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The Effects of Branched Chained Amino Acid Supplementation on Acute Markers of Fatigue
and Performance

A dissertation

presented to

the faculty of the Department of Sport, Exercise, Recreation, and Kinesiology

East Tennessee State University

In partial fulfillment of

the requirements for the degree

Doctor of Philosophy in Sport Physiology and Performance

by

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August 2019

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ABSTRACT

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Joseph Walters

The purposes of this dissertation were to investigate the acute effects of branched-chain amino acids on psychological, physiological, and subsequent performance changes following high volume resistance training. The rationale for this study design was based on abrupt or contiguous training/ competitions that specific athletes encounter in a competitive season. This study design also sought to fill some gaps in the scientific literature concerning the efficacy of BCAAs for subjective fatigue in a resistance training paradigm. To address the purposes of this dissertation, a one-week study was conducted on resistance trained males, in which half of the subjects were randomly selected to receive BCAAs and the other half was a non-supplement group. The subjects in this study performed two high volume resistance training bouts consisting of squat and bench press (5 sets x 10 repetitions at 95% relative intensity) separated by two days. The physiological variables tested in this study were creatine kinase, interleukin-6, C-reactive protein, testosterone, and cortisol. The performance variables tested in this study were static and counter-movement jumps, isometric mid-thigh pull, and Bosco repeated jumps. The primary findings from this study was that subjects in the BCAA group had a statistically significant decrease in muscle damage, indicated by levels of CK. Additionally, there was a statistically significant increase in T:C ratio for the BCAA group compared to the NS group. Concerning performance variables, BCAAs had a small to moderate effect on rate of force development; however, this result was not statistically significant. There were no differences in psychological

variables between the groups. Based on the findings of this dissertation, BCAAs mitigate levels of muscle damage and rate of force development. To conclude, BCAAs may provide a competitive advantage for athletes when training volume and competitions become contiguous.

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DEDICATION

Colossians 3:23

“²³ Whatever you do, work at it with all your heart, as working for the Lord, not for human masters”

I dedicate this work to the one who makes all things possible, my Lord and Savior Jesus Christ. Despite the many trials that I have faced, and the trials that we all will face in life, You are the master of our peace. You have protected, directed, and corrected me in this world. May all things be for Your glory. Amen.

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In pursuit of my Ph.D. I have had many individuals guide my decisions and growth as a student in the classroom and in life. Attaining my Ph.D. has been A long term pursuit but could not be possible without the help of my mentors, past relationships, friends, and family.

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interaction with Dr. Stone, he has impacted my thoughts, knowledge, and creativity in the field of sport and exercise science. I've spent many hours scouring through his literature and videos. Anyone who has ever accomplished their Ph.D. under Dr. Stone knows that it is a trial by fire. Because of his leadership and the situations that he directs us to encounter, we are adequately equipped to face any situation in our career path, and for that, I am indeed grateful for Dr. Stone.

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CHAPTER 1

INTRODUCTION

As an athlete or individual trains, depending on the stimulus, the desired fitness characteristic is typically reduced until subsequent recovery occurs. If the stimulus is applied correctly, an adaptation follows allowing the athlete or individual to improve the desired fitness trait. This circumstance is known as the recovery/ adaptation process. By understanding this process, and how it relates to the athlete, gives insight to coaches on planning subsequent training bouts to optimize the desired fitness quality. However, the recovery/ adaptation process is influenced by multiple factors (e.g. genetics, training, nutrition, etc.), and comprehension of these factors helps us to enhance our knowledge of this occurrence. Perhaps the most complex and least understood element regarding the recovery adaptation process is the immune system. The immune system is altered by multiple factors thus making it difficult to derive conclusions concerning its impact on recovery/ adaptation. Hypothetically, by augmenting the immune system, which also influences other physiological functions (e.g. hormones, cell signaling, etc.), with contemporary approaches such as supplementation (BCAA), could further assist the recovery/ adaptation process in improving training performance.

The immune system is a problematic area of research pertaining to sports performance. The difficulty persists because the immune system involves multiple tissues, cells, and cellular processes that overlap. Also, uptake, redistribution, and marginalization of specific immune cells/ markers are very difficult to interpret for performance. Nonetheless, the immune system has gained attention as a focal area of research for athletes participating in endurance sports (Gleeson, 2006). Observably, many endurance athletes report the occurrence of illness following

an endurance event (i.e. marathon, ultramarathon) (Gleeson, 2006). Currently, immune system research has gained some insight regarding exercise-induced trends from endurance training, but concrete data is still needed. Regarding sports that emphasize strength, power, and size (e.g. American football, weightlifting, throwing, etc.) the research is currently inadequate. By remedying the lack of research of the immune system pertaining to strength/ power sports may provide useful and practical applications to further performance.

One avenue of interest connected to the immune system is inflammatory markers. The rationale for the interests in inflammation is particular inflammatory markers can potentially provide information regarding recovery. Specifically, interleukin - 6 (IL-6) and C-reactive protein (CRP) have been identified as essential factors in the development of inflammatory responses (Fedewa, Hathaway, and Ward-Ritacco, 2017; Nishimoto and Kishimoto, 2006). In pathological diseases such as rheumatoid arthritis, described by levels of chronic inflammation, the expression of IL-6 and CRP are present in higher concentrations (Nishimoto and Kishimoto, 2006). As such, researchers in this field theorize that decreasing the above inflammatory markers may alleviate pathological diseases. Sports scientist and exercise physiologist have extended this theory to the recovery process following training. The expression of IL-6 following exercise, in some instances, is 100-fold higher than basal levels (Lancaster, 2006). Interleukin-6 is also influenced by exercise intensity and the degree of muscle damage acquired from a training bout. Correspondingly, because IL-6 mediates CRP release, it could be beneficial for athletes to find strategies to mitigate IL-6 levels (Gleeson and Robson-Ansley, 2006). Provided that BCAAs have been shown to mitigate tissue damage following exercise, it is possible that these inflammatory markers can be alleviated by supplementing with BCAAs. In turn, BCAA's can potentially optimize recovery leading to better performance.

Another aspect to consider regarding inflammatory cytokines is their influence on hormonal changes and psychological fatigue to training. Currently, we know that when IL-6 is released from the working muscle during exercise, it mediates the release of cortisol for hepatic glucose release (Robson-Ansley, de Milander, Collins, and Noakes, 2004). However, high levels of IL-6 have been shown detrimental, and induce “cytokine sickness”, a state where individuals feel exceptionally fatigued during training (Robson-Ansley et al. 2004). Theoretically, it would be beneficial to the athlete to keep IL-6 from reaching high levels. However, IL-6 has not been studied extensively in resistance training protocols, and its impact, if any, on the athlete or individual during resistance training has yet to be clarified. Hypothetically, high levels of IL-6, despite the exercise modality, would result in elevated cortisol which could affect anabolic-catabolic balance (e.g. testosterone to cortisol ratio). Potentially, supplementing with branched-chain amino acids (BCAA) could reduce levels of IL-6 during resistance training, and thus, aid in recovery/ adaptation.

All things considered, the immune system is influenced and influences many other physiological systems. As mentioned above IL-6 mediates cortisol release, cortisol release influences anabolism. The degree of muscle breakdown also affects these processes. Therefore, training intensity, volume, and exercise selection within the training bout must be taken into consideration. The first phase of the immune system’s response to exercise is defined as the inflammatory phase where a myriad of leukocytes, namely neutrophils and macrophages/ monocytes, occupy the target tissue (Gleeson, 2006; Saladin, Gan, and Cushman, 2018). Neutrophils and monocytes also release IL-6 to signal additional leukocytes to aid in this phase (Gleeson, 2006). Consequently, if muscle damage from the preceding training bout is excessive,

the above responses will rise correspondingly. However, the degree of muscle breakdown can be mitigated with the use of BCAA's. Thus, supplementing with BCAA's could reduce the above responses by mitigating the degree of muscle damage, thereby aiding in recovery/ adaptation.

Considering the above circumstances, the most important factor for athletes is performance. Performance, however, can vary substantially depending on the preceding training bouts. Hypothetically, maintaining high levels of training performance compounded over time would produce superior long-term gains. Again, this is because the athlete or individual could train at higher intensities. A simple and practical method to gauge changes in performance is to track jumps (i.e. static and countermovement). Because rate of force development (RFD) is sensitive to fatigue, drastic changes in jump height specify an athlete's level of preparedness (Sams, 2017). Previous literature has shown that jump performance following training typically declines due to accumulated fatigue (Ratamess et al. 2003; Sams, 2017). In theory, supplementing with BCAA's could mitigate decrements in performance by reducing muscle breakdown and corresponding biomarkers (e.g. IL-6, CRP, cortisol, etc.) thus allowing the athlete to maintain performance. Unfortunately, the literature is scarce concerning immune system biomarkers corresponding with levels of performance involving strength/ power sports.

Generally speaking, immune system research is in its infancy regarding sport and exercise performance. Additionally, the current literature on the immune system to training adaptations has been primarily focused on endurance exercise. By and large, the immune system is influenced by virtually all aspects of its internal and external environment. Consequently, there are many avenues to explore concerning recovery/ adaptation that may hypothetically support

supplementing with BCAAs for recovery efforts. However, direct evidence is lacking that supports the above theories in a resistance training paradigm.

Dissertation Purposes

1. To investigate the acute psychological differences between BCAA and a control group (CG) in response to high volume resistance exercise.
2. To investigate the effects of a clinical grade BCAA supplement compared to a CG on biological markers (CRP, IL-6, CK) associated with fatigue in response to resistance exercise.
3. To investigate the effects of BCAA and a CG on performance changes (SJ, CMJ, IMTP, and Bosco repeated jump test) in response to high volume resistance training.

Operational Definitions

1. Acute Fatigue – inability to maintain or repeat an absolute for output (Stone, Stone, and Sands, 2007)
2. Branched-chain Amino Acids – “free-form” version of the building blocks of protein used for supplementation (Burke, 2001)
3. C – Reactive Protein – an acute phase protein released from the liver that functions to coat foreign objects for opsonization; additionally, CRP is associated with systemic inflammation (Michigan, Johnson, and Master, 2011).
4. Cortisol – A steroid hormone that is released by the adrenal cortex in response to physical and psychological stressors. Cortisol has multiple metabolic functions for homeostasis; mediates the release of additional white blood cells to the area local damage (Zahorec, 2001).

5. Daily Analysis of Life Demands for Athletes – is a composite self-report measure that evaluates an athlete’s stress state and examines contributing factors to this condition (Rushall, 1990).
6. Interleukin – 6 – is a pleotropic cytokine released from nearly all cells of the body (Biffi, Moore, Moore, and Peterson, 1996). Interleukin – 6 is associated with systemic inflammation (Gleeson and Robson-Ansley, 2006).
7. Profile of Mood State Questionnaire – Is a 65-item questionnaire used to gain insight into a persons mood state (Nässi, Ferrauti, Meyer, Pfeiffer, and Kellmann, 2017).
8. Recovery Adaptation Process - the process of homeostasis and long-term physiological augmentations (Stone et al. 2007).
9. Session Rating of Perceived Exertion – a subjective measure of training session intensity (Sams, 2017).
10. T:C ratio – an indicator of anabolic/ catabolic state (Fry et al. 1993).
11. Testosterone – is an anabolic signaling hormone released by the testes/ ovaries. Testosterone plays a key role in protein synthesis. Testosterone is also sensitive to training volume and influences the T:C ratio.

CHAPTER 2

REVIEW OF THE LITERATURE

Improving athletic performance is a multifactorial discipline that requires a clear understanding of the recovery/adaptation process. The recovery/adaptation process can be complex; therefore, it is paramount that the athlete or coach has a sound monitoring program in place to evaluate fatigue. The term fatigue, from a sports performance perspective, can be somewhat ambiguous. One characteristic of fatigue is acute fatigue and is described as the inability to maintain or repeat an absolute force or power output (M. H. Stone et al. 2007). By understanding the mechanisms contributing to acute fatigue the athlete or coach can implement recovery strategies to mitigate decrements in performance.

The underlying factors contributing to fatigue can be physical, psychological, and physiological. These factors are often linked to a number of different conditions that affect the body's ability to perform at its best. Nutritional supplements offer a way to promote recovery and manage fatigue by various mechanisms that include reduced muscle breakdown, reduced perceived exertion, and improve focus. One of the most popular supplements is branched-chain amino acids (BCAA) (Williams, 2005) and has been used for years for improving athletic performance. The benefits of BCAAs include improved strength, endurance, and fatigue, etc. However, the reported benefits for BCAA claims vary depending on the type of exercise being performed (e.g. resistance training vs. endurance running). Despite the popularity of BCAAs, there are still some issues about their effectiveness for performance and fatigue management. Additionally, the assumed benefits for BCAAs have focused mainly on endurance type exercise. Because acute fatigue is not a single entity but rather multiple factors, it is essential to consider how BCAAs might interact with the different elements contributing to fatigue.

Psychological State

Fatigue can be affected, not only by physical training but also by psychological factors (Meeusen et al. 2013). Life events and daily stressors can affect the ability to perform at a high level. Therefore, incorporating a measure to evaluate psychological state can help improve the monitoring program. Auersperger et al. (2014) found that psychological responses preceded that of physiological changes to training. Additionally, psychological responses are more sensitive to training loads than biochemical markers and can detect levels of stress earlier than physiological changes. It also appears that psychological changes are more consistent with training loads than physiological markers (Raglin and Wilson, 2000; Saw, Main, and Gastin, 2016).

Branched-chain amino acids appear to have an impact on psychological state and mental performance during exercise. The rationale for this is that BCAAs interact with the central fatigue theory. By increasing the concentration of BCAAs in plasma effectively reduces tryptophan uptake that leads to the perception of drowsiness and fatigue induced by serotonin during exercise (Blomstrand, Hassmén, Ek, Ekblom, and Newsholme, 1997a; Blomstrand, Hassmén, and Newsholme, 1991; Burke, 2001; Greer, Woodard, White, Arguello, and Haymes, 2007). Several studies have investigated the effects of BCAA's on the psychological state in various training models in order to determine whether BCAAs can affect performance by reducing the perception of fatigue. The most arduous study was conducted by Takahashi, Suzuki, Takahashi, and Sato, (2000) where they had 19 male college athletes (long-distance runners) perform 1600m relay run for 24hrs consecutively. The athletes were divided into two groups, one group that was trained with BCAAs and the other with an equivalent placebo drink. Each participant was given 1g of BCAA or PLA after each 1600 m relay bout. Ratings of perceived exertion and category rate of pain scale (CPS) was recorded after each relay and POMS was

recorded pre, mid, and post-session. Despite the POMS score showing no difference between the groups, the results for RPE and CPS showed that the athletes who were trained with BCAAs reported a lower sensation of exertion and pain than those who were on the PLA. These findings suggest that the athletes who had trained with BCAAs mitigated the sensation of perceived exertion and pain.

In the previous study, BCAAs had no observable effect on POMS' responses. This observation could be due to the fact the athletes received the BCAA dosage in an irregular manner (1g after each 1600m bout). The effective dosage of BCAAs reported in the literature is 48 to 72mg/ kg and is usually given before exercise (Frank, Patel, Lopez, and Willis, 2018) and could explain why there was no noticeable effect on psychological state indicated by Takahashi et al. (2000). However, Hsu et al. (2011) demonstrated positive effects of BCAAs on POMS' responses after exercise. This study was a cross-over design, and subjects performed a single exhaustive bout of treadmill running (Bruce protocol). The subjects were given a BCAA drink or a PLA equivalent after exercise. The subjects were then asked to complete the POMS questionnaire to determine differences in psychological state. The main finding was that the BCAA trial was effective at reducing levels of fatigue indicated by the POMS questionnaire, and these responses were more pronounced 2 hrs post exercise compared to the PLA trial. The results from this study show that BCAAs reduce the subjective feeling of fatigue, but may also have applications to improve mental preparedness in athletes who train twice a day.

