CHAPTER

28

Effects of β-Alanine Supplementation and Intramuscular Carnosine Content on Exercise Performance and Health

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β-Alanine is a nonproteogenic amino acid that has been widely used as a nutritional supplement by exercise enthusiasts all over the world [1]. Numerous research investigations have supported the use of β-alanine as a potential ergogenic aid for improving athletic performance, and it remains readily available as a dietary supplement in most health and nutrition stores. However, research also has discussed the potential benefits of β-alanine supplementation for several other populations, ranging from improving cognitive and physical performance in soldiers [2,3] to aiding with overall health and well-being [4]. This chapter will aim to discuss the ergogenic properties of β-alanine supplementation for exercise performance, review its potential benefits for health, and provide information regarding special considerations for improving athletic performance.

PHYSIOLOGICAL MECHANISMS BEHIND β-ALANINE SUPPLEMENTATION FOR EXERCISE

Carnosine Formation and Buffering Capacity

The primary physiological mechanism behind the ergogenic effects of β-alanine supplementation is the potential for β-alanine to combine with another amino acid, histidine, within body tissues such as the brain and skeletal muscle. On the combination of β-alanine and histidine, a cytoplasmic dipeptide, known as carnosine, (β-alanyl–L-histidine) is formed by the enzyme carnosine synthase [5] (Fig. 28.1).

Carnosine has been shown to act as an intramuscular buffer of H^+, which is especially beneficial for preventing exercise-induced acidosis and the resultant fatigue during high-intensity exercise [6]. When combined with β-alanine, the acid dissociation constant of the imidazole ring of the histidine molecule of carnosine increases slightly, making it capable of accepting H^+ within the body's physiological range. As exercise intensity increases, an increase in the

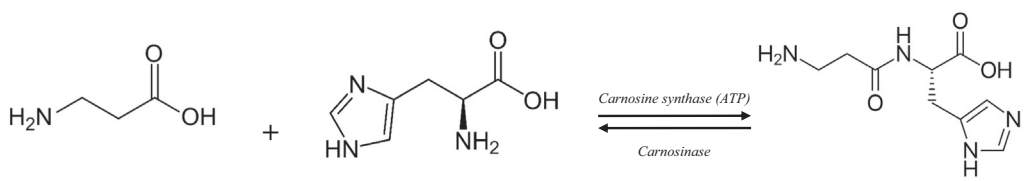

FIGURE 28.1 Chemical structures of β-alanine, L-histidine, and carnosine.

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production of lactate and consequent elevation in H^+ concentrations leads to a decrease in the pH of the muscle [7]. Exercise-induced acidosis alters numerous metabolic processes, eventually leading to a decrement in force production and an increase in fatigue [6]. Specifically, an increase in H^+ concentrations in muscle has been shown to decrease actin and myosin cross-bridge formation, impairing skeletal muscle contraction [8,9]. Research has also shown that exercise-induced acidosis may interfere with the resynthesis of phosphocreatine [10], which is an essential source of phosphate ions for ATP production during intense exercise. Additionally, increases in H^+ release during exercise may hinder the glycolytic energy pathway by decreasing the affinity of phosphofructokinase [11–13]. Furthermore, significant increases in acidosis during high-intensity exercise can cause H^+ to move from the exercising muscle into the circulation, reducing the amount of oxygen transported on hemoglobin molecules and impairing oxygen delivery to the brain. This eventually leads to cerebral hypoxia, resulting in increased symptoms of central fatigue [14]. Research has shown that increases in exercise-induced acidosis and concomitant levels of central fatigue severely diminish exercise tolerance and increase ratings of perceived exertion for a given exercise intensity [15,16]. Therefore higher intramuscular carnosine content aids in preventing the decline in pH associated with intense exercise, delaying fatigue and thereby improving high-intensity exercise performance.

Although there is considerable evidence supporting pH buffering ability of carnosine, others have suggested that carnosine may also act as a diffusible Ca^{2+}/H^+ shuttle. This shuttle is proposed to help increase force production during high-intensity exercise [17,18]. This carnosine shuttle hypothesis is predicated on several physiological changes that occur during intense exercise. During such exercise, H^+ accumulation at the sarcomere increases because of an increase in ATP production via anaerobic glycolysis. The need for H^+ removal from the sarcomere and transport to the sarcolemma, therefore, increases drastically. Concurrently the requirement for Ca^{2+} delivery from the sarcoplasmic reticulum to the sarcomere increases as Ca^{2+} is essential for actin–myosin cross-bridge formation and resultant force production. The carnosine shuttle hypothesis suggests that because carnosine can bind both Ca^{2+} and H^+, an increase in H^+ production at the sarcomere would induce Ca^{2+} unloading, increasing the amount of available Ca^{2+} for cross-bridge formation and therefore force production. Additionally, H^+ delivery to the sarcoplasmic reticulum is increased through the carnosine shuttle, amplifying the drive for H^+ export out of the muscle fiber, which would, in turn, lower the intramuscular pH [17,18].

Others have demonstrated that higher intramuscular carnosine concentrations may increase the Ca^{2+} sensitivity of the contractile apparatus in both Type I and Type II muscle fibers, equating to a substantial increase in force production for a given amount of Ca^{2+} release [19]. However, this investigation was conducted in vitro, examining the effects of skinned muscle fiber contractility through exposure of the muscle to Ca^{2+}-buffered solutions after the acute exposure to a carnosine solution [19], which may limit the interpretation of these findings and their practicality in vivo. For example, investigations in humans contradict these findings as they showed that carnosine content did not affect force production or Ca^{2+} sensitivity or release [20,21]. However, these researchers did find a reduction in relaxation time of skeletal muscle, which may be beneficial for repeated exercise performance. These findings suggest that carnosine may also augment exercise performance through improvements in muscle relaxation.

β-ALANINE SUPPLEMENTATION AND INTRAMUSCULAR CARNOSINE CONCENTRATIONS

Effects of β-Alanine Supplementation on Carnosine Content

Carnosine is formed through the combination of the amino acids β-alanine and essential histidine. Although considered essential, histidine is highly abundant in the human body, whereas β-alanine is much more scarce [22]. Endogenous β-alanine production occurs in minute quantities mainly through hepatic uracil degradation, which is insufficient in producing ample amounts of carnosine [23,24]. The enzyme carnosinase, which is present in the gastrointestinal tract, acts to hydrolyze carnosine into its constituent amino acids; therefore exogenous supplementation of carnosine has been proven ineffective for increasing muscle carnosine levels [7]. Therefore β-alanine is thought to be the rate-limiting precursor to carnosine production in vivo [5,7,25,26]. An investigation conducted by Blancquaert et al. [26] supported this hypothesis as these investigators showed that histidine supplementation alone did not increase muscle carnosine content, whereas β-alanine supplementation alone and β-alanine supplementation combined with histidine significantly increased muscle carnosine. Nevertheless, β-alanine can also be obtained from the diet, primarily through the consumption of meat and fish products [5]. Dietary β-alanine consumption, however, provides only relatively small increases in the plasma bioavailability of β-alanine. For example, ingestion of about 150 g of turkey breast has been shown to provide the equivalent increase in the bioavailability of β-alanine as an 800-mg

supplement [5]. Most of the research showing the ergogenic effects of β-alanine supplementation has been conducted using β-alanine supplementation dosing strategies ranging from 1.6 to 6.4 g/day [27–30]. Large daily meat and fish consumption would likely be required for significant elevations in muscle carnosine content to occur. Additionally, muscle cells do not appear to be capable of directly absorbing carnosine from the circulation [31]. Therefore the most efficient way of increasing muscle carnosine content is through exogenous β-alanine supplementation. Previous research has shown that chronic β-alanine supplementation may increase carnosine content between 59% and 200% from baseline levels (mean = 119.2 ± 41.5%) after 24 weeks of supplementation [1]. The process of carnosine formation in skeletal muscle and brain tissue is depicted in Fig. 28.2.

