Original Communication

Niacin supplementation impairs exercise performance

Greggory R. Davis[1] and Arnold G. Nelson[2]

[1] University of Louisiana at Lafayette, LA, USA
[2] Louisiana State University, Baton Rouge, LA, USA

Abstract: Several pre-workout supplements contain niacin, although the exercise performance effects of niacin are poorly understood. The purpose of the present study was to examine the performance effects of niacin versus caffeine as a pre-workout supplement. Twenty-five untrained males were recruited to complete three identical ramped aerobic cycling exercise trials. Participants were administered caffeine (CA) at 5 mg/kg body weight, 1000 mg niacin (NI), or a methylcelluloce placebo (PL) supplement prior to each trial. NI treatment induced significantly higher respiratory exchange ratio (RER) during exercise compared to the CA treatment, but not the PL treatment (PL=0.87±0.08, NI=0.91±0.08, CA=0.87±0.08; p=0.02). Similarly, exercise time to exhaustion (in minutes) was significantly different between the NI treatment and the CA treatment, but not the PL treatment (PL=27.45±4.47, NI=26.30±4.91, CA=28.76±4.86; p<0.01). Habitual caffeine use (p=0.16), habitual aerobic exercise (p=0.60), and habitual resistance exercise (p=0.10) did not significantly affect RER. Similarly, habitual caffeine use (p=0.72), habitual aerobic exercise (p=0.08), and habitual resistance exercise (p=0.39) did not significantly affect total work performed. The elevated RER and decreased time to exhaustion in the NI treatment suggests limited lipid availability during exercise and impaired exercise performance.

Keywords: Substrate, respiratory exchange ratio, aerobic exercise, performance

Introduction

Niacin, also known as vitamin B3, serves as a precursor to several physiological functions and is commonly found within many pre-workout supplements as well as many foods such as meat, poultry, fish, eggs, and green vegetables [1]. Once ingested, niacin is converted by all tissues into nicotinamide adenine dinucleotide (NAD), which is a coenzyme required by more than 400 enzymes for substrate oxidation or reduction [2]. It also plays a role in the regulation of gene expression and cell signaling [1, 3]. Niacin is also converted into nicotinamide adenine dinucleotide phosphate (NADP) in all tissues, with the exception of skeletal muscle. NADP is involved in cholesterol and fatty acid synthesis and it plays a role in antioxidant function. At supraphysiologic doses, niacin is also used to improve dyslipidemia by decreasing total and low-density lipoprotein (LDL), decreasing triglycerides, and increasing high-density lipoprotein (HDL) [4]. Given the multifaceted physiological functions of niacin, it is not surprising that it is utilized as a dietary supplement to improve overall health.

It is less clear why niacin would be utilized in pre-workout supplements designed to improve exercise performance. Large doses of niacin (1,000–3,000 mg) have been shown to cause flushing of the skin, as well as itching, burning, and tingling sensations in the skin due to vasodilation of small subcutaneous blood vessels [5]. Presumably, this tingling and burning sensation associated with many pre-workout supplements, though the dosage is significantly lower, is caused by niacin, although beta-alanine, which is another common ingredient in pre-workout supplements does elicit similar responses [6]. However, if there is a redirection of blood flow to subcutaneous tissue following niacin ingestion, it stands to reason that exercise performance may actually be hindered to some extent by niacin consumption due to less blood availability to working skeletal muscle. In addition, while it is possible that additional NAD availability in skeletal muscle could mitigate fatigue, if an individual is not niacin-deficient, and therefore has sufficient synthesis of NAD, it is not physiologically possible to speed up enzymatic reactions associated with substrate oxidation by taking an additional niacin supplement. Therefore, we hypothesized that the consumption of a niacin supplement pre-exercise would not affect substrate oxidation nor provide an ergogenic benefit for exercise performance.

