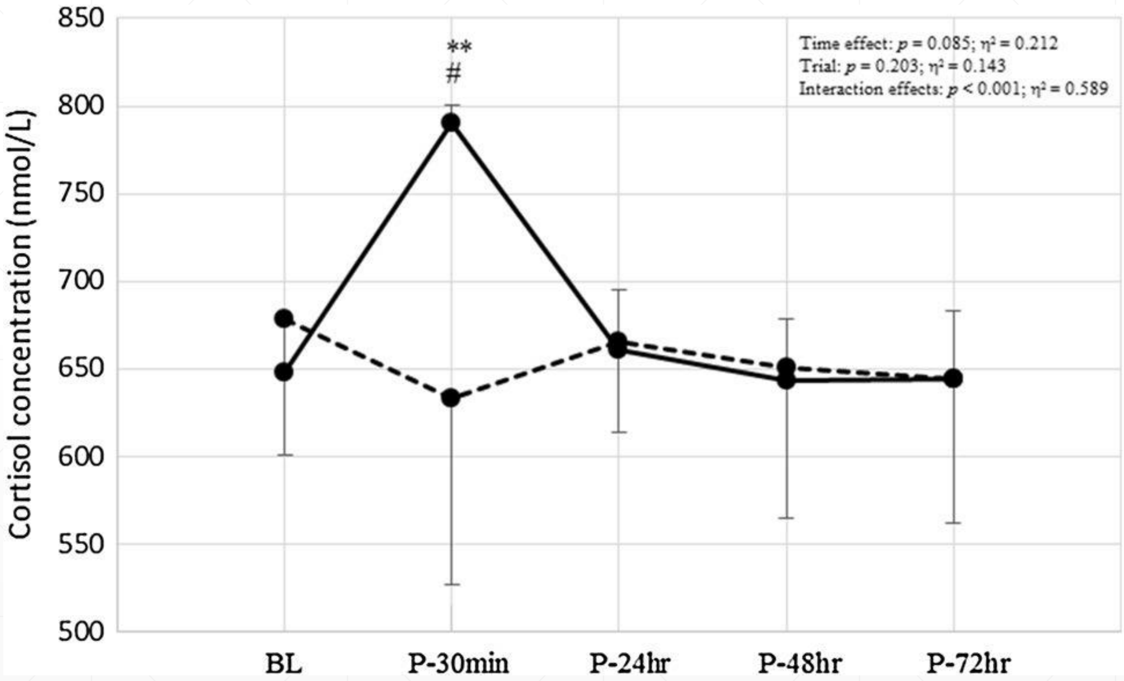
#Indicates a significant ($p \leq 0.01$) difference from BL

##Indicates a significant ($p \leq 0.001$) difference from BL. All data are reported as mean ± SD