Dose Response for β-Alanine Supplementation and Carnosine Synthesis

As previously discussed, many of the investigations demonstrating that β-alanine supplementation has a beneficial effect on elevating muscle carnosine and improving exercise performance have been conducted by using daily β-alanine dosing strategies ranging from 1.6 to 6.4 g/day [27–29,32]. Stegen et al. [33] reported that the incorporation of ingested β-alanine into muscle is very low (about 3%). However, a study by Church et al. [34] reported retention rates of a 6-g daily dose to be 7.9 ± 8.8% which decreases to 5.3 ± 5.6% with a higher dose (12 g/day). Thus increases in muscle carnosine consequent to β-alanine supplementation are dependent on several factors, including training status, supplement dosage, and duration of supplement use.

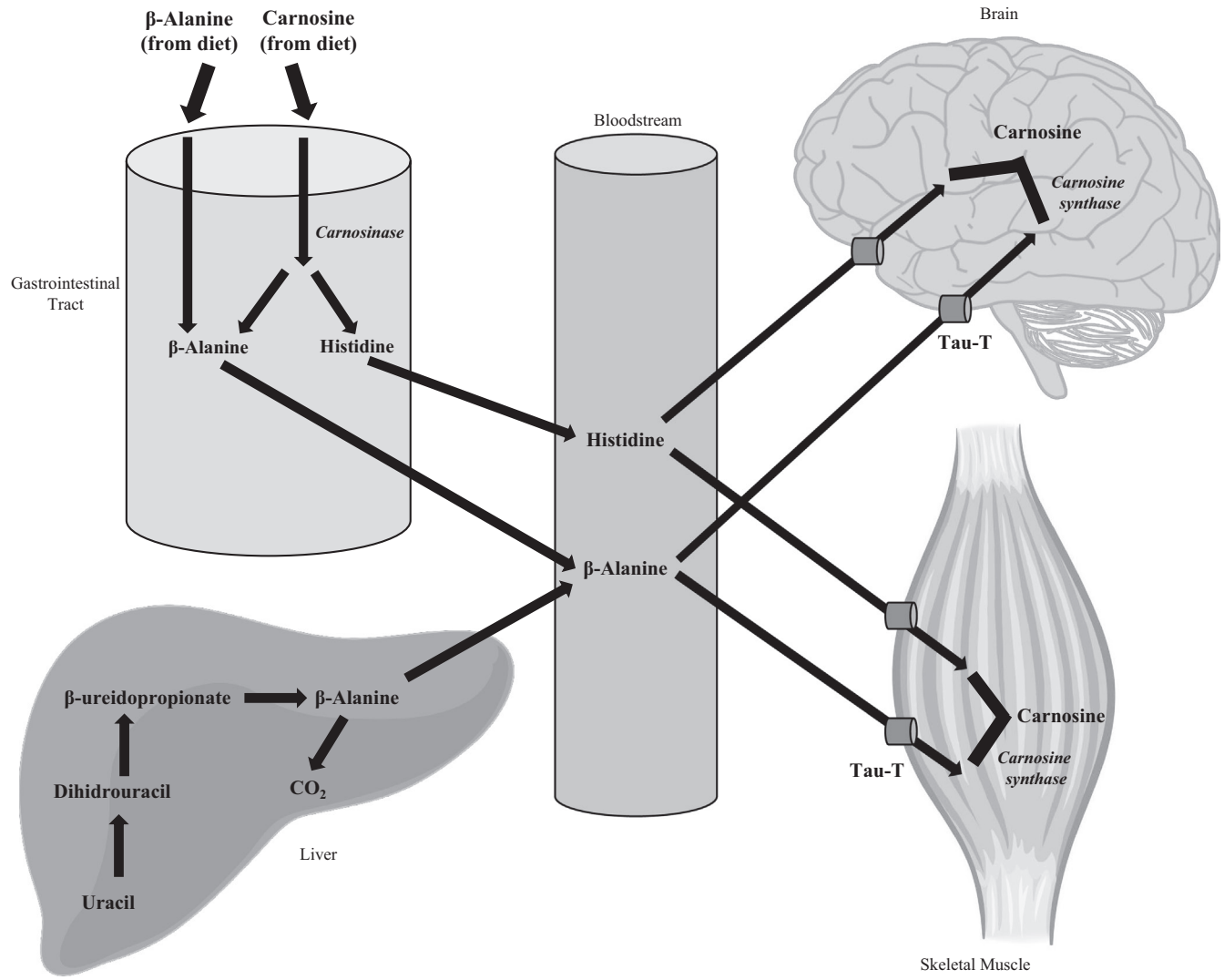

FIGURE 28.2 The process of carnosine synthesis in skeletal muscle and the brain.

A linear dose–response relationship seems to exist to a certain extent between the amount of β-alanine consumed and the increase in muscle carnosine content [32]. Stellingwerff et al. [32] determined that a β-alanine supplementation strategy of 3.2 g/day for 4 weeks increased muscle carnosine content in both Type I and Type II muscle fibers by almost double the amount compared with a dosing strategy of 1.6 g/day. These findings are in agreement with other investigations showing that carnosine content can increase by 20%–30% after 2 weeks of β-alanine supplementation [35] and further elevated by 40%–60% after 4 weeks of β-alanine supplementation [30]. As the daily dose of β-alanine is increased to 6–6.4 g/day, the increase in muscle carnosine content is nearly doubled [34,36]. These empirical observations on the relationship between β-alanine ingestion and muscle carnosine synthesis have been suggested to follow zero-order kinetics with respect to the availability of β-alanine [27]. Interestingly, a study by Church et al. [34] demonstrated that greater daily doses of β-alanine (12 g/day) for 2 weeks could achieve the same level of intramuscular carnosine content as that seen in a 6-g/day dose for 4 weeks. These findings demonstrate that doubling the daily dose of β-alanine can increase carnosine content in half the time [34]. There is evidence that rapid increase in muscle carnosine at the initial stages of supplementation is followed by a decrease in the rate of elevation [37]. This likely reflects the decay in muscle carnosine levels, which has been suggested to follow first-order kinetics [27]. In consideration of zero-order kinetics in regards to carnosine synthesis and first-order kinetics regarding its decay, a plateau will eventually be reached in regards to muscle carnosine elevations consequent to β-alanine supplementation.

A significant degree of variability appears to exist regarding the individual response to β-alanine supplementation [35,38]. Baguet et al. [35] reported that after 6 weeks of 4.8 g/day of β-alanine supplementation, "low-responders" had an elevated carnosine content by only ~15%, whereas "high-responders" increased carnosine content by ~55%. A study by Saunders et al. [38] confirmed these results in the longest β-alanine supplementation studies to date. After 6 months of 6.4 g/day of β-alanine supplementation, individual increases in muscle carnosine content ranged from 59% to 200%. The investigators noted that the greatest increases in muscle carnosine content were seen within the first 4 weeks of supplementation, but carnosine content continued to rise in subsequent months for many of the subjects. Interestingly, the investigators indicated that elevations in muscle carnosine might not have plateaued in all subjects, even after 24 weeks of supplementation as some individuals continued to increase in the final month of supplement ingestion [38].

Once β-alanine supplementation ceases, muscle carnosine content begins to return to baseline levels. This decline appears to be dependent on various factors, including original β-alanine dose and the individual response to β-alanine. A study conducted by Baguet et al. [35] reported that intramuscular carnosine content decreased by nearly a third after 3 weeks of cessation from β-alanine supplementation. Before supplement cessation, participants had consumed 4.8 g/day for 6 weeks. By ninth week after supplement cessation, carnosine content returned to baseline levels. However, the investigators indicated that carnosine washout appeared to be dependent on the individual response to β-alanine. In individuals who were high-responders, carnosine washout time was greater (~15 weeks) than for those who were low-responders (~6 weeks). In a subsequent study Stellingwerff et al. [32] suggested that carnosine washout may take longer (~15–20 weeks) than that reported by Baguet et al. [35] as they demonstrated that carnosine had a decay rate of ~2% per week. Based on available evidence a considerable degree of variability exists regarding the kinetics of carnosine synthesis and washout between individuals.