Another limitation to the current understanding of how niacin affects exercise performance is that most pre-workout dietary supplements contain a combination of several ingredients, including niacin and caffeine. The positive effects of caffeine on exercise performance are well-established [7, 8, 9], but the effects of niacin on exercise performance are currently unknown. In a recent review, it has been suggested that the consumption of dietary supplements that contain both high levels of caffeine and niacin

should be limited [10], and more recently, it has been suggested that the interaction effects may be linked with acute hepatitis and liver failure in healthy adults [6]. In order to determine if niacin has any performance-enhancing (or inhibiting) potential, it is important to examine it as a standalone supplement. Given niacin's role in substrate metabolism, the purpose of this study was to examine the effects of a niacin supplement on substrate metabolism and exercise performance compared to caffeine, a well-established exercise performance-enhancing supplement.

Table 1. Subject characteristics (all males)

n=25	Mean	SD
Age (yr)	21.44	2.27
Height (cm)	177.21	6
Weight (kg)	74.37	13.32
BMI (kg/m^2)	23.36	3.27
Body fat (%)	21.44	0.05
Reg. caffeine (yes)	7	
Reg. aerobic ex.(yes)	12	
Reg. resist. ex.(yes)	14	

Reg. caffeine: regular caffeine consumption=≥ 1 cup of coffee per day; Reg. aerobic ex.: regular aerobic exercise=≥ 150 minutes of total aerobic exercise per week; Reg. resist ex.: regular resistance exercise=≥ 2 days/week of resistance exercise per week.

Materials and methods

Subjects

Untrained males (n=25) between the ages of 18–26 were recruited to participate in the study. All participants were non-smokers, were not taking any medication, and did not regularly perform any type of cycling exercise more than one time per week. Subject characteristics are shown in Table 1. All participants were healthy as indicated by the Physical Activity Readiness Questionnaire (PAR-Q). Informed consent was obtained from all participants prior to the onset of the first exercise trial and the study protocol was approved by the University's Institutional Review Board (Approval #3150).

Study design

Each participant completed three separate exercise trials, with a different dietary supplement consumed prior to each trial (i.e. placebo, caffeine, or niacin). Supplements were administered using a balanced, randomized, double-blind, crossover design. A one-week washout period separated each exercise trial to eliminate any carry-over effect. For the caffeine (CA) trial, each participant was administered an anhydrous caffeine supplement equating to five milligrams (mg)/kilogram (kg) of body weight. This dosage was established based upon previous research [11, 12], which equates two to three cups of coffee, or plasma levels of caffeine around 20–40 μmol/L to five mg/kg [9]. For the niacin trial (NI), each participant was administered 1000 mg of immediate-release niacin. This dosage was established based upon previous research [13], with the understanding that up to 3–4 g of niacin can be nearly completely absorbed at one time [4]. For the placebo trial (PL), each participant was administered a methylcellulose filled capsule. The placebo trial served as both a resting and exercise control. Each supplement was ingested thirty minutes prior to the onset of the blood draws and exercise protocol. This supplement ingestion timeframe was established to keep consistency between all trials, ensure the study remained double-blinded, and at the same time, optimize the highest plasma concentrations of each supplement as possible. Most caffeine supplement studies are performed following a sixty minute absorption time; however, studies have shown that plasma caffeine concentration peaks at approximately thirty minutes following absorption of anhydrous caffeine [14]. Furthermore, niacin plasma concentration from immediate-release capsules peaks approximately twenty to thirty minutes after ingestion [4, 15]. Due to these preceding factors, an absorption time of thirty minutes was established.

Participants were instructed to abstain from caffeine and alcohol consumption 48 hours prior to each trial and were asked to abstain from exercise for twenty-four hours prior to each trial. In addition, participants entered the lab ten hours postprandial and were asked to consume a standard meal of approximately 270 kilocalories (60% carbohydrate, 15% protein, 25% fat) prior to each exercise trial to ensure consistent results across all participants and between each trial.