Bartolomei et al., 2017

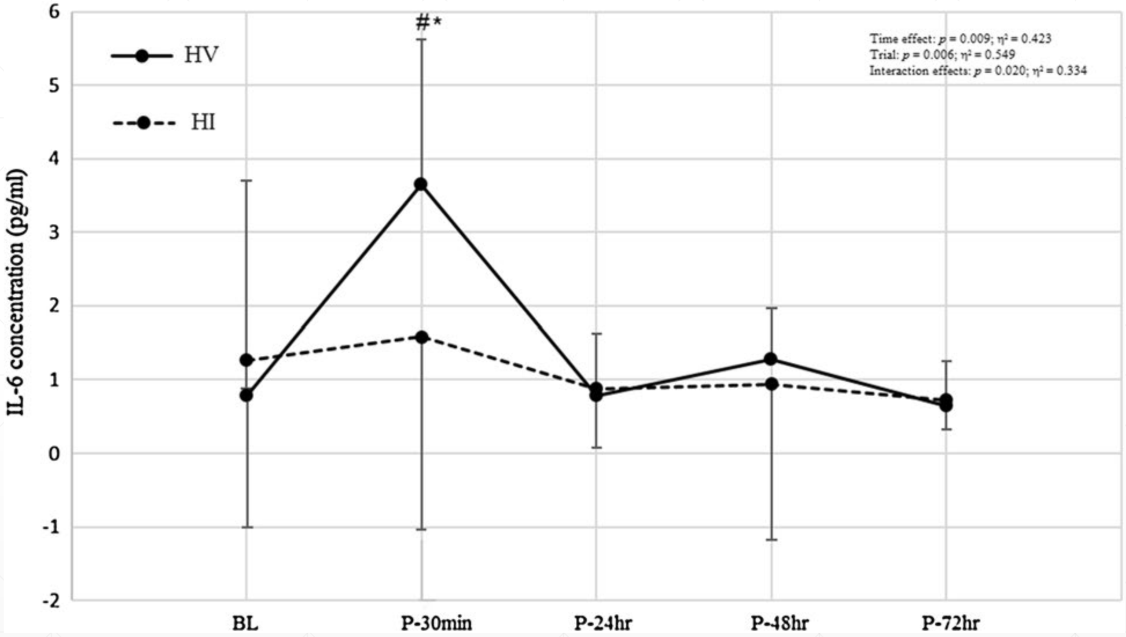
Endocrine Measures

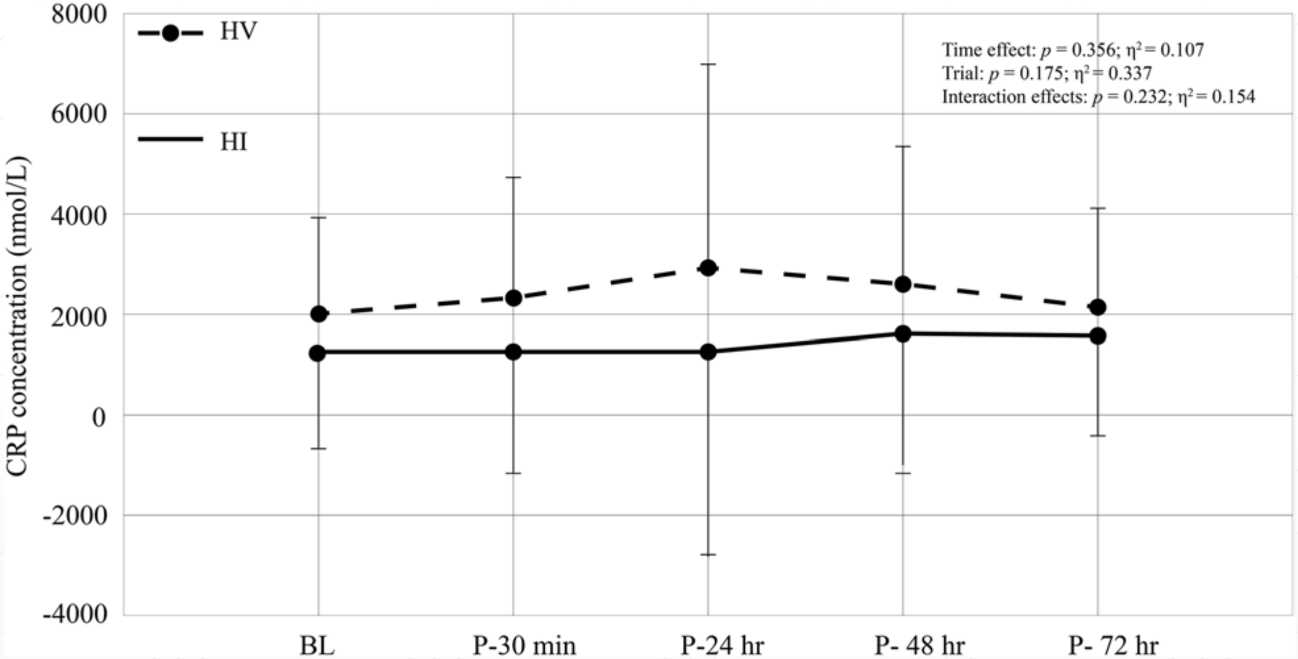




Bartolomei et al., 2017

Inflammatory Measures





Bartolomei et al., 2017

Changes in Muscle Pain and Soreness

Assessment	Trial	BL	P-30 min	P-24 h	P-48 h	P-72 h	Time effect		Trial		Interaction effects	
							p	η^2	p	η^2	p	η^2
PAIN (mm)	HV	0.00	16.17 ± 21.3	26.92 ± 30.3	26.42 ± 0.7	16.33 ± 20.7	0.190	0.498	0.012	0.452	0.240	0.461
	HI	0.00	4.67 ± 8.42	2.58 ± 7.4	1.42 ± 3.6	1.25 ± 3.6						
SOR (mm)	HV	0.00	49.25 ± 24.6##	61.42 ± 23.4##	57.92 ± 21.5##	35.92 ± 17.1##	0.000	0.902	0.000	0.850	0.001	0.711
	HI	0.00	13.25 ± 11.1	23.75 ± 19.6	17.00 ± 14.25	8.50 ± 13.4						

Bartolomei et al., 2017

Muscle Damage Markers

Table 3 Changes in muscle damage parameters

Assessment	Trial	BL	P-30 min	P-24 h	P-48 h	P-72 h	Time effect		Trial		Interaction effects	
							p	η^2	*p*	η^2	*p*	η^2
CK (U/L)	HV	208.10 ± 132.9	259.86 ± 165.1	442.10 ± 297.8	304.24 ± 209.9	305.80 ± 337.0	0.002	0.254	0.079	0.254	0.185	0.145
	HI	169.17 ± 89.1	205.10 ± 102.4	281.28 ± 133.2	219.16 ± 91.6	199.77 ± 50.2						
Mb (ng/mL)	HV	26.25 ± 7.5	59.97 ± 20.8	38.03 ± 24.7	33.65 ± 20.7	38.71 ± 37.1	0.001	0.872	0.383	0.070	0.367	0.091
	HI	26.75 ± 7.1	62.88 ± 18.3	28.34 ± 6.2	27.48 ± 5.6	29.1 ± 6.2						
LDH (mU/L)	HV	704.72 ± 166.7	841.71 ± 257.7	773.24 ± 236.1	757.48 ± 235.8	739.04 ± 237.4	0.012	0.390	0.022	0.390	0.463	0.073
	HI	692.51 ± 185.4	746.50 ± 160.4	728.81 ± 205.7	703.61 ± 198.3	704.11 ± 136.8						

Bartolomei et al., 2017

Study Summary

- Recovery from high volume resistance exercise is slower than recovery from resistance exercise protocols of higher intensity.
- Differences in recovery appear to be related to the greater metabolic stress associated with high volume exercise.
- Reflected by the greater inflammatory response, changes in muscle cross-sectional area, and performance.