EFFECTS OF β-ALANINE SUPPLEMENTATION ON EXERCISE PERFORMANCE

The ergogenic effects (i.e., increased exercise performance) that are associated with β-alanine supplementation are a result of β-alanine binding with histidine to form carnosine in skeletal muscle and not a direct result of β-alanine itself [27]. As previously discussed, carnosine acts as an intramuscular buffer of H^+ and works to offset exercise-induced acidosis [5]. Anaerobic activities primarily rely on the glycolytic energy system for ATP production during high-intensity exercise, increasing lactate production and H^+ release. Evidence has been convincing that an elevation in intramuscular carnosine is most beneficial for preventing exercise-induced acidosis during high-intensity anaerobic activities, where H^+ production is high [6]. An improved intracellular buffering capacity will attenuate fatigue, allowing exercise to continue for a longer duration. β-Alanine supplementation has been shown to be most effective for increasing performance of high-intensity activities lasting from 60 to 240 s in duration [6].

In addition to working as an intracellular buffer, it has been demonstrated that increased carnosine concentrations in vitro may also increase skeletal muscle contractility via an increase in Ca^{2+} delivery to and H^+ removal from the sarcomere [17–19]. However, investigations contradict these findings, showing that 28 days of 6.4 g/day of β-alanine supplementation in males did not affect the force–frequency relationship of the knee extensors [20,21]. These latter studies both concluded that there was no change in Ca^{2+} release from the sarcoplasmic reticulum after β-alanine

supplementation, and increases in exercise capacity and performance after supplementation were not a result of increased Ca^{2+} sensitivity or release. Additionally, these researchers found that time-to-peak tension, electromechanical delay, and maximum and explosive voluntary force production were not affected by β-alanine supplementation. Despite these findings, a reduction in relaxation time was discovered after the supplementation period, which may be attributed to an enhanced Ca^{2+} reuptake into the sarcoplasmic reticulum. An increased action of the sarcoplasmic reticulum Ca^{2+}-ATPase and therefore reuptake of Ca^{2+} has been shown to be the rate-limiting factor in muscle relaxation speed [39]. Considering that muscle relaxation is reported to consume a large proportion of the total energy expenditure [40], a decrease in relaxation time may be especially beneficial to exercise requiring short, repeated contractions, improving force output and subsequent exercise performance [21]. The effects of β-alanine supplementation on exercise performance are summarized in Fig. 28.3.

Effects of β-Alanine Supplementation on High-Intensity Exercise Performance

The ergogenic effects of β-alanine supplementation are most pronounced during high-intensity activities that are accompanied by an increase in lactate production and H^+ accumulation. As discussed earlier, β-alanine supplementation seems to be most effective for high-intensity activities lasting from 1 to 4 min [6]. Although high-intensity activities lasting less than 60 s have a considerably large anaerobic contribution, research has shown that the highest levels of acidosis occur during high-intensity exercises lasting longer than 1 min [41,42].

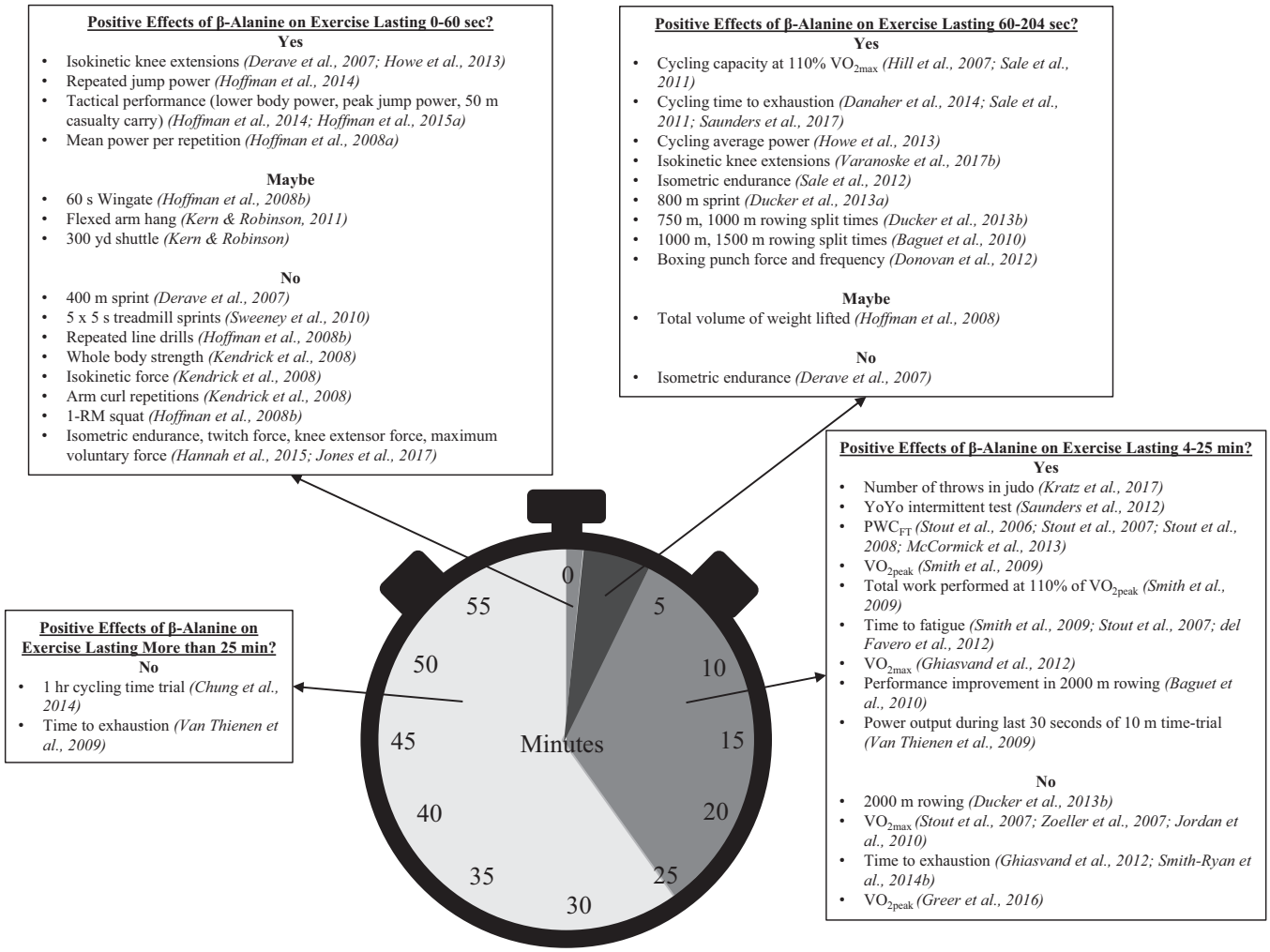

FIGURE 28.3 The effects of β-alanine supplementation on various modes of exercise performance of different durations. The *darker-shaded areas* of the clock represent the duration of exercise during which β-alanine supplementation is most effective. "Yes" indicates that an improvement was seen after β-alanine supplementation, "No" indicates that no improvement was seen after β-alanine supplementation, and "Maybe" indicates that a mild but nonsignificant improvement was seen after β-alanine supplementation. *PWC_{FT},* physical working capacity at fatigue threshold.

An investigation by Hill et al. [37] demonstrated that 10 weeks of β-alanine supplementation (provided in graded dosages increasing from 4.0 to 6.4 g/day by week 4) increased cycling capacity and time to exhaustion at 110% of maximal power by 13% and 16%, respectively. These results were supported by subsequent studies showing improvements in time to exhaustion during cycling exercise after β-alanine supplementation [38,43,44]. Howe et al. [45] provided β-alanine (65 mg/kg BM per day for 4 weeks) to highly trained cyclists and observed a 44% improvement in average power output during a 4-min cycling time trial, a significant increase in average power and a significant decrease in fatigue rate during 30 consecutive isokinetic contractions of the knee extensors. Similarly, Derave et al. [46] showed that 4 weeks of β-alanine supplementation (4.8 g/day) was effective at significantly increasing knee extension torque during the last two of the five sets of 30 maximal isokinetic contractions. These findings were supported by Varanoske et al. [47], who reported an attenuation of muscle fatigue during the latter phases of five sets of 50 maximal isokinetic contractions in females with a high muscle carnosine content compared with those with a lower muscle carnosine. An additional investigation demonstrating similar results discovered an attenuation of exercise fatigue during isokinetic knee extensions in both males and females after β-alanine supplementation (6 g/day for 4 weeks) [48].