Upon arrival to the testing site, all baseline measures were obtained (Table 1). Height and weight were measured using a Detecto medical scale (Cardinal Scale Manufacturing Co., Webb City, MO), body fat was measured via the seven-site skinfold technique (ACSM's guidelines, 2010) using Lange skinfold calipers (Beta Technology, Inc., Cambridge, MD), and a questionnaire regarding exercise habits was completed. Regular aerobic exercise was considered ≥ 150 minutes of total aerobic exercise per week.

Exercise protocol

Following the completion of baseline testing, resting respiratory exchange ratio (RER) data was obtained through indirect calorimetry (Moxus Modular VO_2 System,

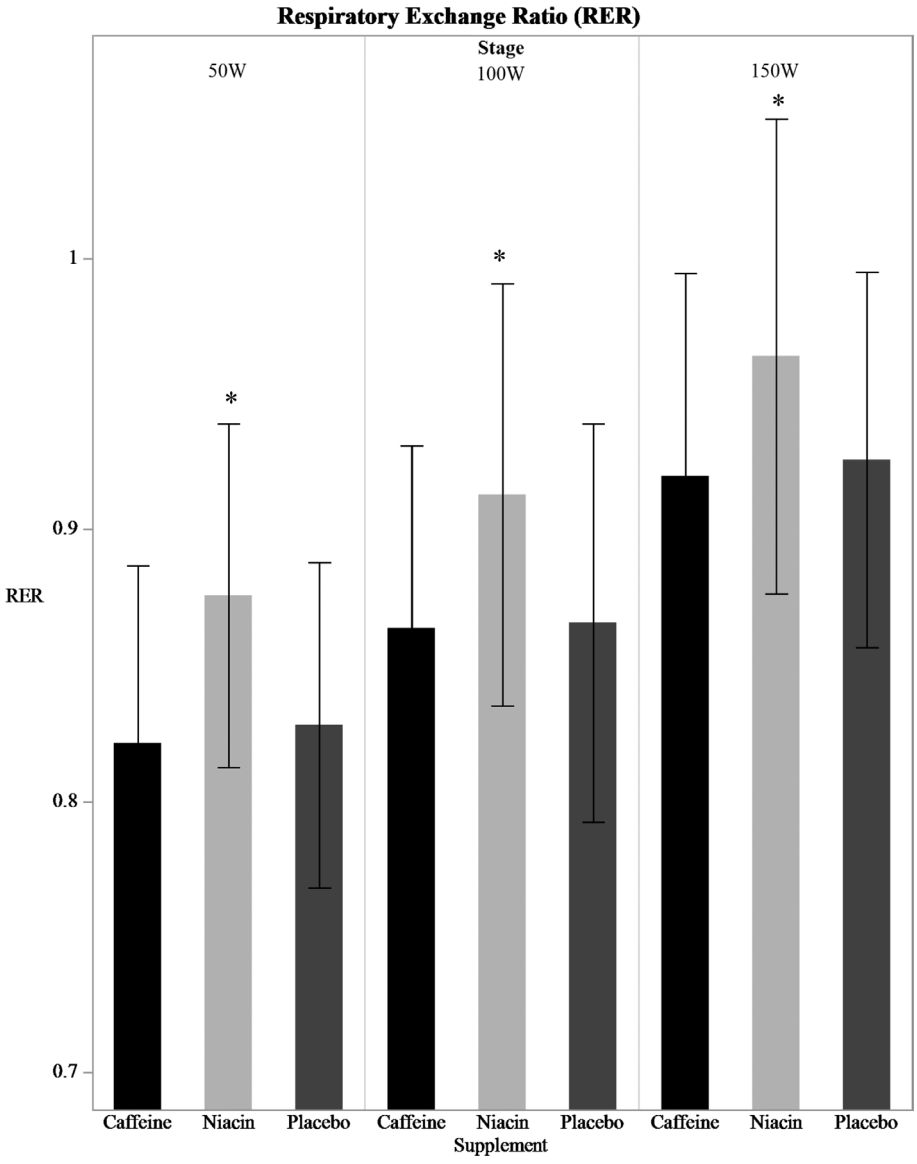

Figure 1. Substrate utilization during exercise. Comparison of respiratory exchange ratio (RER) at 50, 100, and 150 W for placebo, niacin, and caffeine exercise trials. *p<0.05 compared to placebo and caffeine treatment. Values are presented as mean, error bars represent SD (n=25).