One of the most evident effects of BCAAs is its influence on alleviating subjective fatigue. Notably, subjective fatigue is a limiting factor in performance. Several studies investigating the effects of BCAA on psychological state have shown that BCAAs can be used to

reduce subjective fatigue, ratings of pain, and improve mental performance reaction time (Portier et al. 2008; Shimizu et al. 2012). For the most part, the scientific literature investigating the effects of BCAAs on psychological state have unanimously concluded that BCAAs are useful in positively influencing psychological state in some manner (Blomstrand et al. 1997a; Blomstrand, Hassmén, Ekblom, and Newsholme, 1991; Blomstrand, Hassmén, and Newsholme, 1991; Greer et al. 2007; Hsu et al. 2011; Portier et al. 2008; Shimizu et al. 2012). Presently, however, there is still no evidence to support the above results in a resistance training model. Perhaps, this is because the central fatigue theory is based on the duration of exercise. However, reports have shown that levels of tryptophan are known to increase in as little as 30 minutes after exercising (Nybo, Nielsen, Blomstrand, Moller, and Secher, 2003). This amount of time is well within the duration of standard resistance training. Therefore, the question remains if BCAAs impact the psychological state in resistance training paradigms similarly to endurance training.

General Immune Function and Inflammatory Response

Inflammation is a natural occurrence of the body's immune system. From the perspective of resistance training, inflammation occurs in response to the degree of microtrauma induced by the intensity of the training bout (Smith, 2000). The inflammatory response initiates a cascade of signaling events to clear tissue debris, promote adaptive responses (e.g. satellite cell activation, growth factors, cell signaling pathways, etc.), and limit musculoskeletal movement to the localized area to name a few (Saladin et al. 2018; Smith, 2000; Smith and Miles, 2000). As such, the inflammatory response has a considerable impact on acute fatigue and subsequent performance. It is essential to understand the role of inflammation in resistance training to identify the mechanisms that may be responsible for chronic inflammation, underperformance

syndrome, and acute fatigue. Additionally, understanding the inflammatory response to resistance training can help us better understand how inflammation affects our ability to perform repetitive training bouts and competitions.

The magnitude of inflammatory response to resistance training varies depending on the type of exercise, intensity, and duration (Bessa et al. 2016; Blannin, 2006; Smith, 2000). Before the onset of inflammation, there is a cascade of specific immune events that trigger the inflammatory response but are also interlinked to acute fatigue. The initial response in immune function is the occurrence of leukocytosis (Blannin, 2006; L. Smith and Miles, 2000). The most notable change in white blood cell count is neutrophils and monocytes which migrate to the localized area of the body that has been exposed to tissue trauma. These two leukocytes are involved in the release of pro-inflammatory cytokines, more specifically IL-6. Interleukin-6 is a pleiotropic cytokine that has many functions to include: modulation of cortisol release, the signaling of acute phase proteins such as C-reactive protein, and inhibition of anti-inflammatory cytokines (Biffi et al. 1996; Calle and Fernandez, 2010; Lancaster, 2006; Libardi, De Souza, Cavaglieri, Madruga, and Chacon-Mikahil, 2012). Thus, IL-6 is an essential regulator of the inflammatory response of the immune system.

In addition to inflammation, IL-6 may also directly affect fatigue. In a study by Robson-Ansley, de Milander, Collins, and Noakes (2004), they observed that subjects (male distance runners) given a recombinant (lab synthesized) form of IL-6 before a 10km time trial run significantly increased run times. Also, noted by the investigators, was the reported subjective feeling of fatigue and "heavy legs" sensed by the subjects. Increased levels of fatigue and depressed mood states were also observed in resting subjects given a recombinant form of IL-6

(Th-Schwalbe et al. 1998). Also, blocking the IL-6 receptor in patients with chronically elevated IL-6 appeared to suppress debilitating fatigue (Nishimoto and Kishimoto, 2006). Given the effects of IL-6 on subjective fatigue, some scientists consider IL-6 to be a fatigue signal to the central nervous system during exercise (Lancaster, 2006; Nishimoto and Kishimoto, 2006; Th-Schwalbe et al. 1998). As such, IL-6 secretion could have a profound effect on psychological state. Because of the known functions of IL-6, it might be advisable to find strategies to mitigate the release of IL-6 during resistance training (Blannin, 2006).

Another essential aspect to consider concerning inflammation is the "cytokine sickness" theory. This theory is described as the result of an increase in the level of cytokines that are involved in inflammation. The current thought is that excessive exercise-induced tissue trauma elicits a chronic inflammatory response resulting in elevated cytokines. Because cytokines communicate with the central nervous system, this theory proposes that improper recovery can lead to "sickness behavior." The symptoms of "sickness behavior" include negative changes in mood, the undesired to train, and decreased energy levels (Lancaster, 2006; Robson-Ansley et al. 2004; L. L. Smith, 2000). Much of the attention regarding "cytokine sickness" revolves around IL-6 elevation (Paula Robson, 2003) because IL-6 has the most marked changes in plasma levels in response to exercise (Blannin, 2006). This theory provides a mechanism for underperformance syndrome seen in athletes.

It is important to note that the immune system has multiple overlapping and redundant responses to exercise-induced tissue damage. The redundant mechanisms of the immune system make it particularly problematic in isolating known occurrences and the magnitude they have on recovery and acute fatigue. Interleukin-6 has grasped the most attention as discussed above. L. L.

Smith, (2000) describes a physiological response loop to exercise that can help clarify the onset of fatigue. To illustrate, training (whether endurance or resistance) has been shown to elicit leukocytosis and lymphocyte accumulation which contributes to the inflammatory response via cytokines (e.g. IL-6) and other factors. Also, exercising muscle releases IL-6 (A. Steensberg et al. 2001). Interleukin-6, via the HPA axis, leads to an increase in cortisol secretion. Cortisol secretion, concerning the immune function, has been shown to lead to neutrophilia and lymphocytopenia (Zahorec, 2001). Although this event is dependent upon the degree of tissue damage, the increase in neutrophil response can cause further damage (e.g. reactive oxygen species, oxidative burst) to local tissue if left unmanaged. Additionally, neutrophils also secrete IL-6 thus further contributing to the loop described by L. L. Smith, (2000). Taken the above mechanisms into account, there are multiple ways that these events may be associated with acute fatigue. Thus, there are many scenarios in which athletes could exacerbate this loop from multiple training sessions and competitions that are closely scheduled without proper rest.

Another vital aspect to consider for inflammation and fatigue is C-reactive protein (CRP). C-reactive protein is an acute phase protein released by the liver (Kengne, Batty, Hamer, Stamatakis, and Czernichow, 2012). C-reactive protein coats foreign bacteria and tissue debris for phagocytosis (Gleeson, 2006) and adds an additional aspect of immune defense. Notably, CRP is elevated in the presence of tissue damage and is a known indicator for levels of inflammation (Fedewa et al. 2017; Ford, 2002). The secretion of CRP is modulated by IL-6 (Blannin, 2006). Thus, high levels of IL-6 can further contribute to inflammation and acute fatigue based on the mentioned factors. The driving factors for the above events are related to the degree of tissue damage and could be dependent on the intensity of the training bout, frequency (without proper recovery), and duration. It is not uncommon for these factors to occur in a

competitive season in most sports. From a performance perspective, the fluctuations that occur with training and their impact on performance remain understudied.

Equally crucial for regulation of the immune system and inflammatory response is the secretion of hormones. Much of the scientific literature is centered round cortisol secretion and the interaction it has on immune function (Gabriel, Schwarz, Steffens, and Kindermann, 1992; P. Robson, Blannin, Walsh, Castell, and Gleeson, 1999; Zahorec, 2001). In vitro studies show that low levels of cortisol seem to improve immune function; whereas, very high levels appear to have immunosuppressive effects (Blannin, 2006). The importance of cortisol secretion is perceptible when observing the kinetics and proliferation of specific white blood cells. As such, cortisol secretion has been shown to modulate neutrophil count in plasma following training (Gabriel et al. 1992). The rise in neutrophil count, or neutrophilia, arises from bone marrow and is stimulated by cortisol secretion. This occurrence is necessary for the clearance of tissue debris; however, immature neutrophils from the bone marrow have been shown to spontaneously degranulate leading to acute inflammation. As such, neutrophils can be damaging (e.g. oxidative burst, ROS) to host cells by causing a cascade of damage that leads to necrosis (Camus et al. 1992; Zahorec, 2001). Because cortisol secretion modulates neutrophilia, and cortisol secretion is a function of exercise intensity, there could be some beneficial effects on recovery/ adaptation by attenuating cortisol secretion. Although this event is likely extreme and would take a severe training bout to induce, it is speculative that compounded exposure to repeated training bouts and competitions can limit the ability to recover.

Another important consideration to take into account is cortisol's effects on glucose regulation. When exercise duration increases, cortisol secretion also increases via IL6 release to stimulate glycogenetic pathways which include the conversion of amino acids to glucose

(Brownlee, Moore, and Hackney, n.d.; Galbo, 2001). In such events when exercise duration or intensity is high, muscle protein is catabolized to supply metabolic needs such as gluconeogenesis, peptides for immune response, and for the synthesizing of new cells to name a few (Brownlee et al. n.d.; Calder, 2006; Galbo, 2001). For athletes, this would be an adverse scenario especially for those participating in sports that require muscle hypertrophy to perform at higher levels. Thus, the body's ability to regulate these processes is affected by acute training variables (e.g. duration, intensity, and frequency, etc.) and when these variables cannot be controlled, such at times of competition, it may be beneficial for the coach or athlete to supplement with BCAAs to attenuate the above-mentioned issues.

Lastly, the ratio of testosterone and cortisol have been used as an indicator of anabolic-catabolic balance in athletes (Chen, Liao, Chou, Sung, and Tsai, 2017; Plisk and Stone, 2003), and numerous reports show that the T:C ratio is inversely related to training volume (Fry et al. 1993; Häkkinen, Pakarinen, Alén, Kauhanen, and Komi, 1987; Häkkinen, Pakarinen, Alen, Kauhanen, and Komi, 1988). As such, the T:C ratio has provided a useful variable for assessing the level of stress imposed on the athlete. Additionally, although not fully accepted, some reports demonstrate that an increase in T:C ratio is associated with increased strength in athletes (Fry et al. 1993; Häkkinen et al. 1987, 1988). Consequently, if cortisol levels become elevated, the anabolic effects of testosterone on adaptation become masked. Previous literature has shown that increased cortisol response can lower testosterone levels (Doerr and Pirke, 1976); additionally, cortisol may also allosterically interact with testosterone receptors (Mayer and Rosen, 1975) and subsequently affect performance. Because the degree of tissue damage affects the degree of cortisol release, it would be reasonable to assume that supplementing with BCAAs might attenuate the effect of cortisol on muscle growth recovery, and performance.

BCAAs and Immune Function

Training promotes alterations in immune function for homeostasis, growth, and recovery etc. (Cruzat, Krause, and Newsholme, 2014). The response of the immune system to exercise can be thought of like a balancing act between pro-inflammatory and anti-inflammatory signals which are necessary for immune cell kinetics. Multiple studies show that mild to moderate exercise is beneficial for immune function, but when training becomes intensified and prolonged, it may lead to immunosuppressive effects (Calder, 2006; Cruzat et al. 2014; Negro, Giardina, Marzani, and Marzatico, 2008). These scenarios are unlikely for recreational individuals training for health and aesthetics; however, athletes are often exposed to high levels of intense and prolonged training which may disrupt immune cell function and their ability to recover. Therefore the importance of recovery cannot be overemphasized in this regard. More recently, the use of BCAA has been shown to have significant benefits on the immune system by increasing cell proliferation and improving cell function (Cruzat et al. 2014; Walsh, 2006). Much of this evidence, however, is observed in clinical settings where BCAAs are used to treat patients with sepsis and severe burns (Calder, 2006). In some cases, these catabolic events are noted with urinary nitrogen excretion between 20 to 30 grams in extreme cases (Calder, 2006; Li, Yin, Li, Kim, and Wu, 2007) indicating a massive loss of protein. The extent this event in athletes is unclear, but there is evidence that BCAAs can help mitigate the degree of inflammation from reducing the level of muscle damage caused by resistance training.

The discussion of BCAA supplementation on immune function is an emerging but understudied topic in the field of sport and exercise science. Many of the current studies are conducted for clinical situations, and experimental designs are mainly performed in cultured cell

models (Chuang, Yu, and Wang, 1990; Esposito et al. 1985; Skaper, Molden, and Seegmiller, 1976). For instance, it has been observed *in vitro* that lymphocyte proliferation is impaired when BCAA availability is restricted (Calder, 2006). Other studies show that specific WBC responds to BCAAs in a dose-dependent manner in rodents (Jose and Good, 1973; Tsukishiro, Shimizu, Higuchi, and Watanabe, 2000). It is important to note that these studies do not necessarily provide sufficient evidence for the effectiveness of BCAAs on immune function. However, they do provide some information about the mechanisms underlying immune function and how BCAAs may be used to improve athletic performance. Previous literature investigating the effects of BCAA on immune function have centered around glutamine because glutamine provides an energy substrate for specific white blood cells to function optimally. Although, little has been done to investigate the direct role of BCAAs in immune function for athletic performance. Kephart et al. (2016) conducted a study comparing the effects of BCAA + CHO vs. CHO on immune responses to 3 days of rigorous weight training. Notable findings in this study were that BCAA+CHO mitigated the rise in monocyte response over the three days of weight training. The authors note that BCAA may have anti-inflammatory properties to help with muscle soreness and fatigue (Kephart et al. 2016).

BCAAs and Performance

During a competitive season, athletes are subjected to repetitive training sessions, practices, and competitions that require them to perform consistently at high levels. Unfortunately, their schedules are dictated by the competitive schedule that may not allow for adequate time for recovery between training sessions or competitions. This situation is when the benefits of nutritional strategies are most apparent for recovery and performance. Still, in the

scientific literature, a debate remains regarding adequate protein intake for athletes (American College of Sports Medicine, 2009; Antonio, Ellerbroek, Silver, Vargas, and Peacock, 2016; Schoenfeld and Aragon, 2018). Mero et al. (1997) observed a substantial decrease (~21%) in basal fasting levels of leucine in trained sprinters and throwers subjected to a high-intensity training program for five weeks (Mero et al. 1997). However, this decline was not observed in athletes given a supplemental dose of leucine. In this study, the athletes were consuming 1.26 g/kg of protein which is well above the recommended RDA of 0.8 g/ kg/ day. Thus, this study justifies the use the BCAAs supplementation for athletes, especially during the competitive season.

The question remains regarding the efficacy of BCAAs in enhancing acute performance. The known mechanisms are not entirely clear; however, BCAAs have been shown to reduce markers of muscle damage, ameliorate local inflammation through various pathways, and decrease serotonin levels by increasing the ratio of BCAA: tryptophan ratio to name a few (Bigard et al. 1996; Blomstrand et al. 1997a; Burke, 2001). Thus, based on the above mechanisms, it is possible to improve performance by enhancing recovery. Concerning athletic performance, some of the best indicators of competitive success are measures of RFD (e.g. jumps, sprints, throws, etc). These measures are significant because the actions in sport occur so quickly that max force is not attainable. Not to mention, RFD is more sensitive to acute fatigue than maximum strength (Buckthorpe, Pain, and Folland, 2014; Kraemer et al. 2006; Ratamess et al. 2003). Thus, maintaining high levels of muscle power is paramount for competitive success. Therefore many studies have investigated the effects of BCAAs on jump performance as an indirect measure of sports performance. In many reports, it is hypothesized that BCAAs can have a positive effect on performance by mitigating declines in jump height when subjected to some

form of training stress (Kraemer et al. 2009; Ratamess et al. 2003). However, the evidence to support this hypothesis is inconsistent.

Thus far, only a handful of studies have shown an improvement in performance after supplementing with BCAAs (Bigard et al. 1996; Hoffman, Ratamess, Kang, Falvo, and Faigenbaum, 2006; Kirby et al. 2012; Ratamess et al. 2003). Still, the benefits of BCAAs in these studies are small to modest to the extent that they are still questionable in effectiveness. Perhaps the most substantial evidence for the efficacy of BCAAs was reported by Ratamess et al. (2003). In this study resistance trained males completed four weeks of total body resistance exercises design to induce a state of overreaching. The significant findings of this study were noticed in the first two weeks when subjects in the BCAA group substantially mitigated declines in the 1RM bench, 1RM squat, and peak power in the ballistic bench press and jump squat. The finding from Ratamess makes a strong case for the effectiveness of BCAAs for performance enhancement especially in situations where athletes are exposed to abrupt increases in training volume or sudden competitions. Another substantial study for the effectiveness of BCAAs are works by Shimomura et al. (2010). This study was conducted on untrained adolescent females that performed seven sets of 20 repetition bodyweight squats. To detect changes in performance, the subjects were tested on knee extension isometric peak force. The investigators found that two days after the exercise bout basal levels of peak force returned to baseline in the BCAA trial; whereas, peak force remained depressed (20%) in the placebo trial (Shimomura et al. 2010). These findings are in agreement with data by Waldron et al. (2017) where BCAAs mitigated the decline in knee extension isometric peak force (-5% vs. -20%) compared to the placebo

following hypertrophy training (7 sets of 10 reps at 70% 1RM). As such, these findings suggest that BCAA may be beneficial for mitigating declines in performance.