The effect of β-alanine supplementation on isometric muscle performance has met with equivocal results. Derave et al. [7] found no difference in time to exhaustion during isometric endurance at 45% of maximal voluntary contraction of the knee extensors between subjects supplementing with 4.8 g/day of β-alanine or a placebo for 4 weeks. However, Sale et al. [49] using a 6.4-g/day dose for 4 weeks reported significant increases in time to exhaustion during isometric endurance at 45% of maximal voluntary contraction of the knee extensors. Besides differences in dose, Sale et al. [49] hypothesized that the differences between the studies may be related to a potential discrepancy between the actual intensity of the exercise in the study by Derave et al. [46] and what was intended. The expected hold time at 45% of maximal voluntary contraction is predicted to be about 80 s [50], whereas the presupplementation time to fatigue in subjects in the study by Derave ranged between 175 and 200 s. The actual intensity of exercise in the investigation by Derave may have corresponded to a lower percentage of the subject's maximal voluntary contraction. A study by Varanoske et al. [47] provided further support for Sale's work by reporting that women with high muscle carnosine levels experienced a lower decline in maximal voluntary isometric contraction peak torque and rate of force development from a muscle-fatiguing protocol (five sets of 50 repetitions at 180 degrees/s) than women with low muscle carnosine content.

Many studies examining the effects of β-alanine supplementation on sport-specific performance have demonstrated significant performance improvements after supplementation. A study by Hoffman et al. [51] in strength and power athletes discovered significant increases in the mean power per repetition during the squat exercise, an increase in the total number of repetitions performed, and an increase in the total volume (weight, sets,·repetitions) of weight lifted after 30 days of β-alanine supplementation (4.8 g/day) compared with a placebo. Ducker et al. [52] reported significantly faster 800-m sprint times after 28 days of β-alanine supplementation (80 mg/kg BM per day) compared with a placebo in club runners. Also, they reported that split times for both the first and second halves of the race improved with β-alanine supplementation. However, a subsequent study by Ducker et al. [53] showed that 28 days of β-alanine supplementation did not significantly improve 2000-m rowing times or average power outputs in elite rowers, but significant improvements were seen in 750- and 1000-m split times (1.5–3 min into the race). In an additional study examining competitive rowers, Baguet et al. [54] reported that rowers with greater intramuscular carnosine content had faster split times in the second and third 500-m splits of a 2000-m race (~1.5–4.5 min into the race) compared with those with lower carnosine content.

Other studies have also demonstrated the benefits of β-alanine supplementation on specific components of sport performance. β-Alanine supplementation (6.0–6.4 g/day for 4 weeks) has resulted in an increased number of throws per set as well as a total number of throws in a simulated judo match [55] and an increase in punch force and frequency in boxers [56]. Saunders et al. [57] reported that supplementing with 3.2 g/day of β-alanine for 12 weeks was able to increase performance in the YoYo intermittent recovery test in soccer players. These findings provide further support for the ergogenic effects of β-alanine, in varying dosages and durations, on high-intensity activities.

Significant performance benefits resulting from β-alanine supplementation have not been demonstrated in all studies. Kern and Robinson [58] reported no statistically significant performance effects of 4 g of β-alanine per day for 8 weeks in collegiate wrestlers and football players compared with a placebo; however, favorable results were still found in those consuming β-alanine as sprint times for the 300-yard shuttle decreased (change in time of 1.1 ± 0.94 s and 0.4 ± 2.2 s in the supplement and placebo groups, respectively, $P > .05$) and time to failure for the 90-degree flexed arm hang increased (3.0 ± 0.54 s and 0.39 ± 6.5 s in supplement and placebo groups, respectively, $P > .05$). Hoffman et al. [59] reported no significant changes ($P = .07$) in fatigue during a 1-min Wingate anaerobic power test in collegiate football players. However, they assessed these athletes after only 2 weeks of 4.5 g/day of β-alanine supplementation. Furthermore, the athletes supplementing with β-alanine trended ($P = .09$) towards a greater training volume during their workouts and had

significantly lower subjective feelings of fatigue. Although the investigation by Hoffman et al. [59] was likely not of sufficient duration to cause large increases in muscle carnosine, the trends did indicate changes in the right direction.

The benefits of β-alanine supplementation in repeated sprint events or high-intensity activities lasting between 1 and 4 min have been well documented. However, similar response has generally not been seen in short-duration sprint activities. Derave et al. [46] found no difference in 400-m sprint times (~51 s) in trained sprinters who supplemented with β-alanine (4.8 g/day for 4 weeks), even though muscle carnosine was significantly increased. Sweeney et al. [60] found no differences in peak and mean horizontal power during two bouts of 5 s × 5 s treadmill sprints with 45 s of passive recovery between each sprint between individuals consuming 4 g/day of β-alanine for the initial week and 6 g/day for the next 4 weeks compared with a placebo. Also, Hoffman et al. [59] reported no changes in repeated line drills (30–35 s per sprint) in college football players. However, these assessments in the latter study were performed after only 2 weeks of supplementation (4.8 g/day). Nevertheless, these investigations are consistent with the metaanalysis performed by Hobson et al. [6] that indicated the lack of efficacy of β-alanine supplementation in exercise bouts less than 60 s.

Effects of β-Alanine Supplementation on Neuromuscular Fatigue

Neuromuscular fatigue is an inevitable outcome from participation in sustained physical activity, ultimately resulting in a decrease in performance. A delay in the onset of fatigue is an adaptation indicative of performance improvements or the efficacy of a nutrient supplement. A sensitive method used to assess fatigue is the physical working capacity at fatigue threshold (PWC_{FT}) [61]. This test is performed on a cycle ergometer and measures the electromyographic (EMG) activity of the vastus lateralis during a graded cycle ergometer test. Change in EMG activity is assessed at each stage of increasing power output. The goal of the assessment is to identify the power output that is associated with the onset of neuromuscular fatigue. The PWC_{FT} is the power output that corresponds to the highest nonsignificant change in activation of the vastus lateralis [61]. Investigations examining β-alanine supplementation have reported significant increases in the PWC_{FT} in both men and women [61,62]. In a study of older adults (70.7 ± 6.2 y) McCormack et al. [63] demonstrated that ingestion of two low-dose β-alanine supplementation protocols (800 mg/day and 1.2 g/day) combined with a protein drink for 12 weeks significantly improved PWC_{FT} compared with a placebo. Similarly Stout et al. [64] showed that 90 days of β-alanine supplementation resulted in a 37.3% improvement in PWC_{FT} in individuals aged 55–92 years. These results do provide evidence demonstrating that β-alanine supplementation increases the exercise intensity at which neuromuscular fatigue sets in, thereby improving performance. These findings also demonstrate that β-alanine supplementation may be an especially valuable supplement for maintaining fitness levels and functional performance in older adults.

Effects of β-Alanine Supplementation on Maximal Strength and Power Production

During exercise requiring near-maximal force output, an increase in muscle acidosis is not the primary factor that leads to performance decrements. ATP production during exercise requiring extreme force is primarily produced through the splitting of phosphocreatine, and the decrease in performance is related to a decline in phosphocreatine stores [65]. This is consistent with the conclusion reached by Hobson et al. [6] and discussed earlier regarding the efficacy of β-alanine supplementation for exercise durations of less than 1 min. The lack of efficacy in short-duration exercise protocols has been reported in several studies. Kendrick et al. [28] reported no difference in whole-body strength (total weight lifted in box squat, bench press, and deadlift), maximal isokinetic force production of the knee extensors, and number of repetitions completed during an upper arm curl in individuals supplementing with 6.4 g/day of β-alanine and undergoing resistance training for 10 weeks compared with a placebo. Hannah et al. [20] and Jones et al. [21] found no differences in maximum or explosive voluntary force production, twitch force after stimulation, knee extensor force at low or high frequencies of muscle stimulation, isometric endurance of the knee extensors, twitch electromechanical delay, or time-to-peak tension after 28 days of 6.4 g/day of β-alanine supplementation. A study by Hoffman et al. [51] examining the effects of 12 weeks of resistance training combined with 30 days of either 4.8 g/day of β-alanine supplementation or a placebo in a cross-over trial found no differences in 1-repetition maximum squat between groups. However, a subsequent study by Hoffman et al. [2] did report significant improvement in repeated jump power after 4 weeks of β-alanine supplementation (6 g/day). Interestingly, many of these studies did not directly measure changes in intramuscular carnosine content with β-alanine supplementation, which presents a limitation of the applicability and validity of their findings. Regardless, evidence to date suggests that β-alanine supplementation does not appear to improve maximal strength and power production.

