



Acute Effect of Oral N-Acetylcysteine on Muscle Soreness and Exercise Performance in Semi-Elite Rugby Players

Kate M. Rhodes, Dane F. Baker, Brett T. Smith & Andrea J. Braakhuis

To cite this article: Kate M. Rhodes, Dane F. Baker, Brett T. Smith & Andrea J. Braakhuis (2018): Acute Effect of Oral N-Acetylcysteine on Muscle Soreness and Exercise Performance in Semi-Elite Rugby Players, Journal of Dietary Supplements, DOI: [10.1080/19390211.2018.1470129](https://doi.org/10.1080/19390211.2018.1470129)

To link to this article: <https://doi.org/10.1080/19390211.2018.1470129>



Published online: 29 Jun 2018.



Submit your article to this journal [↗](#)



View Crossmark data [↗](#)

ARTICLE



Acute Effect of Oral N-Acetylcysteine on Muscle Soreness and Exercise Performance in Semi-Elite Rugby Players

Kate M. Rhodes, MHSc^a, Dane F. Baker, MSc^b, Brett T. Smith, PhD^{b,c}, and Andrea J. Braakhuis, PhD^a

^aThe University of Auckland, Discipline of Nutrition, Faculty of Medical & Health Sciences, Auckland, New Zealand; ^bChiefs Rugby Franchise, Ruakura Research Centre, Hamilton, New Zealand; ^cTe Oranga School of Human Development and Movement Studies, University of Waikato, Hamilton, New Zealand

ABSTRACT

N-acetylcysteine (NAC) supplementation may enhance performance and reduce soreness from acute, repeated-sprint, high-intensity exercise. Our aim was to investigate whether semi-elite rugby union athletes may benefit. In a randomized block design, 17 semi-elite male rugby players were assigned to receive either 1 g oral NAC ($n = 8$) or placebo ($n = 9$) for six days. The mean percentage effect of NAC on exercise performance was assessed through completion of a broken bronco exercise test on days 5 and 6 of supplementation. Players self-reported muscle soreness and tolerability to supplements using a modified Muscle Pain and Treatment Satisfaction Questionnaire throughout the supplement duration. NAC produced a likely beneficial performance effect on maximum shuttle sprint time (2.4%; 90% confidence limit $\pm 4.8\%$) but was unclear on total time during back-to-back broken bronco tests compared to placebo. NAC had a likely protective effect on subjective muscle soreness during days 1–4 of supplementation ($-19\% \pm 27\%$) but a very likely harmful effect on days 5 and 6 of supplementation ($71\% \pm 59\%$). Daily supplementation with 1 g of oral NAC for six days produced no adverse side effects, reduced muscle soreness after one bout of damaging exercise, but increased soreness following the second bout. The performance effects were generally unclear apart from maximal sprint time.

KEYWORDS

competition; exercise; N-acetyl cysteine; nutrition; performance; team sport

Introduction

Nutritional supplements are one of the many strategies that athletes adopt to enhance their performance and gain a competitive edge over their opponents. The types of supplements athletes consume range from common vitamins or minerals to more exotic counterparts such as antioxidants, amino acids, herbs, botanicals, or a cocktail of these ingredients (Maughan, 2009). In recent years, there has been an increasing amount of interest in a nonspecific antioxidant called N-acetylcysteine (NAC) within high-performance sport. NAC shows potential to benefit to athletes in improving recovery and performance through several mechanistic actions including direct scavenging of exercise-induced reactive oxygen species (ROS), supplying cysteine for synthesis of an intracellular antioxidant (glutathione), enhancement of potassium homeostasis, preservation of the Na⁺/K⁺ pump activity within skeletal muscle,

CONTACT Dr. Andrea Braakhuis  a.braakhuis@auckland.ac.nz  The University of Auckland, Discipline of Nutrition, Faculty of Medical & Health Sciences, Private Bag 92019, Auckland, New Zealand.