Pittsburgh, PA). Volume of oxygen consumed (VO_2), and respiratory exchange ratio (RER) were monitored for the duration of the study. All exercise protocols were performed on a mechanically braked cycle ergometer (Monark Exercise AB, Norrbotten, Sweden). Before the onset of each exercise session, participants completed a ten-minute warm-up at a twenty-five-watt (W) power output maintaining seventy revolutions per minute (rpm). A pedal frequency of seventy rpm was maintained for the entirety of the warm-up and exercise phases as this pedal cadence was found to be comfortable for the untrained individuals used in the current study. Participants then began the initial workload at fifty Watts. The workload then increased by fifty Watts every six minutes until the participant could no longer maintain his prescribed pedal frequency within five rpm for more than ten seconds. This time point was recorded and deemed time to exhaustion. All subjects were able to complete a minimum of eighteen minutes of exercise, (up to 150W) and therefore, RER data were analyzed for the first eighteen minutes of exercise only for direct comparison purposes despite the ability of several subjects to exercise for greater periods of time. Total work volumes were compared to analyze differences between trials.

Statistical analysis

A repeated measures ANOVA was used to determine differences in RER, fat oxidation, time to exhaustion, and total

work between the three trials. Fat oxidation was calculated using previously established methods [16]. Correlations of co-variables were tested using a one-way ANOVA and significant differences were identified using Tukey post-hoc tests. $p<0.05$ was considered significant. All data were checked for normality with a Shapiro-Wilk test, any W statistic with a $p<0.05$ indicated non-normal distributions. A Levene's test was used to test homogeneity of variance, any F statistic with a $p<0.05$ indicated unequal variance. A linear regression was performed to verify that order effects of supplementation did not affect outcome variables. All values are presented as mean±SD. All statistical analyses were completed using JMP Pro v14.0 (SAS Institute, Inc. Cary, NC).

Results

The niacin treatment yielded significantly higher average RER values compared to the placebo and caffeine treatments. PL=0.87±0.08, NI=0.91±0.08, CA=0.87±0.08 (Figure 1). The effect for supplement was significant (F=4.37; p=0.02), a Tukey post-hoc test revealed that niacin was significantly different from the caffeine supplement (Cohen's d=0.69). Similarly, the calculated average percentage of fat oxidation was lower for the niacin treatment throughout the exercise trial. PL=3.39±1.64 $g \cdot min^{-1}$, NI=2.12±1.96 $g \cdot min^{-1}$, CA=3.89±2.03 $g \cdot min^{-1}$. (Figure 2). The effect for exercise stage was significant (F=32.32; $p<0.01$), a Tukey post-hoc test revealed that all stages were significantly different (Cohen's d=1.33, 0.78, and 0.55 for stage 1, 2, and 3, respectively). The interaction effect for supplement and stage upon RER values were not significant (F=0.10; p=0.98). Given an alpha level of 0.05, a sample size of 25, and three repeated measures for a single group, and the effect size for each outcome, the statistical power achieved for each RER outcome was > 0.8. Order effects did not significantly affect RER (F=1.27, p=0.28).

Time to exhaustion (in minutes) was significantly different (F=4.93; $p<0.01$) between the caffeine and niacin supplements, as determined by a Tukey post-Hoc analysis. PL=27.45±4.47 minutes, NI=26.30±4.91 minutes, CA=28.76±4.86 minutes (Figure 3). Similarly, total work (in Watts·min) was significantly different (F=4.70; p=0.01) between the caffeine and niacin supplements, as determined by a Tukey post-Hoc analysis (Cohen's d=0.50). PL=3908± 1220 Watts·min, NI=3673±1270 Watts·min, CA=4309±1330 Watts·min (Figure 4). Given an alpha level of 0.05, a sample size of 25, and three repeated measures for a single group, and the effect size for each outcome, the statistical power achieved for work was 0.97. Order effects did not significantly affect time to exhaustion (F=0.05, p=0.95) or total work (F=0.03, p=0.97).