Effects of β-Alanine Supplementation on Aerobic Performance

During endurance exercise, ATP production is achieved primarily through oxidative phosphorylation, decreasing the demand for higher amounts of intramuscular carnosine because H^+ accumulation is no longer a limiting factor for performance. However, evidence does exist suggesting a modest effect of β-alanine supplementation on aerobic performance, especially in events that are of short duration (less than 25 min) [6]. An investigation by Smith et al. [66] compared aerobic power (VO_{2peak}), total work performed at 110% of VO_{2peak}, and time to fatigue in recreationally active men undergoing high-intensity interval training consuming either a placebo or β-alanine (6 g/day for the first 21 days, then 3 g/day for the next 21 days). The investigators reported improvements in all three performance variables for both groups after 21 days of supplementation; however, additional improvements were observed after 42 days of training in the individuals consuming β-alanine only. Others have reported that β-alanine supplementation can improve time to exhaustion [61] and increases in ventilatory threshold during graded exercise tests [61,67]. Changes in time to exhaustion have also been significantly correlated with increases in muscle carnosine content [68]. However, others have reported no effects of β-alanine supplementation on time to exhaustion [69,70] or ventilatory threshold [70,71]. Although β-alanine supplementation may have some potential effects on fatigue-related measure of endurance performance, most investigations report no improvements in maximal oxygen consumption (VO_{2max}) consequent to β-alanine supplementation [61,67].

Interestingly, Baguet et al. [54] reported significant correlations between intramuscular carnosine content and 100-m ($r = .600$), 500-m ($r = .661$), 2000-m ($r = .677$), and 6000-m ($r = .705$) rowing times. These results provided evidence that greater intramuscular carnosine content was associated with better rowing performance, not only for races of shorter duration but also for those of longer duration. In the same investigation an increase in intramuscular carnosine content after β-alanine supplementation (5 g/day for 7 weeks) was significantly correlated with the performance improvement in 2000-m rowing times, providing further support for the role of carnosine in endurance exercise performance.

One potential explanation for a possible improvement in aerobic performance with β-alanine supplementation is a possible relationship between increases in muscle carnosine and a potential increase in the anaerobic threshold [61,67,72]. Although these studies did not measure changes in muscle carnosine, their results do provide some insight into the potential relationship between those variables. Anaerobic threshold, also known as the lactate threshold, is the exercise intensity at which the body switches from using primarily aerobic pathways for ATP production to using primarily anaerobic pathways for ATP production, resulting in an increase in lactate and H^+ production. β-Alanine supplementation may increase the intensity of exercise at which anaerobic threshold is met, allowing for a lower production of H^+ for a given exercise intensity [61,67,72]. As a result of an increase in muscle carnosine, the internal environment of the muscle cells become less acidic, permitting exercise to continue for a longer duration and at a higher force output [73]. This hypothesis was supported by Jordan et al. [72], who discovered an increase in the exercise intensity at which blood lactate began to accumulate after β-alanine supplementation (6 g/day for 4 weeks) compared with a placebo. Additional support was provided by Zoeller et al. [67] who found a significant increase in power output at anaerobic threshold during a graded exercise test in subjects supplementing with 1.6 g/day of β-alanine for 4 weeks.

Another potential mechanism associated with enhancing endurance performance consequent to β-alanine supplementation is of an indirect nature. Increases in intramuscular carnosine content and the associated improvements in muscle buffering capacity have been proposed to increase aerobic performance by improving the quality of the training stimulus [27]. For instance, an increase in muscle buffering capacity can improve the quality of anaerobic training (i.e., high-intensity interval training) by allowing for greater stress to the metabolic system and strengthening aerobic capacity and cardiovascular function. Furthermore, an increase in muscle buffering capacity, in itself, may be advantageous for endurance athletes, particularly at the end of a race or competition, where the anaerobic push during the final stages may be the crucial determining factor for performance. In support, Van Thienen et al. [74] reported significant increases in peak and mean power output during a 30-s isokinetic sprint that followed an exhaustive 110-min simulated cycling race and 10-min time trial in individuals who consumed β-alanine (2–4 g/day for 8 weeks) compared with a placebo. This study provides support that β-alanine supplementation may be useful for increasing anaerobic performance at the end of an aerobic event, leading to an overall increase in performance.

Most aerobic activities of longer duration do not benefit from β-alanine supplementation. Chung et al. [75] found no improvements in a 1-h time trial in trained cyclists after supplementation, despite significant increases in muscle carnosine content. Furthermore, an investigation by Van Thienen et al. [74] reported no differences in time to exhaustion (in a cycling trial lasting ~50 min) after 8 weeks of β-alanine supplementation. Evidence to date suggests that β-alanine supplementation may benefit shorter duration aerobic activities (~25 min); however, these effects are not present with endurance activities of longer duration (>1 h).

Effects of β-Alanine Supplementation on Tactical Performance

Efforts have begun to focus on the potential effects of β-alanine supplementation on tactical populations. Sustained military operations and simulated operational training are often accompanied by periods of prolonged wakefulness, malnourishment, and extreme physical and cognitive fatigue. Decreases in physical and mental capabilities can increase the risk of accidents and errors in decision-making, which may ultimately lead to a failed mission. A study by Hoffman et al. [2] reported that β-alanine supplementation (6 g/day for 4 weeks) in elite combat soldiers was effective in improving lower body power, psychomotor performance, peak jump power, target engagement speed, and shooting accuracy during intense military training. In a follow-up study by the same research team, using the same dosing protocol, significant increases in muscle carnosine content were reported, which were correlated ($r = .633$) to changes in fatigue rate [3]. Soldiers supplementing with β-alanine also experienced a significantly lower time for a 50-m casualty carry and improved cognitive function [3]. These results provided the initial evidence to support the use of β-alanine supplementation for improving tactical performance in soldiers.

Effects of β-Alanine Supplementation on Body Composition

Numerous investigations have examined the effects of β-alanine supplementation on body mass and body composition. The results of most studies show that β-alanine supplementation alone does not significantly alter body mass or body composition [5,37,59,61,68,76]. However, others have suggested that β-alanine supplementation may increase lean body mass when used in conjunction with exercise training. For example, improvements in lean body mass have been reported in collegiate wrestlers and football players after 8 weeks of 4 g/day of β-alanine supplementation [58]. Smith et al. [66] discovered an increase in lean body mass but no changes in body mass, body composition, or fat mass after 6 weeks of high-intensity interval training combined with β-alanine supplementation (6 g/day for the first 21 days, then 3 g/day for the next 21 days). Furthermore, Hoffman et al. [77] reported significant improvements in both percent body fat and lean tissue accruement after 10 weeks of daily ingestion of 3.2 g of β-alanine and 10.5 g of creatine compared with creatine only or a placebo. The investigators suggested that these changes were related to the significantly greater volume of training experienced by the combined β-alanine and creatine group compared with creatine alone or placebo groups.

These results suggest that β-alanine supplementation alone will not likely alter body mass or body composition but when combined with training, increases in lean mass may be greater than those seen with training or supplementation alone. As discussed, positive changes in lean body mass with the combination of β-alanine supplementation and training is likely related to the benefits of an improved muscle buffering capacity allowing for an increase in exercise training volume.