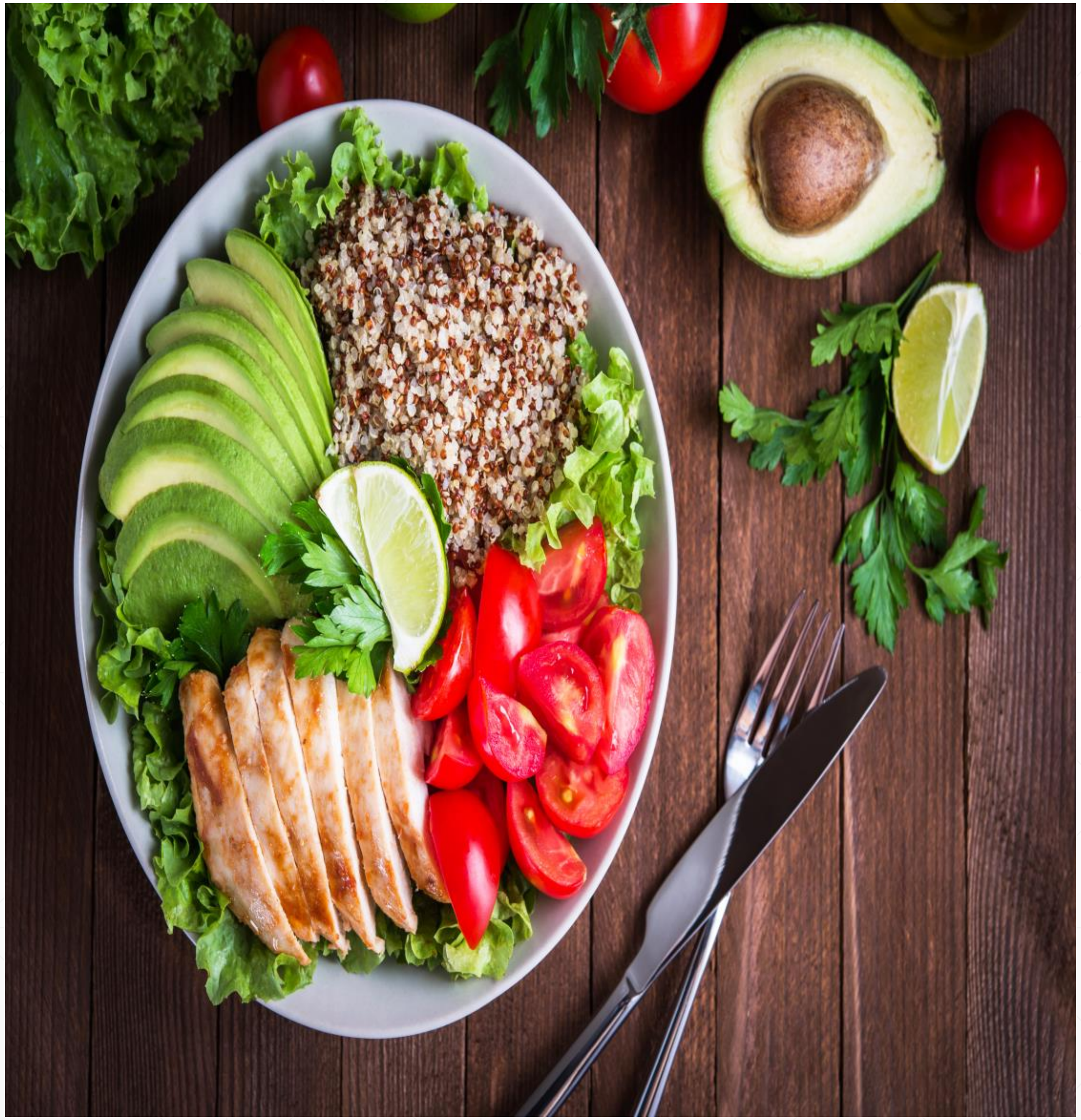
Nutritional Considerations for Enhancing the Recovery Response to Exercise

Nutrition and Recovery

- Nutritional considerations are an important component for accelerating recovery from exercise.
- For many nutritional organizations, recommendations have generally been focused on the athlete’s meal plan but recently have acknowledged the importance that strategically timed nutritional supplements may provide for enhancing recovery.
- Nutritional supplements may provide the athlete with an ability to accumulate specific nutrients within skeletal muscle or other tissues in the body (i.e., the brain), to a greater magnitude than can be provided by regular meal consumption only, thus providing an advantage for enhancing recovery from exercise.