On the contrary to the above studies, multiple reports reflect BCAAs show no difference in measures of performance. For instance, Escobar et al. (2016) had ten resistance trained males perform ten sets of 8 repetitions of eccentric squats at 70% 1RM followed by five sets of 20 split squat jumps. Performance measures consisted of vertical jumps, maximal voluntary contraction, and jump squats. Despite BCAAs showing favorable signs for markers of muscle damage and subjective soreness, there were no differences in performance between the groups. A similar study conducted by Jackman, Witard, Jeukendrup, and Tipton, (2010) showed similar findings in knee extensor MVC. Ten sets of 12 repetitions of knee extension were conducted with an eccentric overload at 120% of 1RM in 24 untrained males. Again, even though BCAAs mitigated subjective feelings of muscle soreness, there were no performance differences between the groups. Multiple studies show that BCAA has no significant effect on performance (Howatson et al. 2012; Jackman et al. 2010; Skillen et al. 2008; Spillane, Emerson, and Willoughby, 2013).

The focus of the above studies has been on the effects of BCAA on acute performance regarding explosive movements and strength, or measures that elude to muscle function. What makes it challenging to fully elucidate the effects of BCAA on performance is the fact that many studies use BCAAs in combination with other supplemental sources (e.g. CHO, whey protein, caffeine, etc) (Hoffman et al. 2006; Kraemer et al. 2006; Willoughby, Stout, and Wilborn, 2007). Therefore, it is difficult to determine the effects of BCAAs on performance alone. Additionally,

the protocols used in many of these studies differ in their methodology. Therefore, there are many limitations to inferring the effects of BCAA on acute performance.

Summary

In summary, the factors that contribute to fatigue in athletic performance are numerous. Psychological, physiological, and physical factors all play an important role in fatigue and acute performance. As such, the coach or athlete should be aware of these factors and take appropriate actions to reduce unnecessary fatigue. Through various mechanisms, BCAAs can potentially affect performance by reducing fatigue on the aspects mentioned above. Numerous studies show that BCAAs have a profound effect on subjective feelings of exertion and fatigue. This finding alone may be enough benefit for athletes to consider supplementing with BCAAs to improve their performance.

Recently, BCAAs have been used to treat clinical patients (e.g. sepsis, severe burns, etc.) (Calder, 2006). As such, the use of BCAAs are not limited to just physical and psychological aspects but may also have applications for improving immune function. Thus, the use of BCAAs for improving sports performance by enhancing recovery through immune function has gained some interest in the sport and exercise field. However, much of the work on BCAA supplementation and immune function for sports enhancement is in its infancy. Through known mechanisms of the immune system 's response to BCAAs, researchers have found that certain white blood cells are more abundant and active; however, this has been shown mainly in cell cultures (Calder, 2006). As such, much of the current work on immune function for sport remains speculative.

Paradoxically, the benefits of BCAAs for athletes are starting to be recognized more for recovery rather than performance (Negro et al. 2008). It is assumed that improving recovery would subsequently improve performance. However, multiple studies show improved psychological and physiological outcomes from BCAAs without concomitant benefits to performance. Of course, there are methodological limitations to some of these studies that may lead to conflicting results. As such, BCAA research for acute performance concerning strength/power athletes warrants further attention.

CHAPTER 3

THE EFFECTS OF BRANCHED CHAIN AMINO ACID SUPPLEMENTATION ON PSYCHOLOGICAL STATE IN RESPONSE TO RESISTANCE TRAINING

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ABSTRACT

PURPOSE: The purpose of this study was to examine the acute effects of BCAAs on subjective psychological fatigue and soreness following multiple resistance training bouts in resistance trained males. **METHODS:** Seventeen (Ages: 25.2 ± 3.5 ; BM: 92.7 ± 12.0) resistance trained males were randomly assigned to either a BCAA group or an NS group. The subjects performed resistance training bouts (squat and bench press; 5 sets x 10 reps at 95% RI of their 1RM) on two occasions within the same week. The POMS was given on day 0 and day 6. The DALDA, sRPE, and soreness survey were given on day 0 - 6. **RESULTS:** Our results indicate that there was no statistically significant difference between the groups at any time-point for all subjective measures. **CONCLUSION:** Our findings indicate that BCAAs do not have any impact on psychological fatigue or subjective feelings of soreness in resistance trained males following two resistance training sessions.

Keywords: *psychological fatigue, profile of mood state, branched-chain amino acids, daily analysis of life demands*

INTRODUCTION

Preparing an athlete for competition is a process that relies on numerous factors such as physical fitness, physiology, technical and tactical strategies, and psychology (Stone, Stone, and Sands, 2007). Each element is essential; in that, they overlap and contribute to the trainability of the athlete. Of course, some attributes will dominate in their emphasis depending on the stage of the training process, but an athlete's psychological state will always influence the task at hand. For instance, the level of motivation, focus, and arousal, etc. will continually play a role in the approach to training emphasis, and this can have a significant impact on training effort.

When monitoring an athlete's acute fatigue and recovery, a variety of tests and examinations (e.g. blood markers, heart rate, and jumps, etc.) can provide insight as to how the athlete is responding to the training load. However, some of these assessments require special equipment, invasive techniques, and technical laboratory experience. Additionally, these tests may be time-consuming which limits their use to provide immediate feedback. Psychological questionnaires can be completed and analyzed quickly and may provide important information related to athlete fatigue and recovery. In some instances, psychological changes in relation to the training load can precede the detection of biological markers (Meeusen et al. 2013). Early detections is crucial for assessing non-functional overreaching and central fatigue. Thus, the psychological state is an important variable to monitor for an athlete's wellbeing, motivation, and training effort.

One proposed method to help manage the psychological strain experienced from training is using nutritional supplementation. Supplementing with branched-chain amino acids (BCAA) is a potential approach that could be used by athletes for the proposed benefits of reducing perceived effort and mental fatigue (Burke, 2001). The rationale for BCAA usage among athletes

is to decrease the systemic tryptophan: BCAA ratio which is known to influence perceptual fatigue (Jeukendrup and Gleeson, 2004). The literature exploring the effects of BCAAs on psychological state in response to endurance exercise has been, for the most part unanimous, in that BCAAs typically have a positive effect on alleviating perceived exertion and mood state (Greer, White, Arguello, and Haymes, 2011; Hsu et al. 2011; Portier et al. 2008; Shimizu et al. 2012; Takahashi et al. 2000; VanDusseldorp et al. 2018). For example, Takahashi et al. (2000) had trained endurance athletes supplement with either BCAA's (1g after each 1600m bout) or a placebo drink. In this study, the athletes performed a 1600m relay run for a consecutive 24 hours. They found that BCAAs dramatically decreased rate of perceived exertion (RPE) and category rate of pain scale (CPS) compared to the placebo. Hsu et al. (2011) reported similar findings in fatigue response indicated by the POMS questionnaire after having subjects complete an incremental treadmill run to exhaustion. Greer et al. (2011), investigated the effects of BCAA's on perceived exertion on subjects completing multiple 90 min cycling bouts followed by 15 min time trials. Notably, the BCAA group reported lower RPE's than the placebo group.

The studies examining BCAA's effect on psychological state are mainly from an endurance context. Based on preceding literature, there are assumptions that BCAA's would help reduce perceived exertion and mental fatigue in all categories of sport and training. However, inferences from endurance-based studies may be inadequate for strength power-sports. Currently, there has yet to be a proposed study examining the effects of BCAA's on psychological state using a resistance training model. Therefore, the purpose of this investigation was to examine the effects of BCAA on acute perceived soreness, Profile of Mood Disturbance, Daily Analysis of Life Demands for Athletes (DALDA), and rating of perceived exertion (RPE) following resistance training.

METHODS

Experimental Approach to the Problem

To evaluate the usefulness of BCAA's effect on acute fatigue and recovery concerning psychological aspects this investigation was designed in a randomized approach. The study was one week in duration and required subjects to perform a series of psychological questionnaires, resistance exercise, and muscular performance test (figure 2). The basis of this study design was to introduce an abrupt increase in training volume that would cause muscle damage and muscle soreness. By doing so, the study design would allow the researchers to detect psychological changes between the BCAA group and a non-supplement group (NS) in response to resistance exercise.

Subjects

Seventeen recreationally trained males participated as subjects. Inclusion criteria for subject participation were at least one year of resistance training experience and the ability to properly perform resistance training exercises (squat and bench press). The subjects were randomly assigned to either the BCAA group (n = 8): ages 26.2 ± 3.5 ; body mass 90.9 ± 3.5 ; and a non-supplement group (NS) (n = 9): ages 24.0 ± 3.3 ; body mass 95.3 ± 13.7 . All the subjects were screened for physical health issues using the NSCA health/ medical questionnaire to determine eligibility further. There were no physical issues reported to consider any of the subjects as ineligible. All subjects were notified of the potential risk/ benefits of this study and signed informed consent. The study was approved by the East Tennessee State University Institutional Review Board.

The subjects in this study assigned to the BCAA group were given 0.17g/ kg of BCAA (Ajipure Fusi-BCAA pharmaceutical grade, made by Ajinomoto) with 20 oz of water mixed with

a non-caloric sugar-free flavor (Propel zero calorie mix). The BCAA's were given on each day of the study and were required to be taken 30 minutes before performance testing or training. Additionally, a second identical BCAA mix was given to the subjects on days when resistance training took place. The second mixture was provided just before the training session started and consumption was finished just before the end of the session. A diet log was recorded for each participant retrospectively for the day prior. The diet log was gathered on each day of the experiment (6 days).

Questionnaires

To assess the psychological state of the subjects, POMS, DALDA, soreness survey, and sRPE data were gathered during the study. The test-retest reliability for POMS and sRPE have been reported in the literature as 0.95 and 0.82, respectively (Lamb, Eston, and Corns, 1999; Mastro, French, and Hall, 1987). Figure 2. outlines when each questionnaire was completed by the subjects. The POMS (short form 40 item) scale was used to assess the following criteria: tension, depression, anger, vigor, fatigue, and confusion as described by Grove and Prapavessis (1992). Since the POMS should be a weekly assessment, subjects also completed the DALDA days 1 through 6 to assess daily stressors (Rushall, 1990). A soreness survey (figure 1) was given to each subject on days 0 thru 6 to identify localized muscle soreness (Sands, McNeal, Murray, and Stone, 2015). Lastly, session RPE was evaluated after each training and testing session using Borg's CR-10 scale (Egan, Winchester, Foster, and McGuigan, 2006).

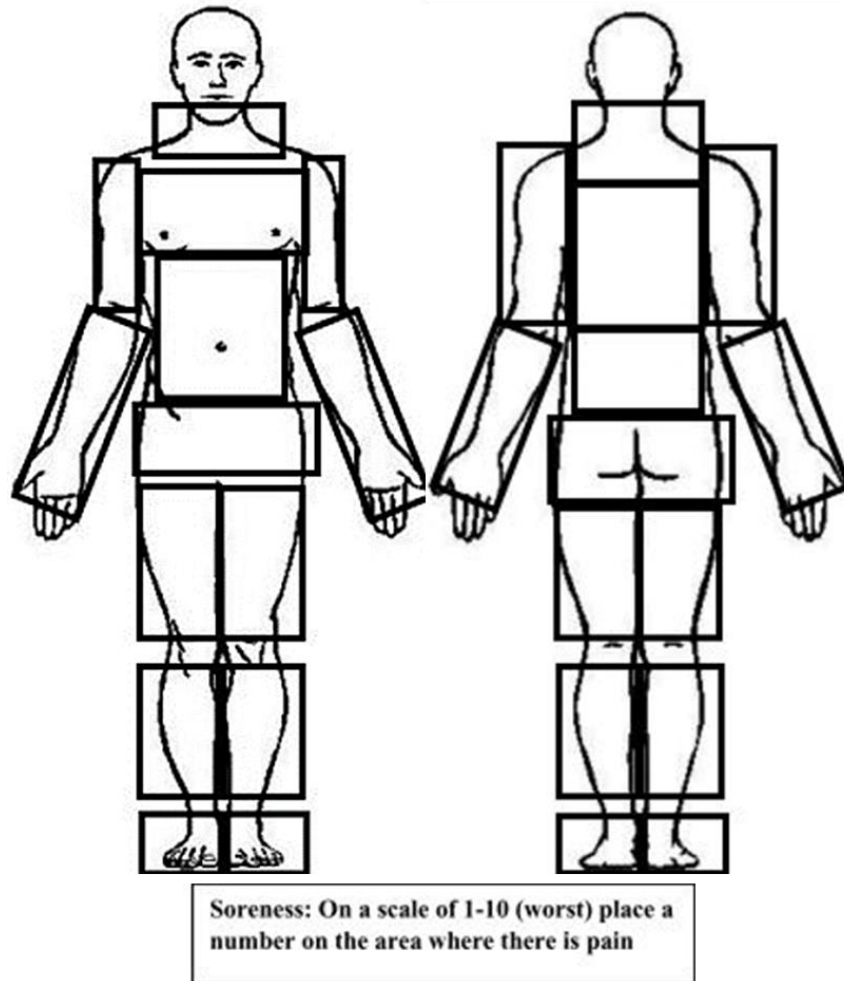


Figure 1. Example of perceived soreness survey

Experimental Design

An overview of this design is further described in figure 2. The study was 7 days in length (Days 0 – 6, day 0 was familiarization). The subjects were required to fill out psychological questionnaires on each day of the study. Each day commenced at approximately 6 am; therefore, psychological state would be marginally influenced by daily events. To isolate differences between the BCAA and NS groups, all subjects were required to take each questionnaire fasted; however, subjects assigned to the BCAA group were instructed to drink

their BCAA mix while answering the questionnaires. The POMS questionnaire was only answered on days 0 and 6. The DALDA, soreness survey, and sRPE were answered on days 1 – 6. The DALDA and soreness survey were answered prior to any performance testing or resistance training, and sRPE was collected after testing and/ or resistance training. Overall, the study design was conducted to detect changes in psychological state in response to the training load.