© 2018 Taylor & Francis Group, LLC

and inhibition of calcium ATPase oxidation at the sarcoplasmic reticulum (Cobley, McGlory, Morton, & Close, 2011). According to a recently published meta-analysis of the effect of NAC on sport performance, studies to date have been conducted primarily on nonathletes utilizing laboratory-based performance tests such as cycle time to fatigue and report varying degrees of performance benefits with NAC in the laboratory (when adjusted for power output, range -2.5 to 6.4%) (Braakhuis & Hopkins, 2015; Rhodes & Braakhuis, 2017). The typical dose using oral protocols reported in previous studies is 50 to 100 mg/kg, which equates to 5–8 g daily for the average rugby player, taken for anywhere from 2 to 9 days (Braakhuis & Hopkins, 2015; Rhodes & Braakhuis, 2017). While other studies have used a larger NAC dose than in the current study, they also report adverse side effects such as sleepiness, lightheadedness, gastrointestinal reflux, nausea, headache, and diarrhea (Rhodes & Braakhuis, 2017). The dose and days of consumption chosen in this study were based on the maximum allowable by the ethical committee, as a higher dose was deemed for medical purposes only. The current study used a protocol designed to provide a performance benefit while minimizing side effects and remain ethically responsible.

The majority of laboratory studies do not account for the intermittent nature of a field-based rugby game. As such, it is unclear whether performance benefits will be transferred in a field-based, semi-elite sport setting, as this has not been investigated (Bailey et al., 2011; Corn & Barstow, 2011; Matuszczak et al., 2005; McKenna et al., 2006; Medved et al., 2003; Medved et al., 2004; Medved, Brown, Bjorksten, & McKenna, 2004; Zembron-Lacny, Slowinska-Lisowska, Szygula, Witkowski, & Szyszka, 2010). Previous studies by Slattery, Dacombe, Wallace, Bentley, & Coutts (2014); Cobley et al. (2011) evaluated the performance effect of NAC using practical exercise protocols that closely simulated physiological responses to actual sport performed; however, both studies failed to involve semi-elite athletes. Further limiting NAC's use is the lack of comprehensive research and information on its tolerability and the potential it has to cause adverse effects for elite athletes (Ferreira & Reid, 2008). There have been reports of adverse effects including nausea and vomiting with NAC (Braakhuis & Hopkins, 2015; Rhodes & Braakhuis, 2017); however, previous studies have not been specifically designed to investigate the incidence of such events. Clearly, a supplement needs to demonstrate a performance benefit and be tolerable to be considered for further use by athletes.

There is a need for more practical applications and investigations of NAC before it can be advocated for its use in semi-elite sport. Thus, our primary aim was to investigate whether NAC supplementation decreases muscle soreness and enhances performance in a semi-elite sport setting. A secondary aim was to investigate adverse effects and the tolerability of oral NAC supplementation.

Methods

Participants

Twenty-eight semi-professional, semi-elite male rugby players were invited through their senior rugby club to participate in the study; of these, 17 agreed (age = 20.4 ± 0.9 yrs, height = 182.3 ± 7.4 cm, weight = 103 ± 12 kg, Yo-Yo Intermittent Recovery Test Level 1 [YIRT-L1] = 17.14 ± 1.73 level). The teams approached to participate are composed of semi-professional, part-time paid athletes. Of these 17 participants, 13 completed the first broken bronco test, and 11 completed both the first and second broken Broncos. The final performance data included a control group ($n = 7$) and an intervention group ($n = 6$). All 17 players completed

the muscle soreness questionnaire. Players who dropped out simply failed to appear to either day 5 or day 6 testing, for reasons we were unable to ascertain. During the study period, players completed an identical amount of training and intensity; however, the amount of game time performed differed slightly between the two groups (NAC = 54 ± 19.6 min vs. PLA = 45 ± 24.5 min). The players typically train 10–12 hours and play one 90-minute rugby game each week, determined via daily training logs completed by each player and checked for accuracy by coaching staff. The trainings are predominantly of a team-, skill-, and field-based nature, but strength and conditioning trainings are also performed. Prior to the study, all players and team management were informed of the testing procedures and possible risks involved, and all gave written consent. Ethical approval was granted from The University of Auckland Human Participants Ethics Committee (reference no. 013509). Team management agreed the players were suitably fit to participate. We estimated a sample size of 19 would enable the detection of a smallest worthwhile treatment effect of 1.85 in the Yo-Yo test level from week 1 to weeks 2 and 3 (Hopkins, 2006). Preseason data were used to estimate the between-subject standard deviation and retest reliability of the YYIRT-L1 test. Cohen's effect size of 0.2 was used to calculate the smallest worthwhile effect (Hopkins, 2006). In the sample size calculation, the between-subject standard deviation was calculated to be Yo-Yo level 9.25 and the retest reliability as Pearson correlation = 0.97, and these values calculated a typical error of 1.6.