Macronutrient Intake and Recovery

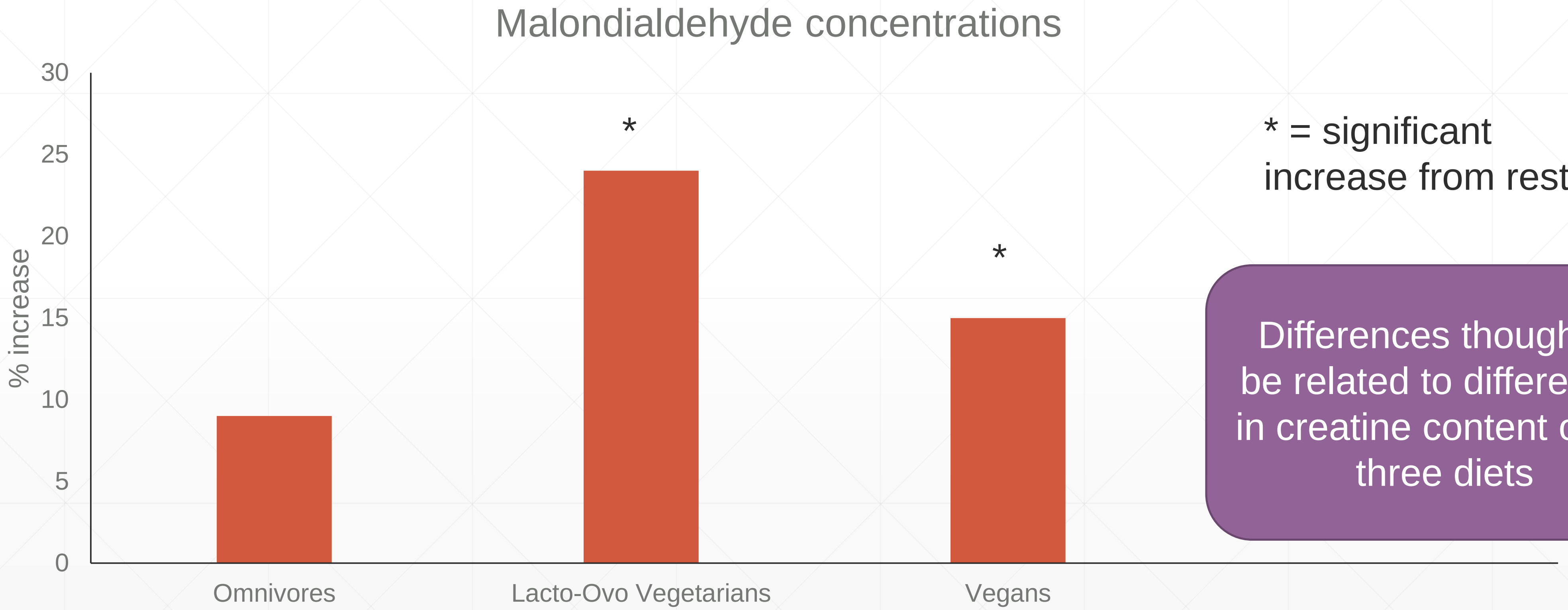
- The dietary habits of competitive and recreational athletes appear to be quite variable, ranging from athletes that follow a traditional omnivore diet to those that prefer a more extreme diet such as vegetarian, ketogenic (high fat low carbohydrate) or carnivore (very high protein).
- The focus of these diets are generally is on a specific macronutrient (e.g., fats or proteins) or a dietary restriction (e.g., no meat or animal products).
- There have been only limited attempts to examine the effect of a specific diet on recovery aspects of performance, and even less has been published on dietary comparisons and recovery from exercise.
- Exercise is known to cause an increase in oxidative stress that causes an increase in the production of free radicals and lipid peroxidation, resulting in cell damage and a potential cascade of events that impacts the health and well-being of the athlete (Bloomer et al. 2005).
- At rest, the body’s antioxidant system is sufficient to remove these harmful oxidants; however, during exercise, this system can be overwhelmed, and an imbalance can occur resulting in the accumulation of antioxidants that can negatively affect recovery.



Nutrition and Recovery

- It is thought that a diet rich in antioxidants such as vitamins C and E, polyphenols and β-carotene can enhance one's ability to combat oxidative stress (Craddock et al. 2020).
- Polyphenols may have the richest concentration of antioxidants, and they are abundant in plant-based foods.
- **Individuals who were vegetarians for more than 20 years had a lower degree of oxidative stress compared to omnivores** (Kim et al., 2012).
- Whether this provides vegetarians an advantage in term of recovery from exercise is not clear, especially considering that meat contains specific nutrients that are also considered to be antioxidants, such as carnosine and creatine.

Oxidative Stress Response during Exercise



* = significant increase from rest

Differences thought to be related to differences in creatine content of the three diets

Nebl et al., 2019

Is there any benefit of a vegetarian diet to enhance recovery?

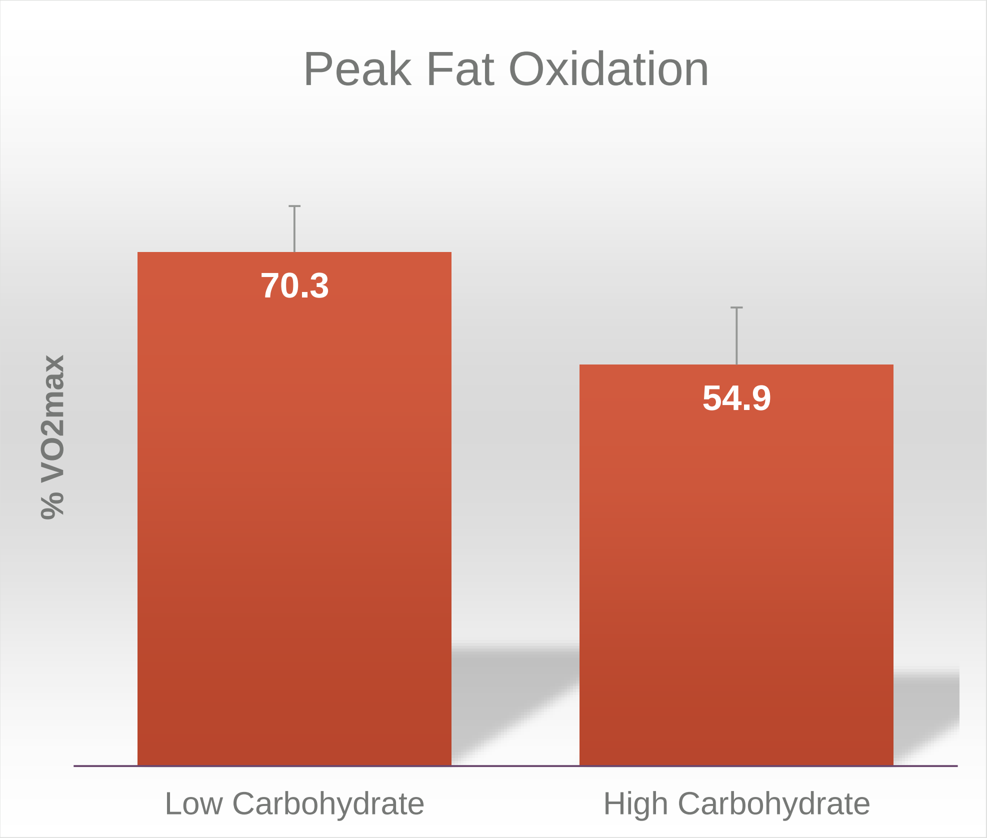
- Vegetarian diets high in polyphenols
- Diets high in fiber reduce bioavailability of polyphenols
- C-reactive protein (marker of inflammation) – lower in both lacto-ovo vegetarians and omnivores compared to vegetarians (Vanacore et al., 2019).
- No scientific evidence to support the benefits of a vegetarian diet for enhancing recovery from exercise.
- Quality of protein in a vegetarian diet?
  - Without animal protein the quality of protein intake may be inferior for a vegetarian compared to an omnivore.