Statistical Analysis

Differences in psychological variables were analyzed using a mixed method analysis of variance with repeated measures. Tukey post hoc test were used for pairwise comparisons between the groups for each variable and time point. Violations of assumptions were mediated by transformation of all datapoints within a dataset. Sphericity was assessed using Mauchly's test. If sphericity was violated a Greenhouse-Geisser correction was applied to the corresponding F ratio. Additionally, Hedge's g effect size (ES) with 95% confidence interval (CI) was calculated to examine the standard difference in group means (BCAA vs NS) at each time point. The effect size scale used to determine magnitude of effect was the following: 0.0 - 0.2 trivial, 0.2 - 0.6 small, 0.6 -1.2 moderate, 1.2 - 2.0 large, and 2.0 - 4.0 very large (Hopkins, 2006). Statistical analysis was conducted using Jamovi statistical software (ver. 0.9.5.11) and Microsoft Excel XLSTAT (ver. 16.0)

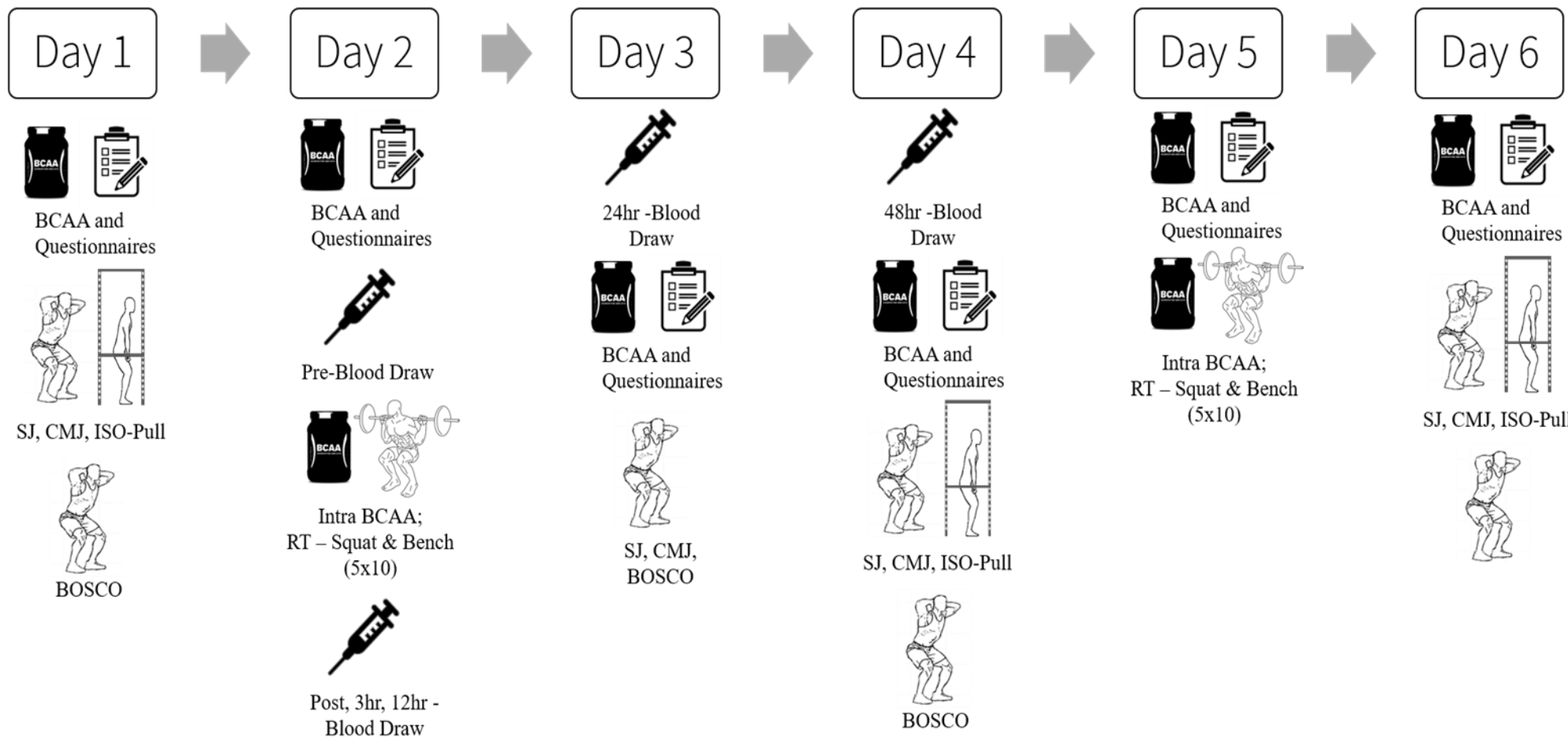


Figure 2. Diagram of testing procedures

- POMS taken on days 0 and 6 (day 0 not shown in diagram)
- DALDA, sRPE, soreness survey taken on days 1-6
- Resistance training (5x10 Squat and Bench) day 2 and 5
- BCAAs given every day of the study and twice on RT days

RESULTS

Profile of Mood

The POMS questionnaire was analyzed using the total mood disturbance score (TMD). The TMD is a sum of POMS criteria defined in the questionnaire. A mixed method repeated measures ANOVA indicates that all effects were non-statistically significant at $p < 0.05$ (**Figure 3**).

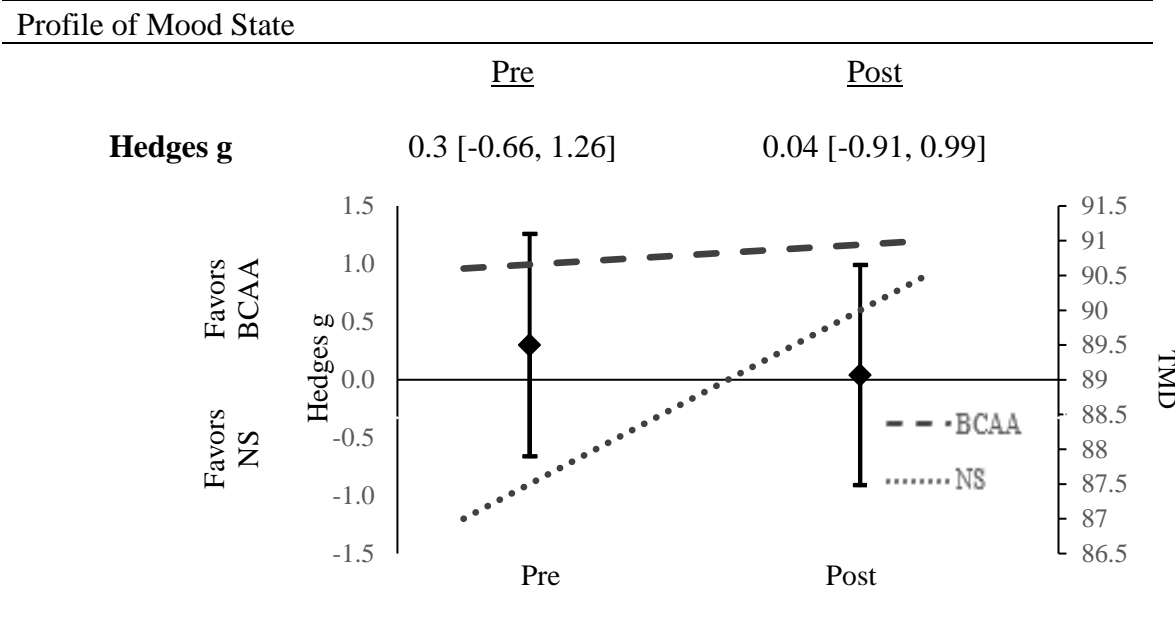


Figure 3. Profile of Mood State Questionnaire – Total Mood Disturbance Score

- X-axis shows the changes in TMD pre-to post for the BCAA and NS group
- Y-axis shows the ES with 95% CI for the respective time-point

Daily Analysis of Life Demands

Daily Analysis of Life Demands were analyzed by taking sum of the “less than normal responses” between the groups. A mixed method repeated measures ANOVA indicates all effects for DALDA responses were non-statistically significant at $p < 0.05$ (**Figure 4**).

Soreness Rating

Soreness rating was analyzed by summing the perceived local muscle responses. A mixed method repeated measures ANOVA showed a statistically significant difference in soreness responses compared to Day 1, $F(5, 75) = 10.2, p < 0.0001$. A Tukey post hoc test reveals that Day 3 soreness ratings were statistically significantly different from Day 1 soreness ratings, $p < 0.0001$. However, there was no statistically significant difference between groups at any timepoint at $p < 0.05$ (**Figure 5**).

Session Rating of Perceived Exertion

A mixed method repeated measures ANOVA showed a significant difference in sRPE throughout the study compared to Day 1, $F(5, 75) = 11.1, p < 0.0001$. However, there was no statistically significant difference between groups at any time point (**Figure 6**).

Daily Analysis of Life Demands for Athletes

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Hedges g	-0.44 [-1.41, 0.52]	-0.68 [-1.66, 0.29]	-0.8 [-1.79, 0.18]	-0.59 [-1.56, 0.37]	-0.28 [-1.24, 0.67]	-0.51 [-1.47, 0.46]

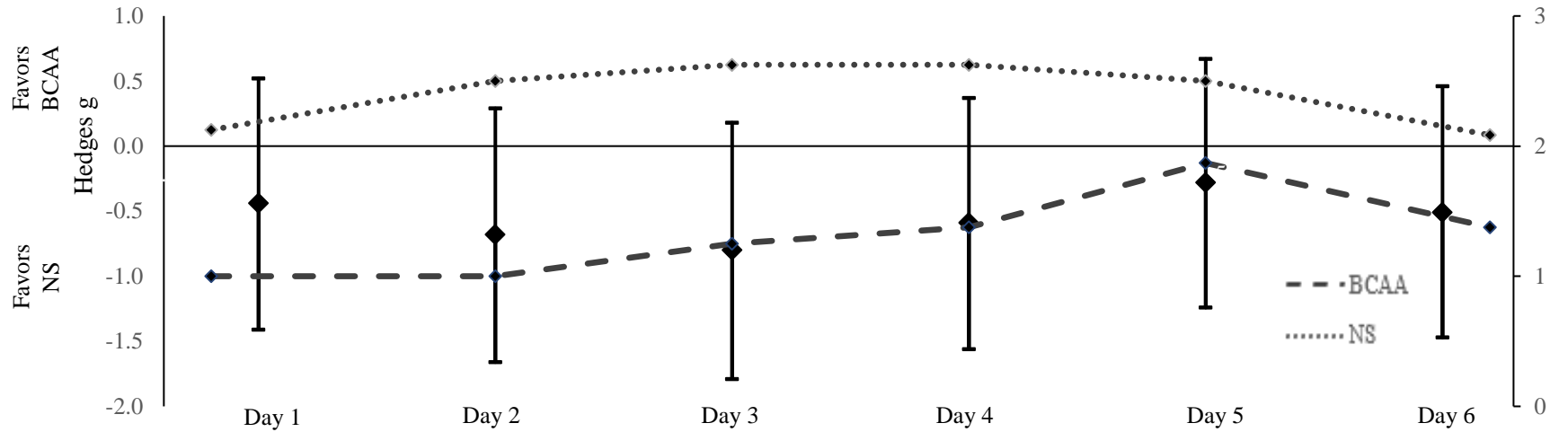


Figure 4. Daily Analysis of Life Demands for Athletes – sum of “worse than normal” responses

- *x-axis* shows the sum of “worse than normal” responses Day 1 – Day 6 for the BCAA and NS group
- *y-axis* shows the ES with 95% CI for the respective time-point

Session RPE

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Hedges g	0.06 [-0.89, 1.01]	-0.14 [-1.1, 0.8]	-0.18 [-1.13, 0.76]	-0.48 [-1.45, 0.47]	0.1 [-0.84, 1.05]	0 [-0.95, 0.95]

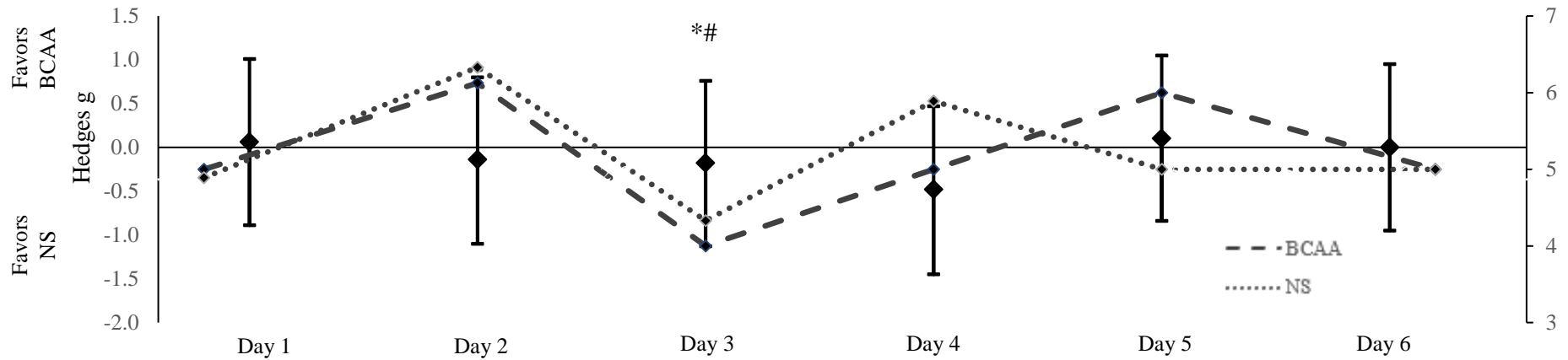


Figure 5. Session Rating of Perceived Exertion

- *x-axis* shows the sum of perceived soreness responses Day 1 – Day 6 for the BCAA and NS group
- *y-axis* shows the ES with 95% CI for the respective time-point
- * indicates statistical difference from Day 1 perceived soreness responses
- *# indicates statistical difference from Day 2

Perceived Soreness

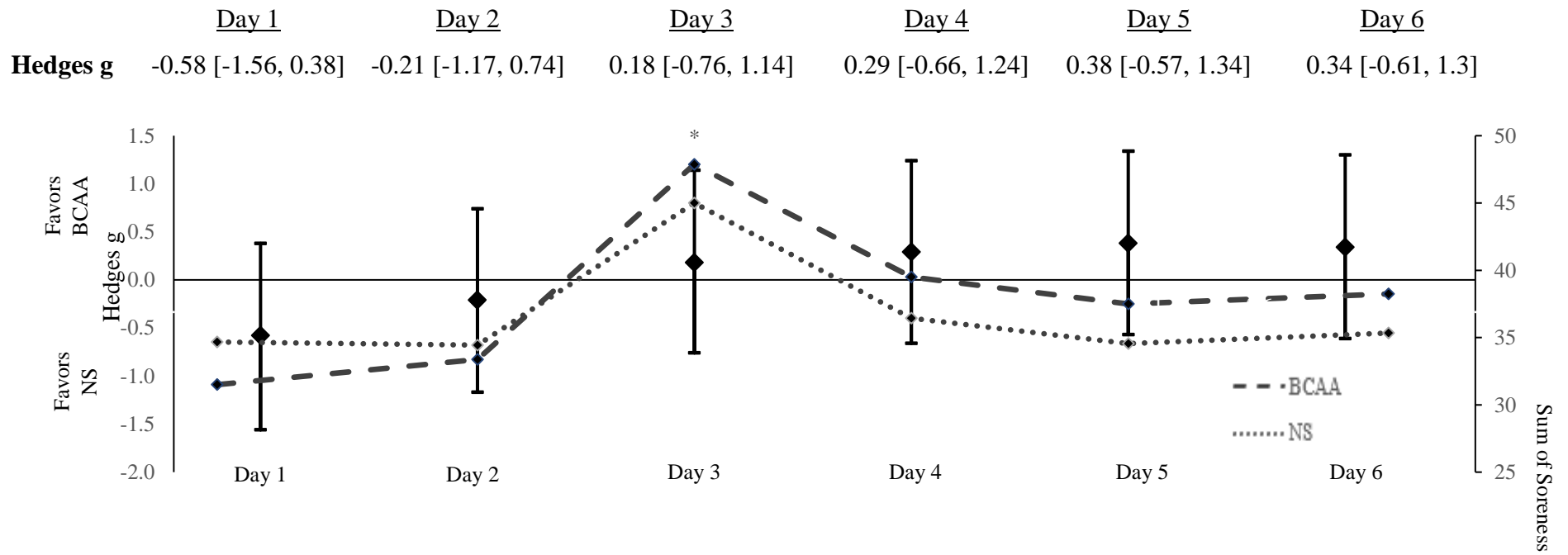


Figure 6. Perceived Soreness

- *x-axis* shows the sum of perceived soreness responses Day 1 – Day 6 for the BCAA and NS group
- *y-axis* shows the ES with 95% CI for the respective time-point
- * indicates statistical difference from Day 1 perceived soreness responses

DISCUSSION

Many in the field of sport and exercise science believe that psychological changes could be the first indication an athlete may be non-functionally overreached or over-trained (Meeusen et al. 2013). Although the intent of the study was not to investigate overreaching/ over-training, acute changes in psychological state are a function of overall recovery. The purpose of monitoring psychological state is to potentially gauge recovery, prevent non-functional overreaching, and provide an ideal circumstance to maximize training. This study aimed to investigate the effects of BCAA's on psychological state and to what extent they may affect recovery.

In the study, we used several psychological questionnaires to estimate psychological state in response to high volume resistance training. Our results show that there was no statistical difference between the BCAA and NS group for any effect (e.g. group and group x time) for any of the subjective measures. Although there was no statistical difference between the groups, standard mean difference (i.e. effect size) show fluctuating outcomes as the study progressed. Neither the BCAA or the NS group showed consistent results to substantiate the effect of BCAA's on psychological state. Perhaps the most substantial outcome of the study was the rise in TMD scores. The TMD trend suggests that BCAA's had a mitigating effect on overall mood disturbance which may give some credence for their use; however, this was only shown in one facet of the psychological measurements (i.e. POMS questionnaire).