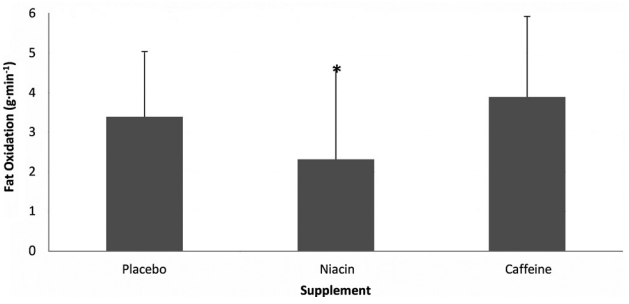

Figure 2. Comparison of fat oxidation at 50, 100, and 150 W for placebo, niacin, and caffeine exercise trials. Values are presented as mean, error bars represent SD. *$p<0.05$ compared to placebo and caffeine treatment (n=25).

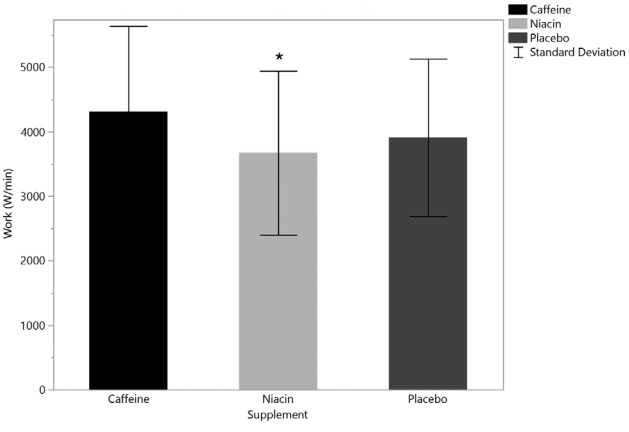

Figure 3. Time to exhaustion and total work. Comparison of time to exhaustion for placebo, niacin, and caffeine exercise trails in minutes (min). Values are presented as mean, error bars represent SD (n=25).

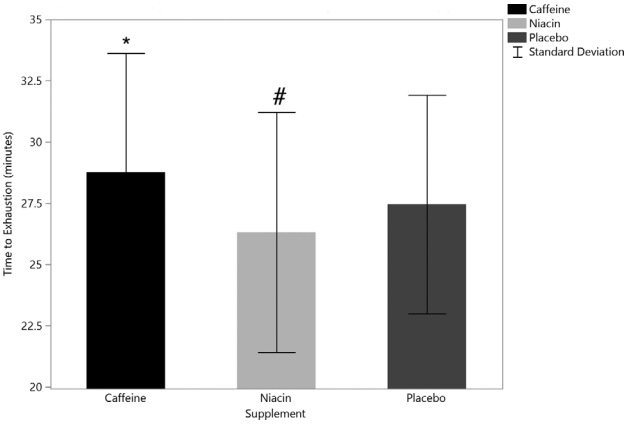

Figure 4. Comparison of total work performed for placebo, niacin, and caffeine exercise trails in watt minutes (Watt·min). Values are presented as mean, error bars represent SD. *$p<0.05$ compared to placebo treatment. #$p<0.05$ compared to caffeine treatment (n=25).