HEALTH BENEFITS OF β-ALANINE AND CARNOSINE SUPPLEMENTATION

Besides acting as an intramuscular buffer, carnosine has shown to have various other physiological roles in the body, including potentially acting as an antioxidant, antiglycating agent, and ion chelator [78–81]. During high-intensity exercise, significant oxidative stress is imposed on the body, resulting in increases in reactive oxygen species (ROS), causing inflammation and cellular damage [82]. The ability of carnosine to work as an antioxidant is seen through its scavenging of free radicals and ROS, specifically superoxide anion, singlet oxygen, and peroxyl radicals [80,83]. Research has also demonstrated that carnosine can act as an ion chelator, preventing ions such as copper, iron, and zinc from reacting with peroxides that may lead to lipid peroxidation and cause further cellular damage [81,84]. Therefore possessing greater amounts of intramuscular carnosine may be beneficial for preventing oxidative damage associated with exercise and in aiding with the recovery process after exercise. However, most of the research examining the effects of carnosine content on oxidative stress has been explored in vitro, and limited research has been conducted in humans. Although animal and in vitro studies have suggested that β-alanine supplementation may reduce lipid peroxidation and damage caused by ROS after exercise, actual evidence is lacking in human studies. The limited number of studies conducted have failed to demonstrate any significant effect on reducing oxidative stress after β-alanine supplementation [85,86]. Further research is necessary to elucidate the effects of β-alanine supplementation on oxidative stress in humans.

Other investigators have proposed that carnosine may have antiaging and antidiabetic properties as carnosine seems to reduce the formation of advanced end glycation and lipid peroxidation products, resulting in lower levels of cellular dysfunction and damage [87–89]. Evidence has demonstrated that carnosine may have beneficial effects on many diseases associated with aging, including decreasing insulin resistance in individuals with type 2 diabetes [90]

and improving neurological symptoms in patients with Parkinson's disease [91]. Elevated muscle carnosine, carnosine supplementation, or β-alanine supplementation have been reported to improve the quality of life and overall well-being of older adults [4,92], improve episodic memory [93,94], increase cognitive functioning [95], reverse the downregulation of the brain serotonergic system [92], and decrease symptoms of schizophrenia [96]. Research has also suggested that carnosine may protect against cancer, especially in the colon [97–99].

Investigations using a rodent model have reported that carnosine supplementation might also reduce kidney disease, improve renal function, and decrease plasma triglycerides and atherosclerotic plaque in diabetic mice [100–102]. Furthermore, carnosine supplementation has also been shown to suppress mitochondrial monoamine oxidase A activity in the brains of rats [92], consequently providing antidepressant actions by maintaining norepinephrine levels [88,103]. In vitro cultures exposed to physiological carnosine solutions have also demonstrated prolonged lifespans and reduced symptoms of senescence [104].

Research has demonstrated that β-alanine supplementation can increase brain carnosine content in rodents and may provide a degree of protection for the brain when exposed to a traumatic event. Murakami and Furuse [105] reported that a β-alanine–supplemented diet in mice could increase brain carnosine concentrations in the cerebral cortex and hypothalamus and increase the concentration of brain-derived neurotrophic factor (BDNF) in the hippocampus. These changes were also accompanied by significantly greater activity of the mice in the open arms of an elevated plus-maze test, suggestive of a decrease in depression. Others have reported that 30 days of β-alanine (100 mg/kg body mass) in Sprague–Dawley rats was effective in increasing carnosine levels throughout the brain and decreasing levels of anxiety and symptoms of posttraumatic stress disorder (PTSD) [106]. Elevations in carnosine concentrations in the various brain regions were inversely associated with anxiety index (r's ranging from −.471 to −.550, P's < .002) and positively associated with improved time spent in the open arms of an elevated plus-maze test (r's ranging from .453 to .521, P's < .003). Rats provided with β-alanine and exposed to the stress were also able to maintain BDNF expression in the hippocampus compared with rats that were fed a regular diet and exposed to the stress. A subsequent study by Hoffman et al. [107] provided the same dosing protocol in rats before exposing them to a low-pressure blast wave. Exposure to a low-pressure blast wave has been demonstrated to be an effective model to elicit distinct behavioral and morphological changes that simulate mild traumatic brain injury (mTBI)–like, PTSD-like, and comorbid mTBI-PTSD–like responses [108]. Thirty days of β-alanine ingestion in rats was reported to be effective in reducing the incidence of mTBI-like phenotype after exposure to a low-pressure blast wave [107]. Animals supplemented with β-alanine and exposed to the blast wave experienced a significant reduction in symptoms associated with mTBI-like behavior compared with animals consuming a standard diet (26% vs. 46%, respectively). In addition, rats fed with β-alanine appeared to have a reduced inflammatory response and a higher BDNF expression in the hippocampus compared with rats that were exposed to the blast wave but fed a standard diet. The results of these studies suggest that elevations in brain carnosine provide a protective effect on BDNF expression in the hippocampus likely by reducing the inflammatory response. The outcome of these investigations provides exciting evidence in regards to β-alanine's protective effect and its ability to increase resiliency to both PTSD and mTBI. However, additional research examining a human model is warranted. In addition, no investigations are known that have examined the efficacy of β-alanine as a potential treatment modality for individuals diagnosed with PTSD or mTBI.

DETERMINANTS OF SKELETAL MUSCLE CARNOSINE

β-Alanine consumption has a potent effect on increasing muscle carnosine levels. However, changes in muscle carnosine content are affected by various factors aside from β-alanine supplementation. The section below highlights a few of the important determining factors of endogenous carnosine levels. Fig. 28.4 depicts the determinants of skeletal muscle carnosine and its effects on exercise performance.

Diet

Intramuscular carnosine content is affected by diet. Increases in dietary protein intake are suggested to be related to higher skeletal muscle carnosine content [47,109,110]. Because most dietary β-alanine is derived from meat and fish products, vegetarian diets are deficient in β-alanine [111]. Endogenous β-alanine production occurs primarily through hepatic degradation of uracil [112]. This results in a minimal production of β-alanine and can result in vegetarians having low carnosine levels [111]. Previous studies have demonstrated significantly lower muscle carnosine levels in vegetarians compared with omnivores [5,111]. Additional research has shown that in omnivorous females, those who consumed the highest amount of dietary protein had the greatest skeletal muscle carnosine content [47,110].