Design

The study used a double-blind, pre-post controlled trial design to investigate the effect on muscle soreness and exercise performance as well as the tolerability and adverse effects of oral NAC supplementation. During preseason training prior to recruitment and testing, all players completed a preintervention Yo-Yo Intermittent Recovery Test Level 1 (YIRT-L1). Players were randomized using a computer-generated sequence and allocated via a block design, ensuring baseline fitness scores were equally matched between groups (NAC = 8, CON = 9). To determine block allocation, athletes were listed from highest to lowest YIRT-L1 score, then every second athlete separated. Once the athletes were partitioned into two groups, the groups were block allocated using the computer simulation. The allocation of players to either placebo or NAC was completed by a secondary researcher (AB) and then coded on named opaque envelopes. The researcher responsible for athlete allocation had no personal contact with participants. Players then began a six-day supplementation period of the respective supplement. During supplementation, players conducted usual training as previously described. Players completed a “broken bronco” shuttle test on day 5 of supplementation and then again on day 6.

The players' muscle soreness and tolerability to 1 g oral NAC was monitored through a modified version of the validated Muscle Pain and Treatment Satisfaction Questionnaire for Medication by Aitkinson and colleagues (Hopkins, 2006). The questionnaire inquires about muscle damage, providing a 1–10 Likert scale and three open-ended treatment satisfaction questions including specific questions of physical and mental side effects. This questionnaire was modified so that the questions could be sent via a daily TXT message by a blinded researcher. This TXT would ask the player to reply with the following:

- Their subjective muscle soreness score out of 10, with 1 being “no soreness” and 10 being “unbearably sore” (Atkinson et al., 2004).
- “Y” if they experienced side effects and “N” if they did not (a follow-up TXT message was sent to those that replied “Y” to the presence of side effects to determine the specificity and severity of the side effect(s) they were experiencing)

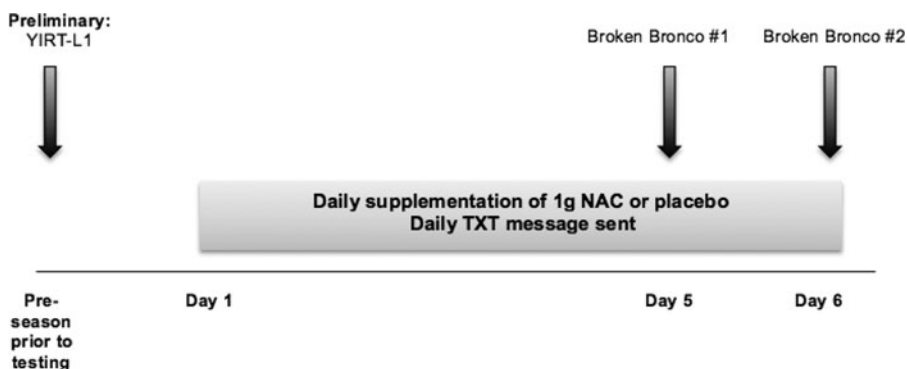


Figure 1. Schematic overview of the experimental design. Preliminary YIRT-L1 performance measures were taken during preseason training, and postsupplementation performance measures were performed on days 5 and 6 of supplementation (NAC or placebo). Side effects and subjective muscle soreness were monitored through a daily TXT message during the supplementation period. NAC = N-acetylcysteine.

Players that failed to reply to the TXT message were followed up in person on day 3, 5, or 6 of supplementation, and their muscle soreness score and side effects information were retrospectively collected by a blinded researcher. We estimate a third of players required follow-up text messages for each follow-up period, days 3, 5, and 6. A player's compliance to the NAC supplements was confirmed if a TXT response was received. [Figure 1](#) shows a schematic overview of the experimental design.