A one-way ANOVA revealed no significant effects for habitual caffeine use (F=1.99; p=0.16), regular aerobic exercise (F=0.27; p=0.60), or regular resistance exercise

Table 2. Effect of aerobic and resistance training on total work

	Mean work ($W \cdot min^{-1}$) for N, C, P	Pooled standard error for N, C, P ($W \cdot min^{-1}$)	Partial eta squared
Habitual aerobic	4168, 4915, 4301	238.90	0.06
No aerobic	3217, 3751, 3547	143.82	0.05
Habitual resistance	3541, 4078, 3717	175.49	0.04
No resistance	3841, 4605, 4153	245.60	0.05

N: niacin; C: caffeine; P: placebo.

(F =2.94; p=0.10), with habitual caffeine RER values of PL=0.89±0.01, CA=0.88±0.02, NI=0.92±0.02 and non-habitual caffeine RER values of PL=0.87±0.01, CA=0.86 ±0.02, and NI=0.91±0.02 (Partial eta squared=0.07). Similarly, habitual caffeine use (F=0.13, p=0.72), regular aerobic exercise (F=3.30; p=0.08), regular resistance exercise (F=0.76; p=0.39) was not significantly related to total work performed. Means, standard deviations, and effect sizes for work versus regular aerobic and resistance exercise are reported in Table 2.

Discussion

When compared to placebo ingestion, neither caffeine nor niacin elicited significant changes on substrate metabolism or exercise performance. However, when compared to the caffeine supplement, the niacin supplement significantly increased RER, lowered the calculated fat oxidation during cycling exercise, decreased time to exhaustion and total work performed. These results suggest that niacin may inhibit aerobic exercise performance.

Given that one of the physiological roles of niacin is to increase NAD production, which is subsequently utilized for substrate oxidation, it is unlikely that the ability to oxidize substrate was limited following niacin ingestion, but rather these results may suggest limited lipid availability compared to the caffeine supplement, ultimately leading to higher RER and lower lipid oxidation values. This notion is supported by previous studies which demonstrate that niacin treatment acutely decreases circulating free-fatty acids and inhibits lipolysis in adipose tissue [17, 18]. This is in contrast to chronic high-dose niacin ingestion, which has been shown to induce a muscle fiber type transition to more oxidative characteristics due to a rebound effect on lipolysis in adipose tissue and an increase in lipid availability in skeletal muscle [19, 20, 21]. Therefore, findings of the current study are in agreement with previous research and suggest that acute high-dose niacin consumption limits lipid availability in skeletal muscle during exercise.

Conversely, caffeine has been shown to have lipolytic properties [22] and logically demonstrated lower RER values and higher fat oxidation rates compared to niacin in the current study. However, it has also been suggested that the ergogenic effects of caffeine are primarily driven by its effects on the central nervous system, as opposed to alterations in lipid metabolism [23]. The current study did not reveal any significant differences between the placebo and caffeine trials when examining RER or fat oxidation, which is in agreement with the aforementioned review and suggests that the significant differences between caffeine and niacin may have been more driven by niacin's inhibitory effect on lipid availability as opposed to caffeine's stimulatory effect on lipid availability.

As expected, for each exercise trial, substrate utilization was the same at the point of exhaustion since the body relies almost exclusively on carbohydrate metabolism to meet energy demands at maximal exercise intensity [24]. However, RER was significantly elevated during the majority of the niacin exercise trial, indicating an overall shift in metabolism toward a greater reliance on carbohydrate metabolism. This reinforces the theory that niacin consumption may limit the ability to utilize fat as a substrate during exercise.

The limited ability to utilize fat during exercise may limit performance, particularly during longer duration aerobic exercise [25]. Data from the current study, which was relatively short in duration, suggest there are significant differences in performance, as measured by total work or time to exhaustion, following caffeine ingestion compared to niacin ingestion. It is worth noting that time to exhaustion and total work performed for the placebo trial were not significantly different from the niacin or caffeine trials. The reason for the lack of differences between these trials but significant differences between the niacin and caffeine trials are likely related to substrate utilization, which, as measured by RER, also demonstrated significant differences between caffeine and niacin trials but not between placebo and niacin or placebo and caffeine trials. Furthermore, previous research has indicated acute caffeine consumption does not affect RER compared to placebo during exercise [26], which is aligned with current results and further suggests alterations in lipid metabolism following niacin ingestion as opposed to changes in lipid metabolism following caffeine ingestion.