It was anticipated that the BCAA group would display lower outcomes for perceived mood state and soreness among all the subjective measures. However, that was not the observed outcome. Previous literature exploring the effects of BCAA's on subjective measures (i.e. POMS, DALDA, sRPE, perceived muscle soreness, etc.) in response to endurance exercise have

shown favorable results for BCAAs (Bigard et al. 1996; Blomstrand, Hassmén, Ek, Ekblom, and Newsholme, 1997b; Blomstrand, Hassmén, and Newsholme, 1991; Portier et al. 2008; Shimizu et al. 2012; Shimomura et al. 2010; Takahashi et al. 2000). For example, Takahashi et al. (2000) had two groups of endurance athletes perform a relay run of 1600m uninterrupted for 24 hours. In this study BCAA's dramatically reduced signs of fatigue indicated by sRPE and CPS; however, very few sports endeavors bear a resemblance to this model. Although the previous research studies show a decrease in perceived fatigue via RPE, CPS, and perceived soreness, etc. none of them examined the effects using a resistance training paradigm.

Taking BCAA's to reduce fatigue is based upon the central fatigue hypothesis. The central fatigue hypothesis is a common approach, among endurance athletes, in hopes of reducing the conversion of free tryptophan to serotonin which is known to have effects on mood and aggression (Jeukendrup and Gleeson, 2004). The concept of the central fatigue hypothesis is that during prolonged exercise there is an increased mobilization in fatty acids (FA). Fatty acids and tryptophan share the same carrier protein albumin. The mobilization of FA due to exercise leaves fewer binding sites for tryptophan; therefore, the concentration of free tryptophan increases. Furthermore, tryptophan and BCAAs compete for the same transporting molecule across the blood-brain barrier. Consequently, if the free tryptophan: BCAA ratio increases, it is hypothesized that this would lead to an increase in serotonin and as a result increase perceptual fatigue. Thus, supplementing with BCAA's would hypothetically reduce the entry of free tryptophan across the blood-brain barrier and mute serotonin's impact on fatigue.

Correspondingly, the scientific literature supports the notion of the central fatigue hypothesis when applied to subjective measures for endurance exercise (Blomstrand et al. 1997b; Blomstrand, Hassmén, and Newsholme, 1991; Takahashi et al. 2000). However, BCAA's did not

attenuate subjective fatigue in this study. This may be explained by the nature of resistance exercise compared to endurance exercise. Notably, resistance training bouts are intermittent and tax the energy systems differently. It is plausible that the duration or the training load of the resistance training bouts in this study was not long enough to see an effect. Additionally, it could be that central fatigue is not a primary factor for resistance training because of the nature of the exercise.

In the context of this study's findings, it does not appear that BCAA's have a meaningful effect on psychological state in a resistance training model. To the knowledge of this author, this is the only study to examine BCAA's effect on psychological state for a resistance training paradigm. Prior studies examining the effect of BCAA's on psychological state were mainly conducted from an endurance perspective (e.g. cycling, running, soccer match, etc.), and generally, found that BCAA's had a positive effect on subjective fatigue from training (Blomstrand et al. 1997b; Blomstrand, Hassmén, and Newsholme, 1991; Greer et al. 2011; Hsu et al. 2011; Portier et al. 2008; Takahashi et al. 2000). However, this does not imply that BCAA's fail to influence psychological state from a resistance training focus. There are some limitations to this study that may have failed to capture an effect. Notably, the small sample sizes and the number of repeated measures influence the statistical power of capturing an effect between the groups in this study. Other limitations, such as previous resistance training or lack thereof may influence the perceived outcome of each questionnaire. In this study, we did not control previous resistance training before data collection which is a notable factor for the results. Equally important, although each subject had at least one year of resistance training, there were considerable differences in resistance training experience. Some subjects were more concordant with their physical abilities and were able to push themselves to a greater degree, and

thus likely influenced subjective outcomes. Another limitation could be the length of the study. In our investigation, the subjects only lifted twice which may not have been a large enough stressor to elicit an effect. Future studies exploring the effects of BCAA's using this model should control for prior training at least two weeks before data collection and increase the number of training bouts.

CONCLUSION

Branched-chain amino acids do not appear to have a substantial effect on psychological state from a resistance training perspective. This study concludes:

1. BCAAs appeared to mitigate the rise in total mood disturbance scores after 6 days of continuous performance testing and resistance training. BCAAs may have application to resistance trained males for reducing mood disturbance following high volume resistance training.
2. BCAAs showed no consistent differences compared to the non-supplement group in the sum of "less than normal" responses in the DALDA questionnaire throughout the study.
3. BCAA's indicated no apparent effect on perceived soreness compared to the NS group throughout the study.

The effects of BCAA on psychological state were not substantial or consistent throughout the study. Future research investigating the effects of BCAA's on psychological state from a resistance training perspective may require a more extended duration study and an increased number of training bouts.

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CHAPTER 4

THE EFFECTS OF BRANCHED CHAIN AMINO ACID SUPPLEMENTATION ON ACUTE MARKERS OF FATIGUE AND PERFORMANCE

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ABSTRACT

PURPOSE: The purpose of this study was to examine the acute effects of BCAAs on inflammatory markers associated with fatigue and subsequent performance changes following multiple resistance training bouts in resistance trained males. **METHODS:** Seventeen (Ages: 25.2 ± 3.5 ; BM: 92.7 ± 12.0) resistance trained males were randomly assigned to either a BCAA group or an NS group. The subjects performed resistance training bouts (squat and bench press; 5 sets x 10 reps at 95% RI of their 1RM) on 2 occasions within the same week. Performance variables were measured using the isometric mid-thigh pull (IMTP), SJ and CMJ, and Bosco repeated jump test. The blood markers used were CK, IL-6, CRP, T, and C. Performance measure were conducted on days 1, 3, 4, and 6. Blood markers were taken pre, post, 3hrs, 12hrs, 24hrs, and 48hrs following the first resistance training bout. **RESULTS:** There was a statistically significant rise in CK for the NS group 12hrs post exercise ($p < 0.05$). There was a statistically significant rise in T:C ratio for the BCAA group 12hrs post exercise ($p < 0.0001$). There were no differences in IL-6 and CRP between the groups. There were no statistically significant differences in SJ, CMJ, IMTP, and IMTP-RFD. There was a statistically significant rise in fatigue index for the BCAA group throughout the study ($p < 0.05$). **CONCLUSIONS:** BCAAs may have an impact on acute recovery indicated by CK and TC ratio. Although, no statistically significant changes were observed for performance variables, BCAA's did appear to mitigate declines in RFD following RT. Based off our findings BCAAs could be beneficial for athletes' recovery during times of contiguous training and competitions.

Keywords: *branched-chain amino acids, interleukin-6, C-reactive protein, T:C ratio, jump height, isometric mid-thigh pull*

INTRODUCTION

In the last few decades, immune system research in the field of sport and exercise science has been increasing. It is presumptive that the emergence of immunological research was in large part prompted by the occurrence of illnesses observed in endurance athletes following heavy training and competition (Gleeson, 2006). As a result, sports scientist and medical professionals have been investigating the mechanisms contributing to the incidence of illness to alleviate such events. As the research in this area evolved, emerging theories regarding cytokines and acute phase proteins and how they affect inflammation have taken an interest in recovery and performance. Inflammation can be characterized as a defense mechanism necessitated by the immune system (Benaroyo, 1994). C - reactive protein is an acute phase protein released by the liver, and is well established as an indicator of inflammation in the medical literature (Kengne et al. 2012; Sardeli et al. 2018). Another indicator of inflammation is interleukin-6 (IL-6). There is an associated rise of IL-6 in patients with type 2 diabetes and has been regarded as a reference for chronic inflammation (Petersen and Pedersen, 2005; Tilg, Dinarello, and Mier, 1997). Additionally, IL-6 is shown to mediate cortisol release (Robson-Ansley et al. 2004), which in turn, can impact T:C ratio, an indicator of anabolic-catabolic balance (Fry et al. 1993; Kraemer et al. 2006). As such, the above inflammatory markers are often studied in performance research in hopes to gain insight into the recovery process.

The recovery notion surrounding these inflammatory markers is that by alleviating their elevation following exercise would potentially benefit subsequent training and competition performance. By understanding the time course of the above markers could guide recovery and training strategies. A few studies have shown some promising results that support this forgoing theory (A. L. Bessa et al. 2016; Pournot et al. 2011). To illustrate, Pournot et al. (2011),

investigated the time course of inflammatory markers in a simulated trail run (45 min treadmill run with cycles of uphill, downhill, and flat every 3 min) with endurance athletes. Immediately following exercise, they incorporated cryotherapy or passive recovery as a treatment to examine the effects this would have on inflammation. Seemingly, a noticeable trend was apparent with inflammation post-exercise; additionally, cryotherapy dramatically alleviated the rise in inflammation. This finding gives credibility to find recovery strategies to alleviate CRP and IL-6 that may aid in athletic performance. On the contrary to these findings, however, previous literature has shown altering the inflammatory process to training may have detrimental effects on subsequent muscle adaptation (Mackey et al. 2007; Mikkelsen et al. 2009). Therefore, it is important to consider how altering the inflammatory process may affect the athlete long-term.

Branched-chain amino acids are a “popularly” used supplement to increase muscle protein synthesis, decreasing muscle breakdown, and alleviating mental fatigue, etc (Jackman et al. 2010; Takahashi et al. 2000; Tipton, Ferrando, Phillips, Doyle, and Wolfe, 1999). Creatine kinase (CK), an indicator of muscle damage, substantially increases after exercise but can be mitigated by supplementing with BCAAs (Coombes and McNaughton, 2000; Kraemer et al. 2006). This finding suggests that BCAAs alleviate the degree of muscle damage induced by exercise. As such, this concept could extend to the degree of inflammation accumulated by training. In theory, supplementing with BCAAs, by way of reducing muscle damage, could mitigate the accumulation of inflammation induced by exercise.

Concerning the above statements, there are some gaps in the scientific literature, however. The time course of specific inflammatory cytokines has been mainly studied in models with an endurance emphasis (A. L. Bessa et al. 2016; A. Bessa et al. 2008; Pournot et al. 2011; Robson-Ansley et al. 2004). Differences in blood flow, catecholamine response, tissue damage,

etc. would likely affect the distribution and magnitude of inflammatory markers found in plasma from varying training models (resistance vs. endurance). Additionally, there has yet to be a clear indication of the impact that inflammatory markers have on performance with healthy athletes/ individuals, as most of the data surrounding data on IL-6 and CRP are conducted on individuals with pathological issues. Therefore, the purpose of this study is threefold using resistance trained subjects: (1) to investigate the time-course IL-6 and CRP following a resistance training model, (2) to investigate the effects BCAAs would have on IL-6 and CRP, and (3) to investigate the effects BCAAs would have on subsequent performance.

METHODS

Experimental Approach to the Problem

To evaluate the usefulness of BCAA's effect on acute fatigue and recovery on physiology and performance a randomized study design was used. This study was one week in duration and required subjects to perform a series of psychological questionnaires, blood draws, resistance training (RT), and muscular performance test (figure 2). The basis for this study design was to prompt an abrupt increase in training volume that would induce muscle damage potentially impeding performance. By doing so, this study design would allow the researchers to potentially detect physiological and performance changes between the BCAA group and the non-supplement group (NS) in response to exercise.

The subjects in this study assigned to the BCAA group were given 0.17g/ kg of BCAA (L-Leucine 2.5, L-Isoleucine 1.25g, and L-Valine 1.25g per serving) (Ajipure Fusi-BCAA pharmaceutical grade, made by Ajinomoto) with 20oz of water mixed with a non-caloric sugar-free flavor mix (Propel zero calorie mix). The BCAA's ingested given on each day of the study and were required to be taken 30 minutes before performance testing and training. Additionally,

a second BCAA mix was given to the subjects on days when resistance training took place and was required to be finished before the end of the resistance training. A diet log was recorded for each participant retrospectively for the day prior. The diet was gathered on each day of the experiment (6 days) to examine any outcomes not expected from the experimental design.

Subjects

Seventeen recreationally trained males volunteered to participate in this study. Inclusion criteria for subject participation were at least one year of resistance training experience and the ability to properly perform resistance training exercises. Training loads were computed from self-reported 1 RM's from the squat and bench press (squat = $148.4 \text{ kg} \pm 39.6 \text{ kg}$; bench press = $104.3 \text{ kg} \pm 22.2 \text{ kg}$). The subjects were randomly assigned to either the BCAA (n = 8; ages = 26.2 ± 3.5 ; body mass = 90.9 ± 8.5) or NS group (n = 9; ages = 24.0 ± 3.3 ; body mass = 95.3 ± 13.7). Subjects were screened for physical health issues using the NSCA Health/ Medical Questionnaire. No significant strength or anthropometric differences were found between groups, and no physical issues were reported that would make subjects ineligible. Subjects were notified of the potential risks and benefits of this study and signed an informed consent. This study was approved by the East Tennessee State University Institutional Review Board.

Blood Draws

Each subject provided six blood samples from days 2 – 4 of the study. Each blood draw contained ~ 9 mL of blood taken from the median antecubital vein and were collected into a 9mL vacutainer (BD serum separator). A certified phlebotomist performed each blood draw. After clotting (~30min), each vacutainer was centrifuged at 3000 rpm for 15 min. After centrifuging, the serum was extracted into transfer tubes and stored at -80°C until analyzed.

Biological Analysis

Analysis of T, C, and CK was performed by an automated immunoassay system (Immulite 2000). C-Reactive protein was analyzed by a chemistry analyzer (Beckman Coulter AU480). Interleukin – 6 was analyzed by a commercial ELISA kit (RandD systems) in an automated device (DSX Dynex Technologies). Testosterone to cortisol ratio was determined by converting to each variable to nmol/ L ($\text{nmol/ L}_{\text{test}} \div \text{nmol/ L}_{\text{cort}} \times 100$). The test-retest reliability for T, C, IL-6, and CK reported in the literature yield intraclass correlation coefficients (ICCs) of 0.92, 0.82, 0.99, and 0.9, respectively (Bashir and Gropler, 2014; Cauley, Gutai, Kuller, and Powell, 1991; Elder, Ellis, Barclay, and Wetherell, 2016; Harper et al. 2016).

Performance Testing

To evaluate differences in performance, the subjects were required to complete the following performance test: static and counter-movement jumps (2 conditions – 0 kg and 20kg), isometric mid-thigh pull, and Bosco repeated jump test. Each test was selected to assess various elements of fatigue (neuromuscular, maximum strength, endurance, etc.). The test-retest reliability for SJ, CMJ, Isometric mid-thigh pull, and Bosco repeated jump test yield ICCs of 0.99, 0.88, 0.98, and 0.87, respectively (Acero et al. 2011; Dal Pupo et al. 2014; De Witt et al. 2018; Slinde, Suber, Suber, Edwén, and Svantesson, 2008). All test were performed on dual force plates (Rice Lake Weighing Systems, Rough Deck) and analyzed on LabVIEW software (National Instruments).

Experimental Design

An overview of this design is shown in figure 2. This study was seven days in length (Days 0 – 6, day 0 was a preceding day and was not required to be followed consecutively). To examine the acute physiological and performance changes between the groups, the subjects were required to perform a series of tests measuring jump height, rate of force development (RFD), max strength, and strength endurance (fatigue index). Additionally, blood draws occurred on

Days 2 – 4 (pre, post, 3hrs, 12hrs, 24hrs, and 48hrs). Testing for performance variables occurred on days 1, 3, 4, and 6. On testing days, SJ and CMJ occurred first in the order of performance test. Each subject was advised on the jump procedure (i.e. depth, rest time, warm-up) before initiating jumps. Additionally, each subject performed at least two jumps for each protocol unless the most recent jump was 2 cm higher or lower than the previous jump (jumps would continue until the threshold < 2 cm was met). After SJ and CMJ, subjects performed the isometric mid-thigh pull. Each subject pulled at twice unless the 2nd pull was 250N higher or lower than the previous pull. Each pull was separated by 2 min rest. The final test performed was the Bosco repeated jump test. The Bosco repeated jump test consists of repeated jumps for 30 seconds. All respective jumps were initiated from a squat depth ($\sim 90^\circ$ knee angle), and subjects were encouraged to jump for max height for each jump. All performance testing days were identical in procedure except for day three which excluded the isometric mid-thigh pull.