Ketogenic vs Omnivore Diets

- The ketogenic diet has gained tremendous popularity - defined by its low carbohydrate, high fat intake.
- The basis of this diet is to provide a dietary treatment plan to treat obesity and diabetes but is also used by athletes to enhance their metabolic system for competition (Harvey et al. 2019).
- Generally, the macronutrient caloric composition of the ketogenic diet is 80% fat, 15% protein, and 5% carbohydrates (Veech 2004). The increase in ketone bodies from a high consumption of fat is thought to provide a more energy efficient substrate than glucose or fatty acids (Veech 2004; Harvey et al. 2019).

Ketogenic vs Omnivore Diets

- Volek and colleagues (2016) compared a low-carbohydrate diet to a high carbohydrate diet in elite male ultra-endurance athletes performing a maximal graded exercise test and a 180 min submaximal run at 64% VO2max.
- Participants consumed their specific diets for at least 6-months prior to study enrollment.
- The results of the study indicated that peak fat oxidation was 2.3-fold higher in the low-carbohydrate group
- Fat oxidation during submaximal exercise was 59% higher in the low-carbohydrate group than in the high-carbohydrate group.
- Despite these differences in fuel use between the groups, no significant differences were noted in resting muscle glycogen and the level of glycogen depletion after 180 min of running.
- Findings confirmed by Prins et al. in 2019.



Ketogenic Diet and Glycogen Replacement

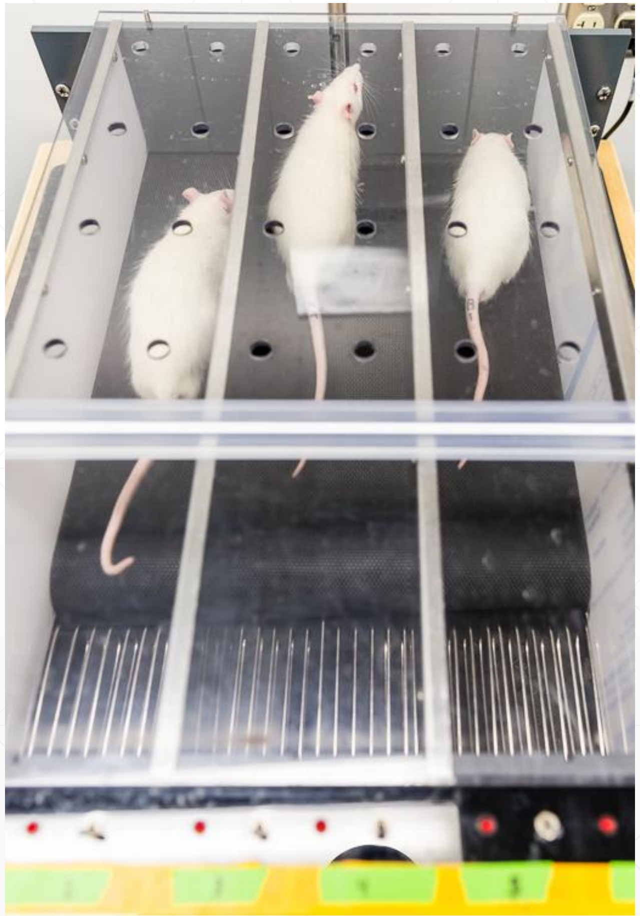
- The low-carbohydrate content of the ketogenic diet has been a major concern for many individuals, as the standard belief was that maximizing glycogen storage was critical for exercise performance.
- Traditional thought - athlete that competes or trains daily - glycogen replenishment is critical for recovery.
- Evidence indicates metabolic adaptations resulting from low-carbohydrate diets do compensate for low muscle glycogen content (Paoli et al. 2015).
  - Low-carbohydrate, high-fat diets usually lead to ketosis when the liver oxidizes high concentrations of non-esterified fatty acids (NEFA) into ketone bodies (McPherson and McEneny 2012).
  - When glycogen stores are depleted glucose levels are maintained through the process of gluconeogenesis resulting in the conversion of molecules with carbon skeletons such as amino acids and lactate to glucose.
  - Glycerol derived from the metabolism of triglycerides can also be a source of glucose (Massicotte et al. 2006).