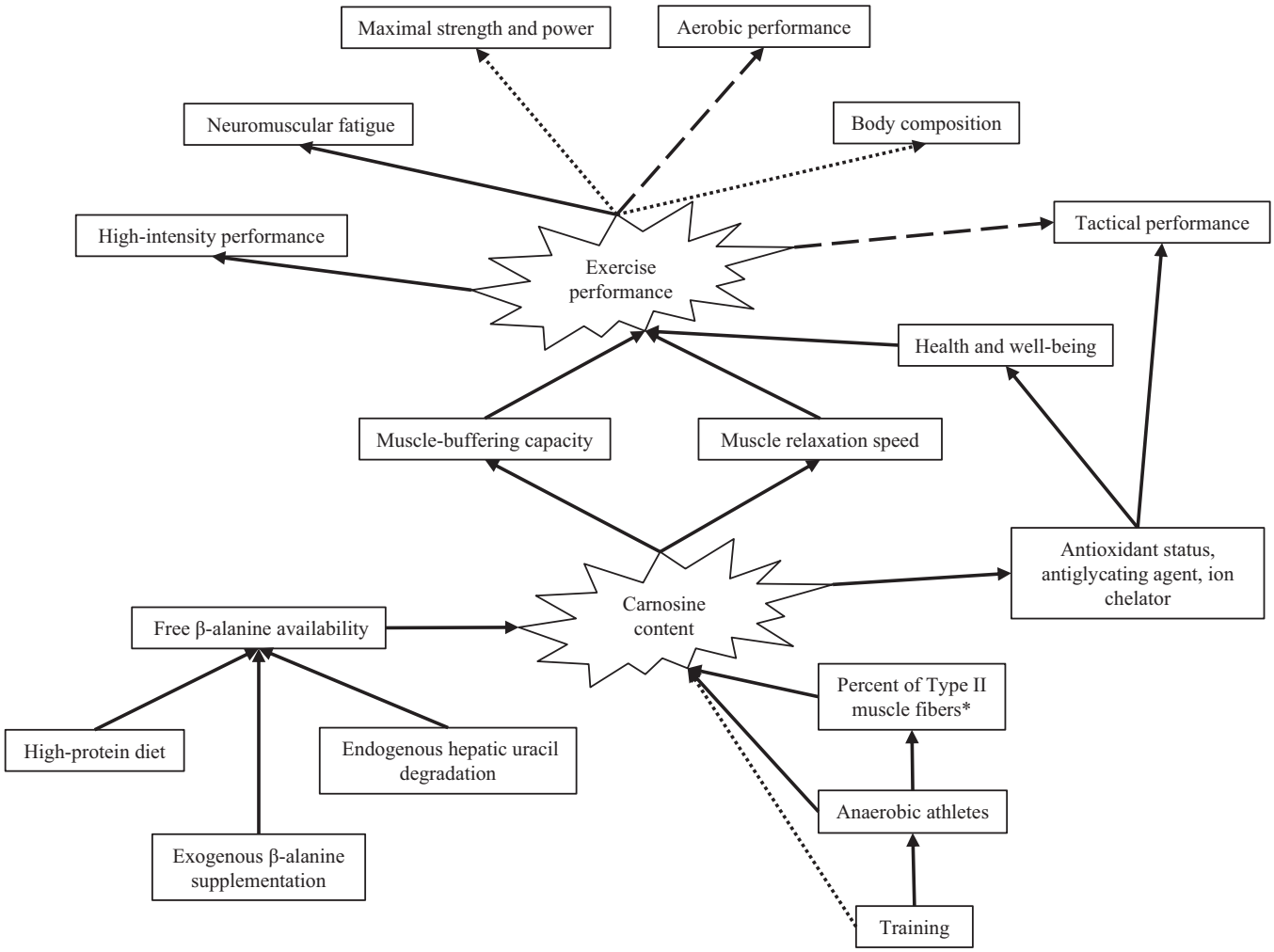

FIGURE 28.4 A schematic representing the determinants of skeletal muscle carnosine content and its effects on exercise performance. *Solid arrows* presented illustrate that the former box in the sequence has a direct positive effect (i.e., improvement or increase) on the latter box. *Dashed arrows* represent a possible positive effect. *Dotted arrows* represent no effect. *Anaerobic training has not been proven to induce a greater percentage of Type II muscle fibers; however, elite anaerobic athletes may display a greater Type II fiber distribution.

In contrast, Everaert et al. [111] reported no difference in skeletal muscle carnosine content between males with high and low amounts of dietary β-alanine consumption. However, these differences may be a result of the total amount of β-alanine consumed. Subjects from the study by Evereart et al. [111] were Belgian males, whose dietary protein consumption is low in comparison to North American standards [113]. It is possible that a threshold level of protein intake is needed to start seeing significant differences in muscle carnosine formation from dietary sources.

Muscle Fiber Type

Significant differences in carnosine content exist between Type I and Type II fibers [29,37,114]. Carnosine content in fast-twitch fibers may be up to 100% greater than that reported in slow-twitch fibers [29,37,111]. Muscle that comprised a greater percentage of Type II fibers would likely have a higher carnosine content than muscle that comprised a greater proportion of Type I fibers. Derave et al. [46] reported that the gastrocnemius muscle, which is predominantly composed of Type II fibers, had a 25% greater carnosine content than the soleus muscle, which is primarily composed of Type I fibers.

Despite initial variability in carnosine content, β-alanine supplementation has been shown to increase muscle carnosine concentrations similarly in both fast-twitch and slow-twitch fibers [29,37,46]. However, when comparing two muscles that have differing carnosine contents at baseline, a similar absolute increase in carnosine would correspond to a higher relative increase in the muscle with lower carnosine content. Therefore research reporting greater relative

increases in carnosine content in Type I fibers compared with Type II fibers may be a function of the carnosine content at baseline in Type II fibers.

Gender

A sexual dimorphism seems to exist with regards to intramuscular carnosine content. Skeletal muscle carnosine content is approximately 20%–25% greater in men compared with women [111,115,116]. Differences in fiber type distribution may play a role in explaining some of the carnosine variability between genders. Men have been shown to have a greater proportion of Type II fibers compared with women [116] and that the size of these fibers is much larger in men [116,117]. Considering that Type II fibers have a higher carnosine content than Type I fibers, and men tend to have a greater percentage of fast-twitch fibers, fiber type distribution is likely a contributing factor to the gender differences observed in carnosine content.

Also, as previously discussed, dietary protein plays a role in intramuscular carnosine production. One of the potential mechanisms behind the gender dimorphism of carnosine content is related to differences in dietary protein consumption between men and women. Research suggests that men consume more protein than women [118]. Greater dietary protein intake would provide for a greater pool of β-alanine to combine with histidine to produce carnosine.

Gender differences in muscle carnosine levels may also be related to differences in circulating testosterone concentrations [119,120]. Research conducted in rats has shown that castration, resulting in a decrease in endogenous testosterone production, results in a significant decrease in muscle carnosine content [119]. Also, exogenous testosterone administration in rats has been shown to result in a 2.5-fold increase in carnosine content [119]. In humans, research has shown that bodybuilders have approximately double the carnosine content compared with control subjects [120] and that carnosine content increases dramatically during puberty in boys but not in girls [121], suggesting that testosterone is a positive determinant of carnosine formation. Carnosine content is also lower in older compared with younger adults, which mirrors the change (e.g., decrease) in circulating testosterone associated with aging [111]. However, some evidence suggests that the gender dimorphism of carnosine content in regards to testosterone concentrations may be related to the differing fiber type ratio in men and women [111] and that additional research is still needed to determine the effects of gender on carnosine content.

Despite differences in baseline carnosine content between men and women, a study examined whether such differences impact carnosine changes during β-alanine supplementation [48]. Results of the study demonstrated no differences between the genders in the absolute increase in carnosine content after 28 days of β-alanine supplementation (6 g/day). This investigation also reported baseline intramuscular carnosine concentrations in both genders that were the highest among those reported in the literature, showing that carnosine content can be increased, regardless of high baseline concentrations.

Training Status

Most investigations appear to be consistent regarding the role that training has on muscle carnosine changes. Evidence to date suggests that intramuscular carnosine content cannot be elevated by exercise training alone [28,29,122,123]. Studies examining the effects of exercise on muscle carnosine content have shown that 4–16 weeks of isokinetic training, cycling, sprint training, and resistance training are unable to elevate muscle carnosine content [28,29,122,123]. Only one study is known that has reported a positive effect of intense training and increases in muscle carnosine; Suzuki et al. [124] reported that 8 weeks of high-intensity sprint training significantly increased muscle carnosine content in young healthy males. However, no other study has been able to confirm that training alone can increase carnosine content.

Regardless of whether or not training can elevate carnosine content, it is evident that elite athletes participating in sports requiring high buffering capacity have the greatest amounts of intramuscular carnosine [125]. For example, sprinters and rowers have greater intramuscular carnosine than marathoners, whereas no significant differences in carnosine content have been found between marathoners and their sedentary counterparts [125]. Olympic speed skaters have also been reported to have some of the highest muscle carnosine content among athletes [126], but the highest carnosine content has been found in bodybuilders [120]. However, androgen use may be a confounding factor influencing the elevated carnosine levels seen in bodybuilders. Regardless, significant correlations ($P < .05$) have been discovered between buffering capacity and carnosine levels, as well as carnosine content and anaerobic performance ($P < .01$) [125], showing that carnosine content may be a potential determining factor for high-intensity performance. Considering that current knowledge suggests that carnosine content cannot be increased by training alone, it is possible that a degree of self-selection may be evident. That is, those individuals who have an inherently

high level of intramuscular carnosine have a natural advantage when participating in high-intensity exercise and therefore choose to partake in those sports [28].