A standardized warm-up occurred before testing and consisted of 25 jumping jacks, 1x5 mid-thigh pull with 20kg bar, and 3x5 mid-thigh pull with 60kg weighted bar. The remainder of the study was conducted as outlined in figure 2. The objective of this study design was to observe any acute performance changes with fatigue in response to RT between the BCAA and NS group.

Collection of physiological variables began on Day 2. On Day 2 subjects reported to the lab fasted (~ 6 AM) and promptly received their pre-blood draw (after hydration testing and questionnaires). After the pre-blood draw, subjects assigned to the BCAA group received their 1st BCAA mix (to be fully completed before starting RT); whereas, the NS group immediately began RT. A second BCAA mix was given to the BCAA group to be ingested ad libitum during RT (2nd BCAA mix fully ingested before finishing RT). The RT bouts were monitored by

certified strength coaches (NSCA – CSCS), and load prescriptions were adjusted as needed. Displacement values were measured for each subject before the study and subjects were advised to perform full range repetitions consistent with displacement depth. Rest intervals between sets were 2-3 min. Post-blood draws occurred immediately after completing the RT. Next, the subjects completed their 3hr and 12hr blood draw relative to the post RT blood draw (Subjects were not required to have fasted for 3hr or 12hr blood draw). On Days 3 and 4, the subjects promptly received their 24hr and 48hr at ~6 AM fasted and carried out the remainder of the study protocol for each day respectively.

Statistical Analysis

Statistical analysis of all performance variables was executed using a mixed method analysis of variance with repeated measures. A Tukey post hoc test was used for pairwise comparisons for each variable and time point. Additionally, a Robust Analysis for Mixed Designs (bootstrapped samples = 2000, trimmed means 10%) was used for variables that could not meet assumptions. The mean difference, hedges g, and 95% confidence intervals were calculated to further examine differences in group means (BCAA vs. NS) at each time point. The effect size scale used to determine magnitude of effect was the following: 0.0 - 0.2 trivial, 0.2 - 0.6 small, 0.6 - 1.2 moderate, 1.2 - 2.0 large, and 2.0 - 4.0 very large (Hopkins, 2006). Statistical analyses were conducted using Jamovi statistical software (ver. 0.9.5.11) and R for robust analysis (ver. R x64 3.5.0)

RESULTS

Testosterone

A mixed method repeated measures ANOVA showed a statistically significant difference in T compared to pre-values, $F(5, 75) = 24.5, p < 0.0001$. A Tukey post hoc test shows that the 3hr and 12hr T values were statistically significantly different from pre-values, $p < 0.0001$. No statistically significant difference was found between groups at any time point (**Figure 8A**).

Cortisol

A mixed method repeated measures ANOVA showed a statistically significant difference in C compared to pre-values, $F(5, 75) = 54.3, p < 0.0001$. A Tukey post hoc test showed that the 3hr and 12hr C values were statistically different from pre-values, $p < 0.0001$. No statistically significant difference were found between groups at any time point (**Figure 8B**).

Testosterone to Cortisol ratio

Testosterone to cortisol ratio was analyzed by a robust mixed design ANOVA. There was a statistically significant interaction effect indicating that the BCAA group's T:C ratio was higher than NS, $\Psi = 11.9, p = 0.002$. A Tukey post hoc test reveals that the BCAA's T:C ratio was statistically higher 12hrs post exercise compared to the NS group ($p < 0.0001$).

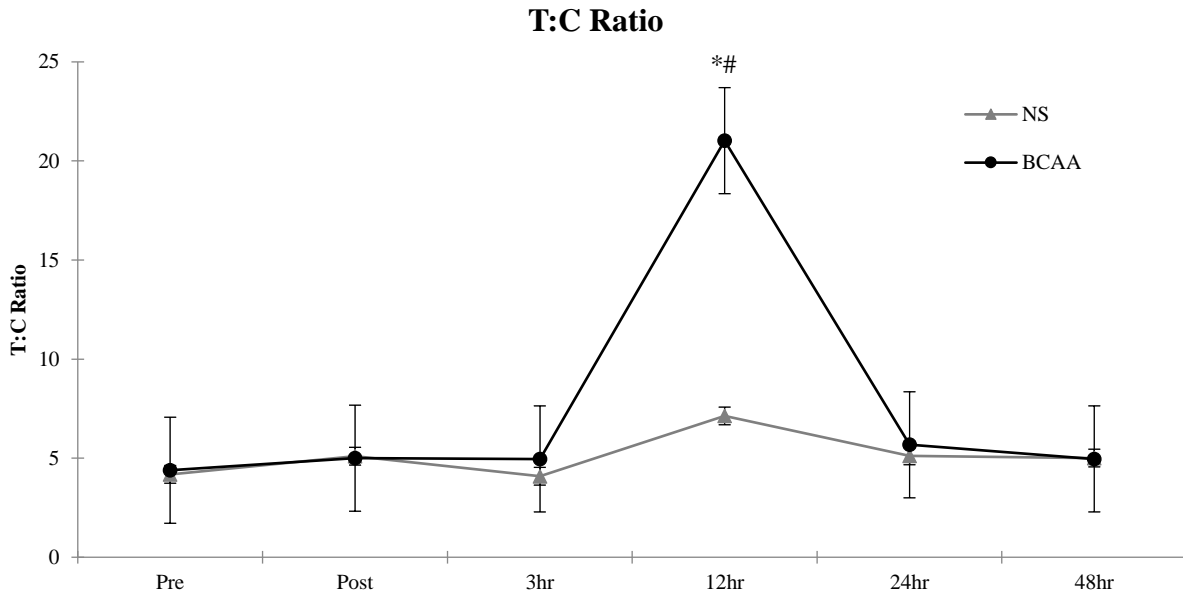


Figure 7. Testosterone-to-cortisol ratio

- * indicates statistical difference from pre-values
- # indicates statistical difference between the groups

Creatine Kinase

A mixed method repeated measures ANOVA showed a statistical difference in CK compared to pre-values, $F(5, 75) = 11.9, p < 0.0001$. A Tukey post hoc test showed that CK values were significantly higher for the NS group 12hr post exercise, $p = 0.009$ (**Figure 9A**).

C-Reactive Protein

A mixed method repeated measures ANOVA showed all effects for CRP were non-statistically significant between groups and time-points to pre-values, $p > 0.05$ (**Figure 9B**).

Interleukin – 6

A mixed method repeated measures ANOVA showed a statistically significant rise in IL-6 compared to pre-values, $F(3, 45) = 3.96, p < 0.05$. However, a Tukey post hoc test revealed there was no statistical difference between groups at any time point (**Figure 10**).

Jump Height

A mixed method repeated measures ANOVA showed that all jump conditions for SJ and CMJ were non-statistically significant between groups and compared to pre-values, $p > 0.05$ (**Figures 12 and 13**).

Iso-pull Peak Force

A mixed method repeated measures ANOVA showed that all effects for iso-pull peak force were non-statistically significant, $p > 0.05$ (**Figure 14A**).

Iso-pull Rate of Force Development

A mixed method repeated measures ANOVA showed that all effects for iso-pull RFD were non-statistically significant, $p > 0.05$ (**Figure 14B**).

Fatigue Index

Fatigue index was measured using the Bosco repeated jump test. A mixed method repeated measures ANOVA showed a statistically significant interaction effect between the groups. The NS group had a lower fatigue index than the BCAA group throughout the study, $F(1, 15) = 3.02, p = 0.04$. A Tukey post hoc suggested that the difference likely occurred on Day 6 of the study, but was not statistically significant, $p = 0.08$ (**Figure 15**).

Testosterone and Cortisol

A. Testosterone	Pre	Post	3hr	12hr	24hr	48hr
Hedges g	-0.1 [-1.05, 0.86]	0 [-0.95, 0.95]	0.25 [-0.71, 1.21]	1 [-0.01, 2.01]	0.29 [-0.67, 1.25]	-0.24 [-1.2, 0.71]

B. Cortisol

Hedges g	-0.15 [-1.11, 0.8]	-0.17 [-1.12, 0.79]	-0.3 [-1.26, 0.65]	-1.17 [-2.2, -0.14]	0.01 [-0.94, 0.97]	-0.24 [-1.2, 0.71]
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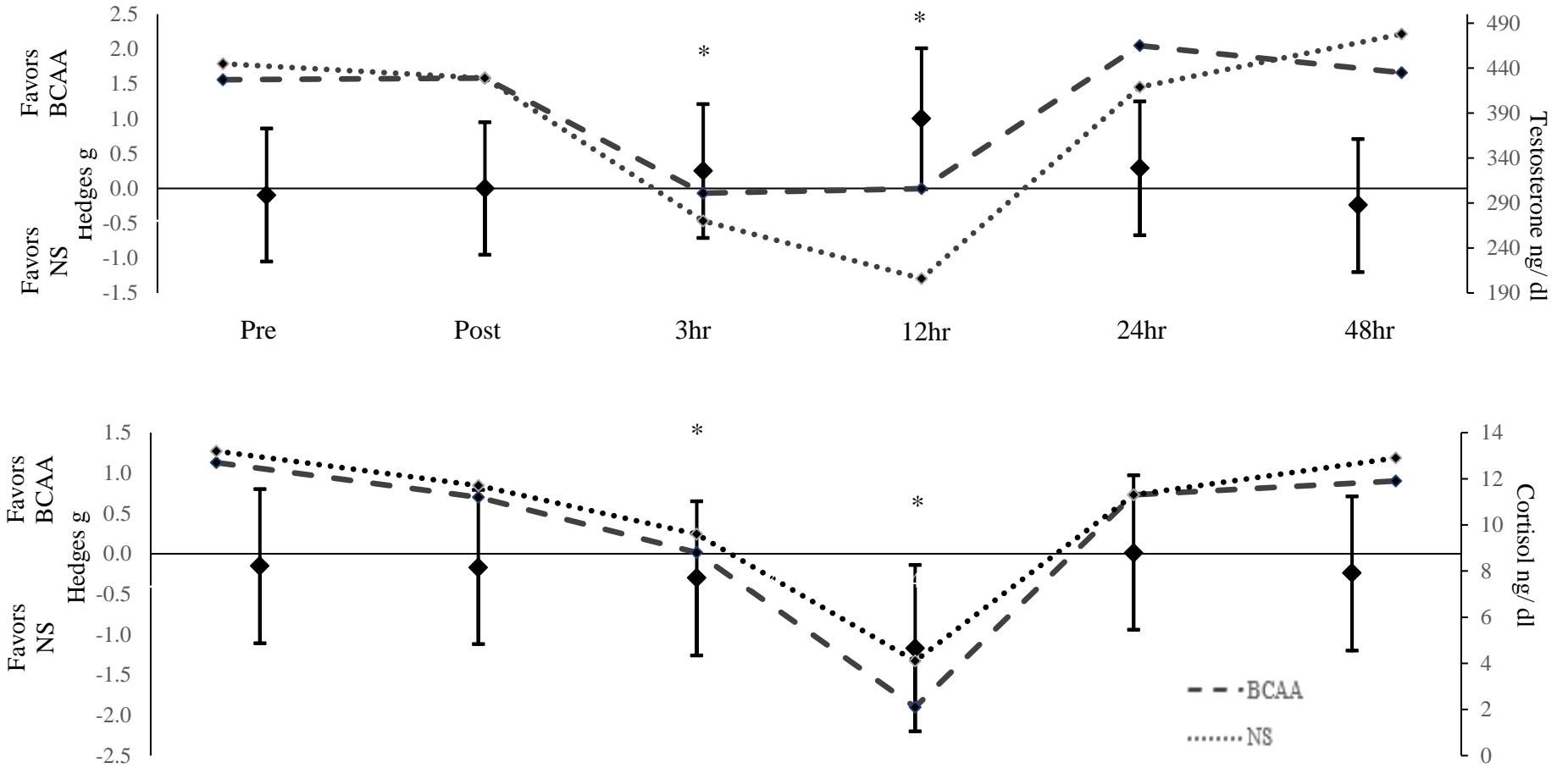


Figure 8. Changes in testosterone B. Changes in cortisol

- x-axis shows the changes in testosterone, cortisol, and ES with 95% CI Pre – 48hrs post resistance training
- * indicates statistical difference from pre-values

Creatine Kinase and C-Reactive Protein

A. Creatine Kinase	Pre	Post	3hr	12hr	24hr	48hr
Hedges g	-0.6 [-1.57, 0.37]	-0.63 [-1.6, 0.35]	-0.76 [-1.75, 0.22]	-0.93 [-1.94, 0.07]	-0.67 [-1.65, 0.31]	-0.48 [-1.45, 0.48]

B. C-Reactive Protein

Hedges g	0.06 [-0.9, 1.01]	0.16 [-0.8, 1.11]	0.15 [-0.81, 1.1]	0.25 [-0.7, 1.21]	0.13 [-0.83, 1.08]	0.31 [-0.64, 1.27]
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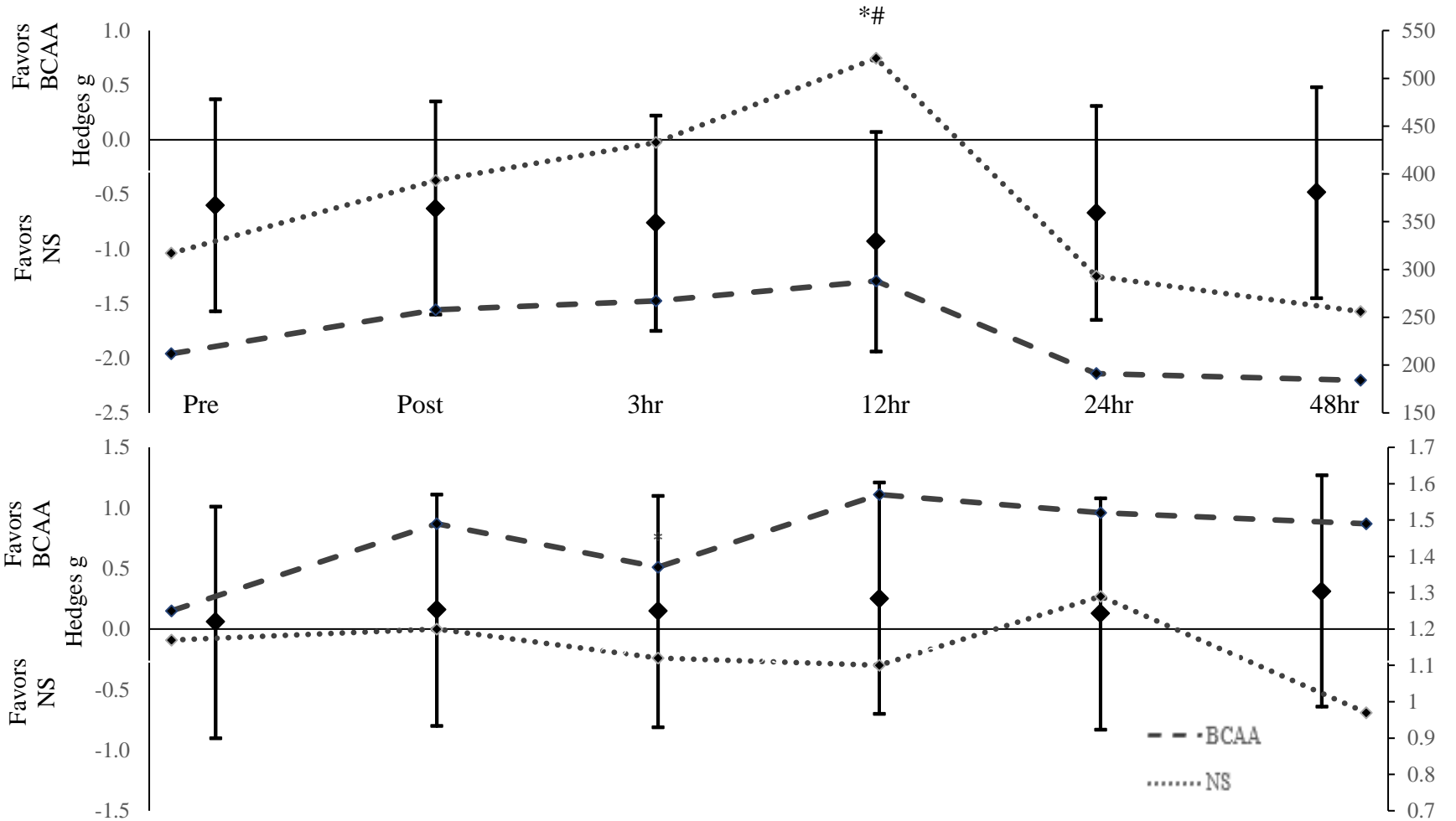