Compared with glucose, the energy produced from ketone bodies appears to be greater (Paoli et al. 2015).

These two sources appear to compensate for the low carbohydrate intake.

Other Benefits Associated with Ketogenic Diet

- Reduced levels of reactive oxygen species (hydrogen peroxide [H_2O_2] and hydroxynonenal [4-HNE]) concentrations.
  - Potential protective mechanism during high intensity training
- Enhanced recovery from exhaustive exercise reported in murine study (Huang et al., 2018).
  - Markers of muscle and liver damage reduced in ketogenic group vs. high carbohydrate fed animals.
- Likely related to high protein content in diet



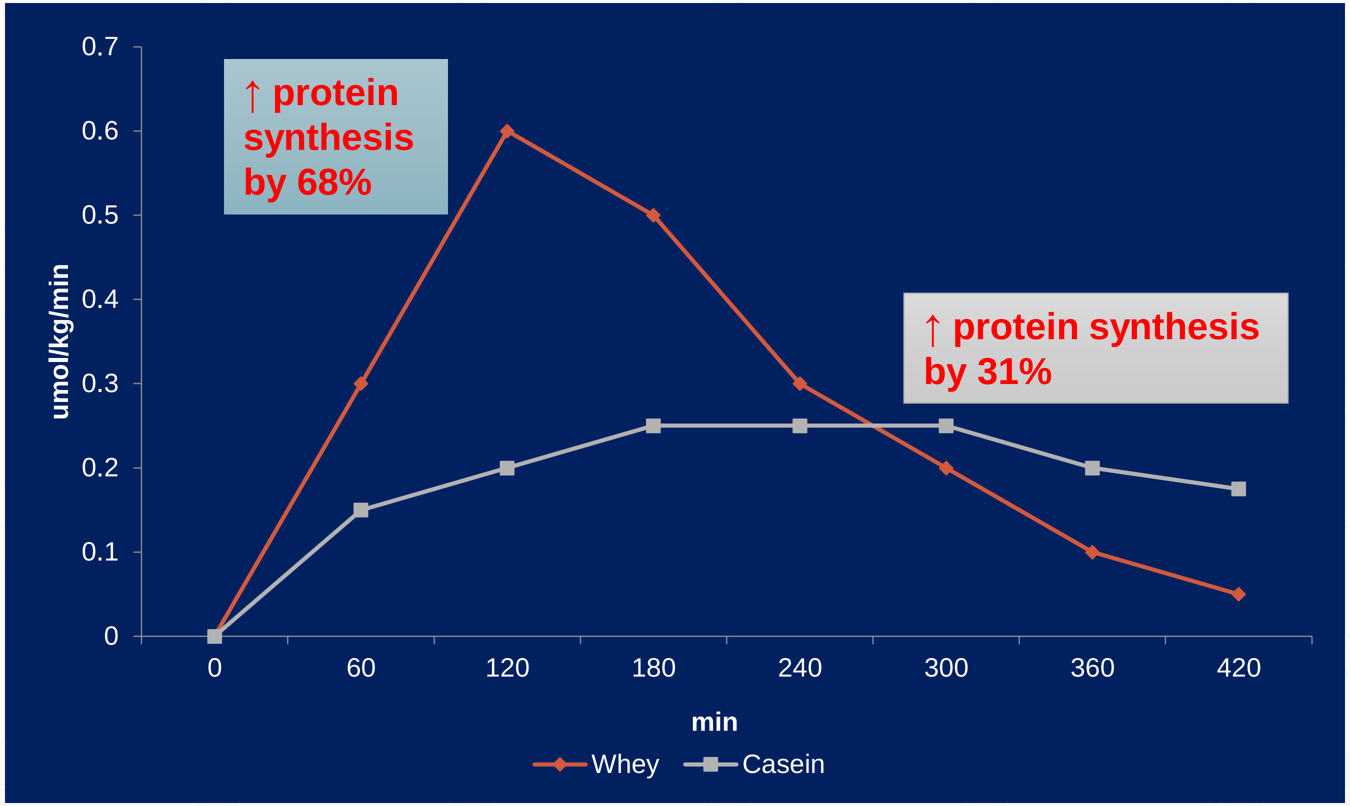
Effect of Dietary Supplementation on Recovery Indices of Exercise

- There are numerous dietary supplements that have been suggested to enhance exercise recovery.
- Focus on the more popular dietary supplements used by competitive athletes:
  - Protein
  - Creatine
  - β-alanine
  - Polyphenols.

Focus on recovery benefits NOT efficacy on enhancing exercise performance

Protein Supplementation

- Protein consumption following an intense workout can enhance the recovery and remodeling processes within skeletal tissue.
- Several studies have reported a decrease in the extent of muscle damage, attenuation in force decrements, and enhanced recovery resulting from protein ingestion following resistance exercise.
- The two most common whole proteins used in dietary supplements are casein and whey - differences related to their differences in digestive properties and amino acid composition.
    - Casein forms a gel or clot in the stomach, which slows down absorption. Whey protein is the translucent liquid part of milk and contains higher amounts of the essential and branched chain amino acids – thus, faster rate of absorption with higher concentrations of leucine
- Heightened sensitivity in skeletal tissue following a workout - ingestion of whey protein immediately following workout most beneficial protein to enhance recovery.
- Whey also reported to enhance glycogen synthesis in both liver and muscle > casein, related to its capacity to upregulate glycogen synthase activity.