Training and β-Alanine Supplementation

There is some evidence to suggest that the combination of β-alanine supplementation and exercise training has a cumulative effect on increasing carnosine content. A study conducted by Bex et al. [127] compared carnosine content in trained athletes (including swimmers, kayakers, and cyclists) with untrained individuals after 23 days of 6.4 g/day of β-alanine supplementation. These investigators reported greater increases in muscle carnosine in the trained muscles of athletes compared with the untrained muscles. For instance, higher increases in muscle carnosine were found in the deltoid muscle of kayakers compared with the gastrocnemius, whereas the opposite pattern was found in cyclists, indicating that the muscles used for a particular sport or activity may be the ones that are most sensitive to elevations in carnosine. The nonathletes had the lowest increase in muscle carnosine in comparison to the athletes [127]. In contrast, Kendrick et al. [29] reported similar increases in carnosine content in both trained and untrained legs after 4 weeks of unilateral isokinetic training combined with β-alanine supplementation (6.4 g/day). These findings indicate that β-alanine supplementation increased carnosine content, but carnosine was not further increased by training [29]. However, it should be noted that the training volume in the study by Kendrick et al. [29] (10 sets of 10 repetitions of knee extensions performed 3–4 times a week) was less than 8 h/week of sport-specific training in the study by Bex et al. [127]. This increase in training volume would significantly increase blood flow, thus increasing delivery of β-alanine to active muscle [127]. It is possible that exercise stimulates β-alanine membrane transporters enhancing β-alanine uptake into the cell or that trained athletes may have greater capillary density, which will enhance β-alanine delivery to the cell. Further research appears to be necessary to determine the effects of both training and supplementation, combined or separately, on changes in muscle carnosine content.

SAFETY OF β-ALANINE SUPPLEMENTATION

Most studies examining the ergogenic effects of β-alanine have used dosing strategies ranging between 1.6 and 6.4 g/day [27,73]. Higher doses have not often been examined because of the greater risk of experiencing symptoms of paresthesia [27], which include flushing, irritation, and pricking of the skin. These symptoms typically occur when 800 mg of β-alanine or more is ingested in a single dose [5], and symptoms last 60–90 min after ingestion [30], with a higher dosages resulting in greater symptoms. Circulating β-alanine is thought to bind to Mas-related G protein–coupled receptor D (MrgprD), which is primarily expressed in the sensory dorsal root ganglion neurons that lie under the skin [128]. These receptors have a high affinity for itch-inducing ligands [128] and thus the binding of β-alanine to MrgprD is thought to induce the itching sensations associated with β-alanine consumption. As such, this has resulted in an ingestion pattern requiring small doses of β-alanine to be consumed multiple times per day [37] or consumption of a sustained-release formulation of β-alanine. The advantage of a sustained-release formulation is that it can reduce symptoms of paresthesia and potentially allow for a higher daily dose to be consumed. Decombaz et al. [129] compared 1.6 g of instant-release and sustained-release formulations of β-alanine and reported no difference in the area under the curve for plasma β-alanine for 6 h after ingestion. Also, the sustained-release formulation resulted in a delay in the peak concentration of β-alanine in plasma and a more extended retention time compared with the instant-release dose. Individuals consuming the sustained-release formulation had significantly lower symptoms of paresthesia compared with individuals consuming the instant-release dose [129]. Additionally, a study by Church et al. [34] reported no differences in symptoms of paresthesia between individuals consuming 12 g/day of sustained-release β-alanine and those consuming a placebo, indicating that the sustained-release form may be an effective and efficient way of increasing muscle carnosine without side effects.

Considering that β-alanine is a nonproteogenic amino acid that the body produces endogenously with important physiological functions, it is likely that β-alanine is a safe supplement to use. The efficacy of β-alanine supplementation has been examined in various populations, including athletes, untrained individuals, and military personnel, as well as younger and older populations, with no adverse health consequences. Harris et al. [5] reported that 3.2 g/day of β-alanine supplementation for 4 weeks had no effect on 12-lead electrocardiogram results and blood biochemistry or hematological data. Similarly, a study by Church et al. [34] showed that 2 weeks of 12 g/day of β-alanine supplementation did not result in any changes in hematological variables or complete blood cell counts. Additionally, longer β-alanine supplementation periods (8–12 weeks of 0.8–3.2 g/day) have shown that β-alanine supplementation appears to be safe for both younger [32] and older populations [63,68].

One of the proposed physiological consequences of chronic β-alanine supplementation in high doses is the potential for a decreased intramuscular taurine concentration and a downregulation of the β-alanine receptor, TauT, in skeletal muscle (See Fig. 28.2). β-Alanine and taurine share the same transporter [5], and dramatic increases in the bioavailability of β-alanine (i.e., through supplementation) may, therefore, inhibit taurine uptake into the muscle because of competitive inhibition. Additionally, owing to the balance of taurine and carnosine concentrations on intracellular osmoregulation, an increase in carnosine concentration may decrease the amount of intracellular taurine, impacting several physiological functions such as oxidative capacity [73,130]. Studies conducted in animal models have shown that intramuscular taurine concentrations decrease after β-alanine supplementation [131]. However, the decrease in taurine did not have any adverse side effects on oxidative capacity, and the β-alanine dosage supplied was much higher than what is typically used in human studies. In older rats though, an increase in oxidative stress and lipid peroxidation was associated with decreased intramuscular taurine after β-alanine supplementation [131]. However, no such results have been reported in humans [5,37]. Harris et al. [5] reported an increase in plasma taurine concentrations but no change in intramuscular taurine after 4 weeks of β-alanine supplementation. On the other hand, an investigation by Saunders et al. [38] found a significant downregulation in TauT receptors on skeletal muscle after 24 weeks of 6.4 g/day of β-alanine supplementation. Carnosine content continued to increase throughout the 24-week period, although the rate of increase decreased over time. These results provide evidence suggesting that the downregulation of TauT, and resultant decrease in β-alanine transport into skeletal muscle, may have led to a decrease in the rate of carnosine synthesis. These results indicate that carnosine synthesis may be more dependent on the amount of β-alanine transported into the muscle than on the activity of carnosine synthase [38]. Intramuscular taurine was not measured in this investigation; therefore it cannot be concluded that the downregulation of TauT led to a decrease in taurine concentrations. However, it is apparent that more research is necessary to determine if long-term supplementation with β-alanine leads to changes in the concentrations of intramuscular amino acids and muscle metabolites.

Another potential consequence of chronic β-alanine supplementation is a decrease in intramuscular histidine concentrations [26]. Although β-alanine is the rate-limiting factor of carnosine synthesis, it has been suggested that when β-alanine combines with histidine to form carnosine, it may potentially cause a reduction in the free histidine pool [26]. A reduction in intramuscular histidine may affect protein metabolism, as well as reduce hemoglobin and hematocrit concentrations [132]. A study conducted by Blancquaert et al. [26] reported that 3.5 g/day of β-alanine supplementation for 21 days resulted in significant decreases in intramuscular histidine. However, when participants supplemented with histidine and β-alanine combined, no significant decreases in intramuscular histidine were seen [26]. In contrast, a study by Church et al. [34] showed that 6 g/day for 4 weeks and 12 g/day for 2 weeks did not alter intramuscular histidine levels and that additional histidine supplementation was not necessary to maintain histidine concentrations. Interestingly, Hoffman et al. [107] reported that β-alanine ingestion resulting in significant elevations of brain carnosine also resulted in significant elevations in brain histidine content. Histidine content across the brain was 86% higher in the animals consuming β-alanine than animals consuming their normal diet. Also, carnosine content was significantly correlated ($r = .75$) to histidine content in the hippocampus. Still, further research appears justified to examine the effects of β-alanine supplementation on changes in intramuscular histidine content.

CONCLUSIONS

The beneficial effects of β-alanine supplementation are a result of the increase in intramuscular carnosine content and not a direct action of β-alanine itself. Owing to the ability of carnosine in buffering H^+, the level of exercise-induced acidosis decreases with β-alanine supplementation, allowing high-intensity exercise to continue for a longer duration. β-Alanine supplementation seems to be most beneficial for improving high-intensity exercise lasting 1–4 min. However, numerous investigations have supported the notion that chronic β-alanine supplementation has a myriad of beneficial effects, ranging from improving exercise performance to increasing health and well-being in various population groups.

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