Figure 9. Changes in CK B. Changes in CRP

- *# indicates statistical difference between groups

Interleukin-6

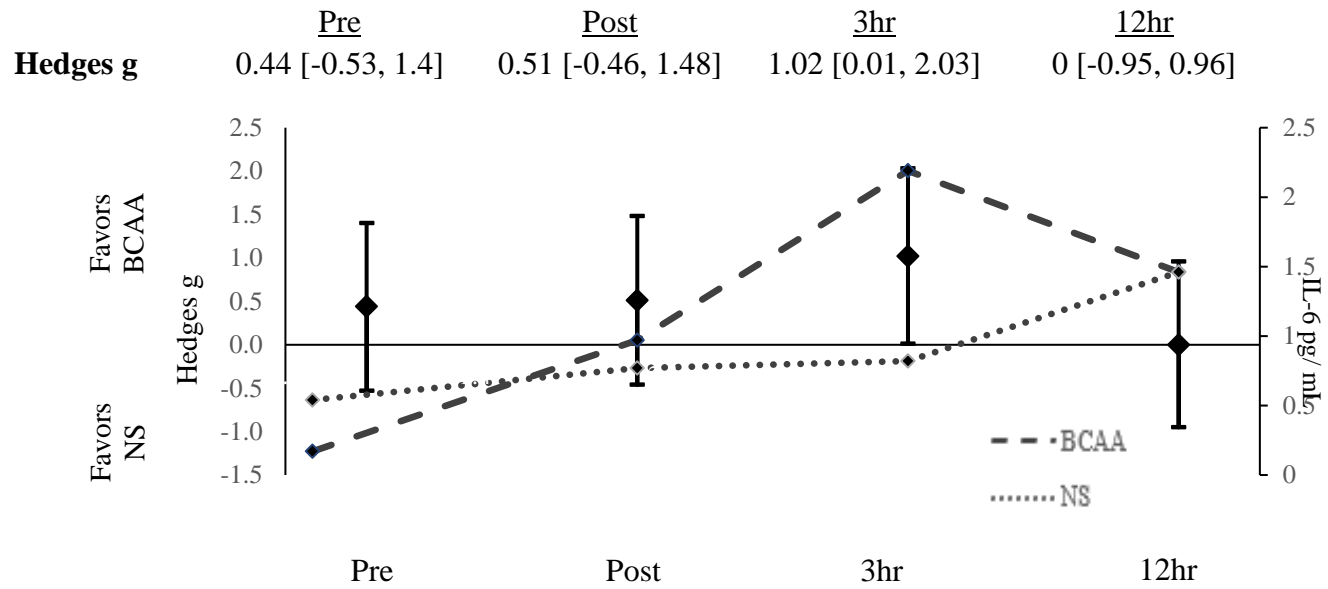


Figure 10. Changes in CK B. Changes in CRP

- x-axis shows the changes in CK, CRP, and ES with 95% CI Pre – 48hrs post resistance training
- *# indicates statistical difference between groups

CK, IL - 6, and CRP

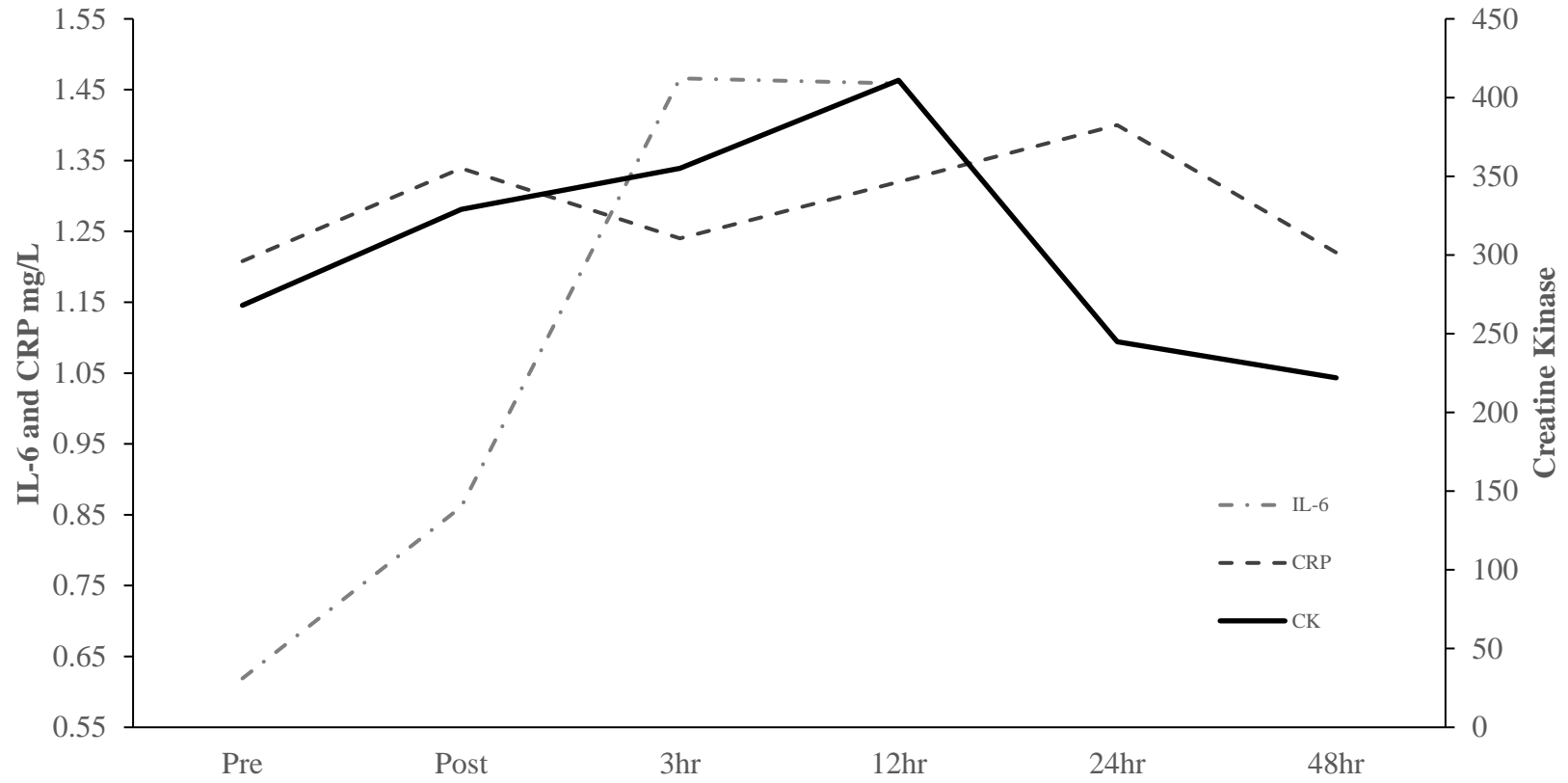


Figure 11. Trend in CK, CRP, and IL-6

- Trend in CK, CRP, and IL-6 in response to resistance training. Interleukin-6 only analyzed from pre to 12hrs.