7 hrs post: casein intake resulted in higher ($p<0.05$) leucine balance

Boirie et al., (1997)

Creatine

- Creatine is a nitrogenous organic compound that is synthesized from the amino acids’ glycine, arginine and methionine primarily in the liver. The efficacy of creatine supplementation has been well documented in numerous studies over the past 20-years.
- In addition to its ergogenic ability, creatine supplementation has also been suggested to enhance recovery from exercise.
  - Creatine has been reported to enhance glycogen replenishment following exhaustive exercise (Nelson et al. 2001).
  - Creatine induced increases in cell volume may be the mechanism responsible for augmenting glycogen synthesis. Increases in muscle creatine (31%) associated with a change in glycogen storage (18 %) following 5-days of creatine supplementation (Van Loon et al., 2004).
- Limited benefits of attenuating muscle damage in untrained participants.
- When creatine supplementation is provided to experienced, resistance-trained individuals performing an overreaching exercise protocol, significant reductions in uric acid (marker of exercise stress) and a greater maintenance of performance was noted in the creatine supplemented group (Volek et al. 2004; Cooke et al., 2009).

Creatine

- Creatine supplementation has also been shown to reduce muscle damage and inflammatory markers following a 30-km road race in competitive marathoners (Santos et al., 2004).
  - Participants provided 20 g of creatine monohydrate per day for 5 days. Blood was obtained immediately prior to- and 24-hours following the race. Although differences in creatine kinase were not statistically different, there was still a 19.2% lower response in runners that supplemented with creatine compared to placebo.
  - Significantly lower lactate dehydrogenase (38%), prostaglandin E2 (66.5%) and TNFα (33.8%) concentrations were noted in the creatine group suggesting a reduction in muscle damage and inflammation resulting from creatine supplementation.
- Results from these investigations do support the benefits of creatine supplementation on enhancing recovery from exercise. Precise mechanism remains unclear.

β-Alanine

- β-alanine is a non-proteogenic amino acid. When ingested it combines with histidine within skeletal muscle and other organs to form carnosine. β-alanine is the rate-limiting step in muscle carnosine synthesis.
- Carnosine is a highly effective intracellular pH buffer that enables a greater tolerance of sustained anaerobic activity.
- Besides serving as an intracellular buffer, carnosine has also been suggested to act as an antioxidant (Kohen et al. 1988; Boldyrev et al. 2004; 2010).
  - Carnosine has been demonstrated to scavenge reactive oxygen species and react directly with superoxide anions and peroxyl radicals in vitro (Boldyrev et al. 2013).
- Carnosine has been shown to behave as an ion-chelating agent, preventing ions such as copper and zinc from excessive accumulation, which may lead to lipid peroxidation and subsequent cellular damage (Trombley et al. 2000).
- Carnosine also reported to act as an anti-glycating agent, preventing the formation of advanced lipid oxidation end-products (Boldyrev et al. 2013).
- Carnosine's physiological role clearly goes beyond those of muscle-buffering capacity and suggest that elevations in carnosine levels may enhance exercise recovery.