It is also worth noting that habitual caffeine use reduces ergogenic effects of caffeine [27], yet the data in the current study suggested that habitual caffeine use did not

significantly affect RER, likely due to minimal caffeine use among participants. Similarly, although RER values differ at low exercise intensities between those that habitually perform aerobic exercise and those that do not [28], RER values are similar at higher exercise intensities used in the current study, thus habitual exercise did not significantly affect RER values. As expected, participants that reported habitual caffeine use, habitual aerobic exercise, and habitual resistance did not exhibit differences in RER or total work performed. Given that the total work performed was relatively low and most participants could not complete the exercise stage at 200 Watts, the participants in the current study can be presumed to all have been untrained aerobically or anaerobically.

Little is currently known about the interactive metabolic effects when niacin and caffeine are consumed together, but from a lipid metabolism standpoint, niacin and caffeine appear to have opposing effects. Although analgesic and catecholamine-mediated effects of caffeine can also affect performance and may therefore outweigh the metabolic effects of niacin, two studies examining acute exercise performance following the ingestion of a dietary supplement containing both caffeine and niacin showed no performance benefit for strength or endurance [29, 30]. Another found an improvement in bench press one-repetition maximum, but no improvement in lower-body one-repetition maximum, muscular endurance, or anaerobic capabilities [31]. Conversely, when caffeine is consumed by itself as a dietary supplement, it has consistently been shown to improve physical performance [32, 33, 34].

One strength of this study was that the niacin supplement was compared to a placebo supplement as well as a caffeine supplement. This allowed for a direct comparison of niacin to caffeine, a well-established performance-enhancing supplement, as well as the comparison of these two supplements to a placebo. Another strength was that the study utilized a double-blind, randomized and counter-balanced design to minimize potential order effects or placebo effects. Another strength was that RER measures were collected throughout the exercise protocol to determine substrate utilization changes at different exercise intensities with different dietary supplements. Of the few studies that have previously examined performance effects of niacin, findings are largely in agreement with the current study, with no significant effects on aerobic performance identified [35, 36] and decreased plasma free fatty acid availability [37].

The primary weakness to this study was that plasma free fatty acids and plasma niacin concentrations were not measured. However, based upon the aforementioned study and the RER data of the current study, it is likely that the high dose of niacin effectively entered into the circulation and decreased free fatty acid concentration. Furthermore, the purpose of the study was not to investigate the physiological mechanisms of niacin, but to determine exercise performance. It should also be noted that food logs were not recorded and while participants were asked to maintain a consistent diet throughout the study, it is possible that differences in food intake 48 hours prior to the exercise trial could have influenced the outcomes of the study. In addition, caffeine intake was only restricted 48 hours prior to exercise. As reviewed by Graham, this timeframe results in minimal detectable levels of caffeine in the blood and withdraw of caffeine consumption 0, 2, or 4 days prior to caffeine ingestion did not affect the ergogenic effects of exercise performance [38]. Thus, it is unlikely that a longer time-frame restricting caffeine would have impacted the outcomes of the study.

The minimal performance effects of supplements containing both niacin and caffeine taken together with current data suggest niacin may slightly worsen performance while caffeine slightly improves it in untrained healthy men, thus the differences between niacin and caffeine, but not between placebo and niacin or placebo and caffeine. Previous data and current data suggest niacin does not have any performance-enhancing benefits and may potentially worsen exercise performance. Caution should be taken when consuming dietary supplements containing high levels of niacin.

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Conflict of interest
The authors declare that there are no conflicts of interest.

ORCID
Greggory R. Davis
https://orcid.org/0000-0003-2410-9070

Greggory R. Davis, PhD
School of Kinesiology
University of Louisiana at Lafayette
PO Box 42210
Lafayette, LA 70504
USA

gregg.davis@louisiana.edu