Static Jump 0 kg and Static Jump 20kg

A. SJ 0kg	Day 1	Day 3	Day 4	Day 6
Hedges g	-0.01 [-0.96, 0.94]	0.02 [-0.93, 0.97]	-0.05 [-1, 0.9]	-0.04 [-0.99, 0.92]

B. SJ 20kg

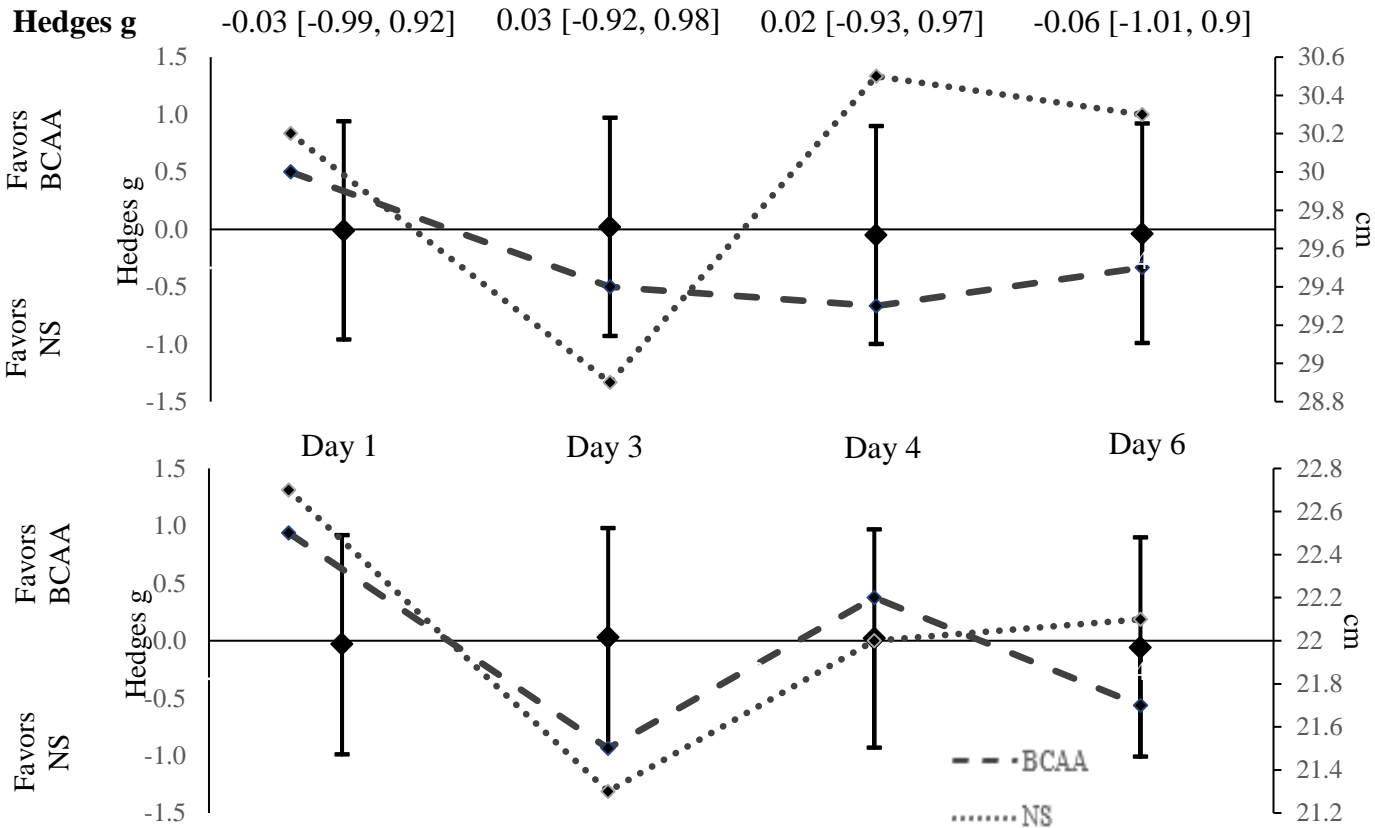


Figure 12. A. Static Jump 0kg B. Static Jump 20kg

Counter-Movement Jump 0kg and Counter-Movement Jump 20kg

A. CMJ 0kg	Day 1	Day 3	Day 4	Day 6
Hedges g	-0.16 [-1.11, 0.8]	-0.05 [-1, 0.9]	0.06 [-0.89, 1.01]	-0.13 [-1.09, 0.82]

B. CMJ20kg

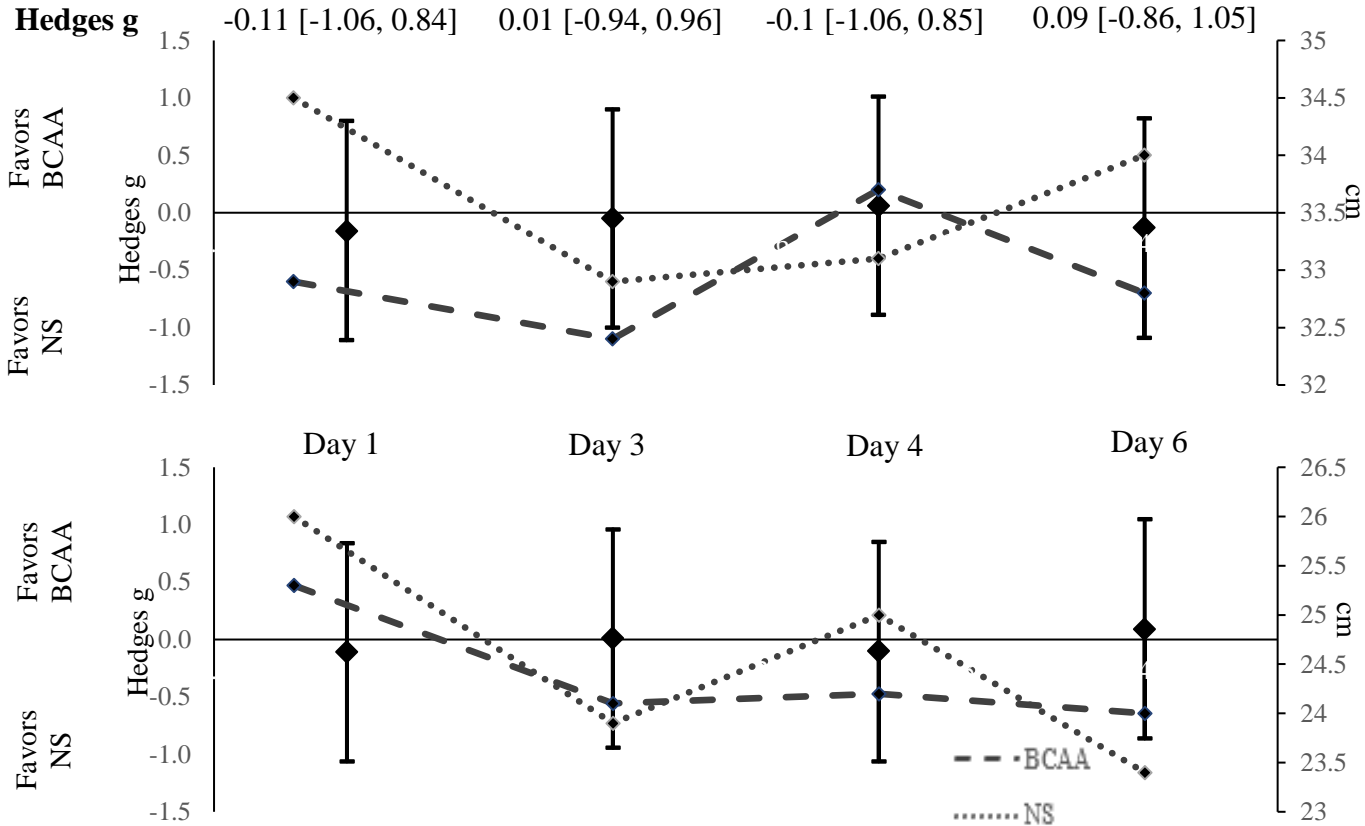


Figure 13. A. Counter-movement jump 0kg B. Counter-movement jump 20kg

ISO-Pull Peak Force and ISO-Pull RFD 250ms

A. Peak Force	Day 1	Day 4	Day 6
Hedges g	-0.14 [-1.1, 0.81]	0.07 [-0.89, 1.02]	-0.09 [-1.05, 0.86]

B. RFD 250

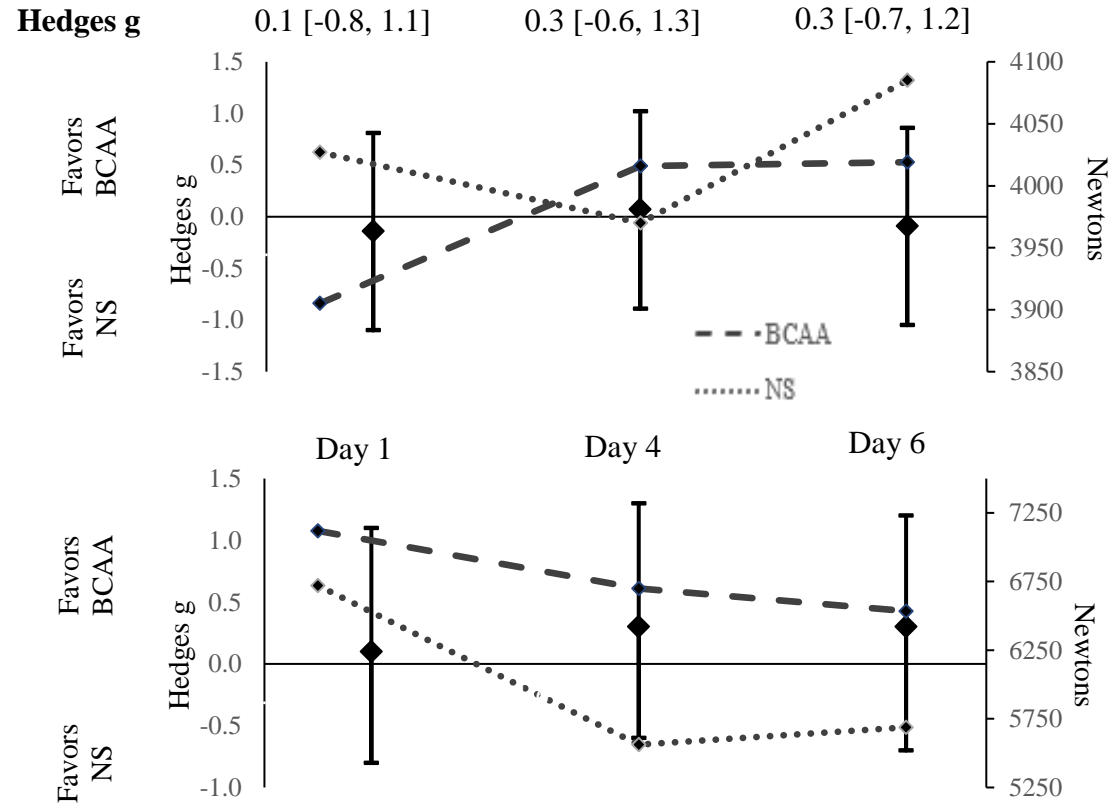


Figure 14. A. ISO-pull peak force B. ISO-pull RFD 250ms

Fatigue Index

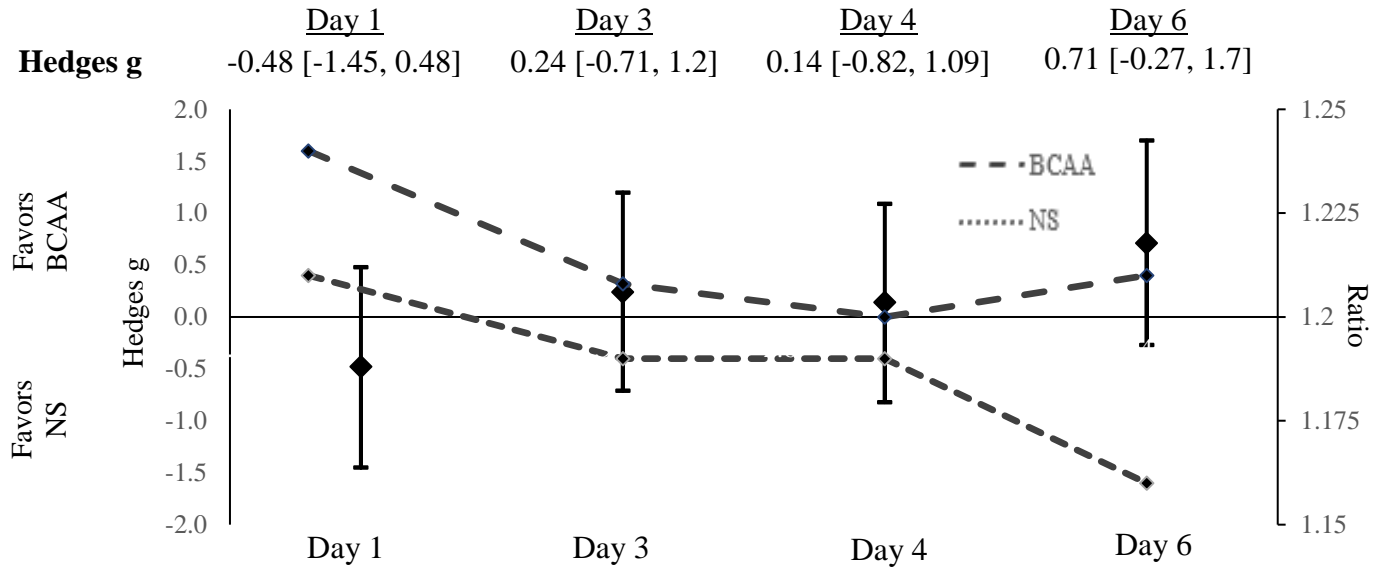


Figure 15. Fatigue Index

DISCUSSION

In this study we had subjects perform an acute high-volume resistance training protocol to investigate the time course of inflammatory markers following resistance training, the magnitude BCAA's would have on inflammatory markers, and determine the extent to which this might affect performance. The motive for our experimental model was to further the understanding of the inflammatory markers and potentially gain information to inform recovery strategies, planning sequential training bouts, and the use of supplementation.

The inflammatory markers investigated were IL-6 and CRP. A comprehensive framework by which these markers function is beyond this discussion; however, it should be noted, IL-6 and CRP are triggered by muscle damage. C-reactive protein is an acute phase protein released by the liver and "coats" foreign debris and necrotic cells for destruction via the complement system. Interleukin-6, in response to tissue damage, is released by neutrophils to signal additional immune cells movement to the localized area (A. Steensberg et al. 2001; Adam Steensberg, Fischer, Keller, Møller, and Pedersen, 2003). Additionally, IL-6 mediates the release of CRP (Steensberg et al. 2003). Therefore, the severity of muscle breakdown influences the extent to which IL-6 and CRP are elevated, and hence, they are used as indicators of inflammation magnitude. Furthermore, we investigated the response of testosterone and cortisol to resistance training. Interleukin-6 mediates increased cortisol concentration which orchestrates the distribution of immune cells in the damaged area. In theory, by minimizing IL-6 release through muscle damage, it would create a superior anabolic environment. In this study, we found that IL-6, CRP, and T:C ratio, to a degree, followed the trend to muscle damage (CK) after resistance training (figure 11). Creatine kinase and IL-6 peaked at 12hrs post-exercise; whereas, CRP peaked 24hrs post exercise. Additionally, the T:C ratio for the BCAA group was superior to

that of the NS group 12hrs post exercise. Ironically, however, IL-6 and CRP exhibited higher values for the BCAA group despite the NS group exhibiting higher CK values throughout the study (figure 11). The results for IL-6 and CRP are surprising, in that, IL-6 is known to mediate cortisol release; however, the BCAA group had higher IL-6 values and lower cortisol response compared to the NS group.

In addition to inflammatory markers and hormones, we investigated how these variables are related to performance. Despite there being statistical differences in CK, the only meaningful performance difference appeared to be the impact BCAA's had on RFD. Our results show that BCAA's mitigated the decline in RFD throughout the study. Thus, it may be beneficial for athletes to supplement with BCAA's when training and competitions are contiguous.

Investigating markers of inflammation provide a general time course and magnitude in which such markers respond to training. This information could be useful to an athlete or coach because it can provide a physiological measurement of recovery, or lack of. Additionally, the knowledge of appearance/ disappearance of specific inflammation indicators, in theory, can help plan subsequent training bouts for optimal recovery. Likely, the response of these markers would be different between training methods (i.e. resistance training, endurance exercise, etc.). It is apparent that inflammatory markers would accompany the rise and fall of muscle damage. Our results show the time course of IL-6 and CRP were largely consistent with that of CK; however, what makes our data troublesome to interpret is that the BCAA group's values for IL-6 and CRP were higher than the NS group, despite the BCAA group demonstrating lower values of muscle damage. The impact this has on recovery remains open for interpretation. Previous literature with similar experimental models showed inconclusive outcomes. For instance, Ispiridis et al. (2008) measured the kinetics of CRP, IL-6, DOMS, and CK after a soccer match in 24 highly trained

soccer athletes. Measurements were taken pre, immediately post, and every 24hrs for four days (24-96hrs post) following the soccer match. Interleukin -6 plateaued immediately post (~400% higher than pre-values) and fell to baseline values 24hrs post-soccer match. C-reactive protein peaked 24hrs post (~200% higher than pre-values) and tapered to baseline 48hrs post. Creatine kinase and DOMS, on the other hand, steadily increased and plateaued 48hrs post-soccer match. The results of this study are puzzling, in that, the inflammatory markers peaked and returned to baseline and preceded the rise in CK. In another related study, Chatzinikolaou et al. (2010) measured the kinetics of CRP, IL-6, and CK following plyometric exercises (5x10 50cm hurdle jumps and 5x10 50cm drop jumps). Similarly, the kinetics of CRP and IL-6 preceded that of CK following exercise indicating that the inflammatory markers preceded that of CK. The results of the earlier studies, in this author's opinion, raises questions as to the usefulness of IL-6 and CRP as indicators of inflammation for these experimental models.

Physiological markers can provide mechanistic insight into recovery but can be challenging to interpret because numerous factors impact their outcome. However, when it comes to athletic performance, physical results are the main concern for athletes and coaches despite alterations in physiological responses. In this study, we noted a marked difference in RFD following resistance exercise. Branched-chain amino acids reduced the decline in RFD during recovery and showed possible trends for improvement compared to the NS group. As for jumps, and ISO-pull peak force, there were no substantial differences between the groups. Throughout the literature, the effects of BCAA's on acute performance and recovery are ambiguous (Gualano et al. 2011; Kerksick et al. 2006; Kraemer et al. 2006; Ratamess et al. 2003; A. E. Smith, Fukuda, Kendall, and Stout, 2010; J. W. Smith et al. 2017). For instance, Fry et al. (1993) reported that BCAA's had no impact on weightlifting performance among elite

weightlifters following one week of high volume training. Waldron et al. (2017) reported similar findings where BCAA's did not affect isometric strength or CMJ performance in resistance trained males. Notably, the preceding tests in the above literature are not equivocal for all fitness characteristics (e.g. strength, RFD, endurance, etc.); however, supplementing with BCAA's appear to decrease declines in power and RFD (Ratamess et al. 2003; Shimomura et al. 2010), although extensive research on this is scarce. Rate of force development is especially important for athletes engaging in sports that involve explosive actions (e.g. basketball, baseball, volleyball, etc.) where rapid movements are paramount for competitive success. Although isometric RFD has been shown to be related to dynamic movement performance, including jumps (Stone et al. 2007), this relationship was not supported in this study.

The findings from our study suggest some interesting conclusions concerning recovery and acute performance; however, the findings are not without limitations. Notably, the effects of muscle damage on inflammation are not yet fully understood, and therefore, the inflammatory markers we investigated may not elucidate the mechanisms that affect muscle function and subsequent performance. For instance, CK has been used as an indicator of muscle damage following exercise; however, it should be noted that CK is a measurement of membrane disruption and may not entirely represent damage to the muscle directly (Jackman et al. 2010; Kirby et al. 2012). In some instances, previous literature has shown statistically significant differences in CK in response to exercise, indicating varying degrees of muscle damage, without an accompanying decrease in performance (Escobar et al. 2016; Howatson et al. 2012). Likewise, in this study we found no differences in performance despite the NS group showing statistically significant higher responses in CK. In parallel, the findings from this study showed a higher increase in IL-6 for the BCAA group despite CK levels being markedly lower. Thus,

interpreting changes in CK in conjunction with measures of inflammation may require a more thorough examination of the mechanisms underlying these changes. Another limitation in this study design was the sample size and number of repeated measures. In this study we had a total of 17 participants with four to six repeated measures for all the physiological and performance variables. Therefore, the number of subjects and repeated measures for this study has limited statistical power to detect any deviations between the groups. As such, the statistical power for capturing an effect in this model was lacking. Future research on this topic could benefit the body of literature by adding additional inflammatory markers that may interact with measures of muscle damage; additionally, future research with similar models could benefit with larger sample sizes.

CONCLUSION

In our experimental model we examined the kinetics of inflammatory markers following resistance training, the effects BCAA's would have on preceding markers, and the effects BCAA's would have on acute performance. We conclude the following:

1. The kinetics of IL-6 and CRP, in this study, did not uncover any meaningful insight into acute recovery or performance.
2. Branched-chain amino acids had no impact on IL-6 and CRP.
3. Branched-chain amino acids relented elevations in CK following resistance training.
4. Branched-chain amino acids mitigated declines in RFD following resistance training.

Branched-chain amino acids may have benefits for sports when competitions are contiguous and optimal recovery is not achievable.

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CHAPTER 5

SUMMARY AND FUTURE DIRECTIONS

The purpose of this dissertation was to examine the acute effects of BCAAs on psychological, physiological, and performance changes to high volume resistance training. The rationale for our experimental model was based on repetitive training bouts that may negatively alter recovery. To accomplish these purposes, we provided BCAAs to subjects on multiple days and had them complete a series of psychological questionnaires, blood draws, and performance tests to examine changes in acute fatigue.

Study one examined the effects of BCAA on psychological changes. We used the POMS, DALDA, RPE, and a subjective soreness survey to fulfill this task. Ultimately, previous literature exploring the effects of BCAA's on subjective fatigue have shown that BCAAs have positive effects on psychological changes (Greer et al. 2011; Shimomura et al. 2010; Takahashi et al. 2000). However, there was no available literature using a resistance training model. Therefore, we sought to rectify the existing literature by conducting a study with a resistance training paradigm. Essentially, our results suggest that BCAAs had no effect on subject fatigue in a resistance training model.

Study two investigated the effects of BCAAs on physiological changes of the immune system associated with fatigue (i.e. IL-6, CRP, T:C ratio). Additionally, we sought to investigate subsequent performance changes based on physiological changes to multiple high-volume resistance training bouts. We hypothesized that BCAAs would mitigate the degree of muscle damage, and therefore, show favorable physiological changes following training. Ultimately, the

favorable changes in fatigue would lead to improved acute changes in performance. Regarding the physiological changes associated with fatigue, BCAAs did not have an effect on all our physiological variables. Branched-chain amino acids mitigated the degree of muscle damage and improved T:C ratio; however, changes in IL-6 and CRP were unaltered. In fact, IL-6 and CRP showed unexpected trends for the BCAA group. Concerning performance, BCAAs had a small effect on RFD. Although this effect was not substantial, from a practical standpoint could be enough of a benefit to justify their use for competitive success.

Overall, our studies showed the following 1) BCAAs did not have an effect on psychological changes to resistance training, 2) BCAAs showed some favorable changes concerning physiological markers (i.e. CK and T:C ratio), and 3) BCAAs had a small to moderate effect on RFD following resistance training. However, our studies are not without limitations. It is the opinion of this author that BCAAs are still beneficial to enhance performance in all facets; although, this was not observed in this research. The limitations in our studies opens the door to future research designs that may satisfy limitations in our model. For instance, our research failed to show that BCAAs had an effect on psychological changes to resistance training. Our model lacked ecological validity to training conducted in a typical sport setting. Future research could remedy this limitation by conducting a similar model on athletes in a complete season. Regarding the physiological markers in this study, more conclusive work needs to be done in this area before practical conclusions are made to real scenarios. Although the markers we used in this investigation are well documented in the literature for clinical patients and endurance exercise study designs, research on immune markers associated with fatigue are lacking for resistance training models. Future research may want to use other markers

associated with fatigue/ recovery, such as neutrophil to lymphocyte ratio, with a similar study design to this research.

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