β-Alanine

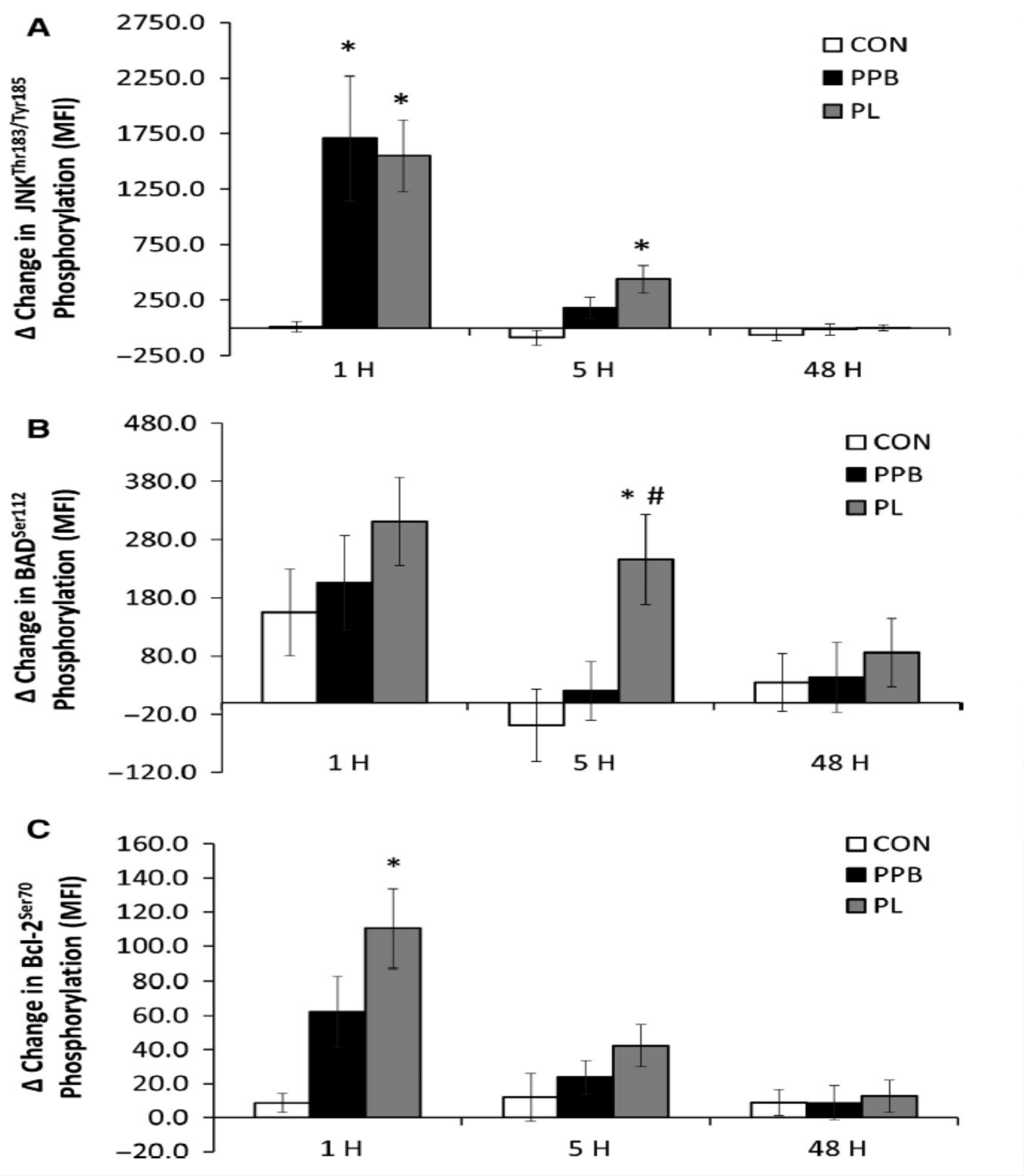
- Investigations examining the role of β-alanine supplementation and oxidative stress have been limited.
- Smith et al. (2012; 2014) examined effect of β-alanine supplementation on markers of oxidative stress,
  - 28-days of β-alanine (4.8 g·day^{-1}) during a 40-minute treadmill run in moderately trained college-aged men and women was unable to attenuate the oxidative stress response.
- Several animal studies have reported that β-alanine may have a role as an antioxidant in the brain.
  - Murakami and Furuse (2010) reported significant elevations of carnosine content in the cerebral cortex and hypothalamus of mice that supplemented with β-alanine for 5-weeks. Increases in brain carnosine were associated increases in brain derived neurotrophic factor (BDNF), and a decrease in 5-hydroxyindoleacetic acid concentrations, a metabolite of serotonin.
  - Hoffman et al., (2015; 2017) have shown that elevations in hippocampal carnosine content resulting from β-alanine ingestion can increase resiliency in rodents exposed to either a predator scent stress (PSS) (e.g., an animal model of post-traumatic stress disorder, PTSD) or a low-pressure blast wave (e.g., an animal model of mild traumatic brain injury, mTBI).
- These results indicate a potential role of β-alanine for increasing resiliency and/or recovery from concussive events in competitive contact sports.
- Whether β-alanine supplementation can provide any anti-inflammatory or antioxidant protection to enhance recovery following intense exercise in competitive athletes requires additional examination.

Polyphenols

- Polyphenols are the most plentiful antioxidant in the diet and are common in many plant-based foods and beverages, such as fruits, tea and coffee.
- There are four main polyphenols, which differ in their structure: phenolic acids, flavonoids, stilbenes, and lignans. Flavonoids are the most common polyphenol supplement that has been investigated.
- Polyphenols are considered antioxidants whose major function is to maintain oxidative balance within the body. Several studies have demonstrated that acute supplementation can attenuate strength deficits following exercise that elicits muscle damage (Panza et al. 2008; Bowtell et al. 2011; Jówko et al. 2012; Jajtner et al. 2016, 2018; Beyer et al. 2017; Townsend et al. 2018).

Polyphenols

- 28-days of polyphenol supplementation in recreationally trained college students (using lower body muscle damaging protocol) using 3 exercises (squats, leg press and leg extension) at 70% of 1RM, with 90 sec of rest between sets. Results revealed that resistance exercise-initiated monocyte recruitment and mobilization was enhanced following polyphenol supplementation, thus possibly enhancing expression on nonclassical monocytes after exercise. A significant attenuation in the inflammatory response and a reduction in apoptotic markers during the recovery period (Jajtner et al. 2016; 2018; Townsend et al. 2018) .
- The 4-week supplementation period also resulted in an increase in total antioxidant capacity compared to placebo, which may have important implications for exercise recovery (Beyer et al., 2017).



Townsend et al., 2018

Conclusion

- The study of exercise recovery is quite complex as a multitude of factors such as age, sex, training experience, muscle fiber type and type of activity performed (i.e., endurance versus resistance exercise) can influence interpretation.
- Investigations of recovery have ranged from performance outcomes to molecular examination of cellular signaling systems describing potential mechanisms of recovery.
- Monitoring the recovery process using validated tools for performance measurement may represent key factors in understanding recovery of different components of performance.
- There does not appear to be any consensus on a specific diet being advantageous with regards to recovery compared to others. However, there is evidence to suggest that the use of several of the dietary supplements (e.g., protein, creatine and polyphenols) are efficacious in enhancing recovery from both endurance and strength/power exercise.
- There is some interesting evidence in animal studies regarding elevated carnosine levels resulting from β-alanine supplementation and enhanced antioxidant status that has been reported to coincide with an attenuated inflammatory response. However, further research still appears necessary regarding β-alanine and its role in recovery from exercise.

Thank you