NAC supplementation

Players received 1 g (2×50 mg capsules) of NAC (Nutrabio Labs Inc, Middlesex, US) or 1 g (2×50 mg capsules) of placebo (sucrose and salt mixture) daily for a period of six days. In New Zealand, Medsafe New Zealand classifies NAC administered in its oral form as a scheduled pharmacy-only medicine at doses above 1 g per day and as an unscheduled dietary supplement for general use at doses below 1 g per day. This constitutes our basis for testing a NAC dose of 1 g per day. We appreciate that oral NAC supplementation has a reduced bioavailability compared to NAC administered intravenously; however, ethical and doping issues in sport preclude the use of IV administration (Holdiness, 1991). All players recorded usual dietary supplements; we requested the players refrain using any potential NAC or antioxidant-containing products for two weeks prior to and during the study.

Players were given the capsules in an opaque envelope by a blinded researcher. The envelopes also contained a written reminder for participants to take two capsules per day with 150 mL water and a paper copy of the muscle soreness scale. The players were instructed to take the final dose in the morning, 1–2 hours prior to the broken bronco test. Blind tasting sessions performed prior to testing confirmed the capsules were identical in size and color and thus indistinguishable from each other. Players were not asked whether they knew what treatment they were on. To provide assurance that the NAC supplement we purchased from Nutrabio Labs Inc. was free from the presence of World Anti-Doping Agency (WADA) prohibited list substances, we contacted Drug Free Sport New Zealand (DFSNZ) for consultation and sent a sample of the product to LGC Standards Proficiency Testing, Lancashire, UK, to be independently tested. The results from both DFSNZ and LGC showed no presence of banned substances.

Broken bronco shuttle test

A broken bronco is an exercise protocol commonly used in rugby teams across New Zealand to measure an individual's ability to perform repeated bouts of high-intensity exercise, and as a training technique to improve an individual's fitness. This test was chosen because it is a practical test that is familiar to the participants and part of their usual training routine; hence, a familiarization broken bronco test was not performed. Repeated sprint ability tests are also well correlated with match-specific physical performance (Currell & Jeukendrup, 2008). The broken bronco test requires players to perform six shuttle runs, all at maximum intensity. Each shuttle consists of running to a 20 m marker and back, a 40 m marker and back, and finally a 60 m marker and back. The test runs for twelve minutes with the players starting a shuttle run on every two minutes (0 min, 2 min, 4 min, 6 min, 8 min, and 10 min). Both broken bronco tests were video recorded using two iPads and then later analyzed using an application called CoachMyVideo (version 3.1, CMV, US) to obtain the elapsed time for each player to complete each 20, 40, and 60 m shuttle. The videos were viewed twice by one researcher using a standardized approach (for example, completion was deemed as the first body part to cross the line, start time from the whistle start). Shuttle times were also manually recorded on handheld timing devices by the team's coach and two blinded researchers as back-up data. The manual back-ups were not needed as the electronic method was fully operational on both occasions. Each broken bronco shuttle test was completed on an outdoor rugby field, with the environmental conditions being similar on both days ($\sim 15^{\circ}\text{C}$, a clear and fine day with little to no wind). Players were given time to warm up for 10 minutes prior to completing each broken bronco shuttle test. All players completed the same warm-up, as per usual training protocol.

Statistical analysis

The performance measure for the broken bronco test was the number of seconds taken to complete the test. Pre-post changes in performance were compared with mean and 90% confidence limit presented, formatted as $X \pm \text{CL}\%$. A higher total time to complete the broken bronco test equates to a lesser performance. Adverse effects were recorded as a count of events (diarrhea, nausea, vomiting, and headache, for example) and muscle soreness a score, presented as mean and standard deviation (SD), later converted to an odds ratio for analysis. Data were log transformed prior to analysis and back transformed for data presentation, with the change in the intervention group compared to the change in the control group. Data were analyzed using the "sports" parallel group trial spreadsheet (Hopkins, 2015), interpreting the adverse effects and muscle soreness score outcomes using the odds ratio clinical inference statement. We added the game time in minutes as a confounding factor in the muscle soreness and performance analysis. This approach takes into account the risk of benefit and harm, rather than the line of no effect, to declare a clear or unclear outcome. Thresholds for small, moderate, and large effects on performance were set at 0.2, 0.6, and 1.2 of the between-competition variation in the performances of elite team sport athletes. The corresponding thresholds used to evaluate the magnitude of the effect on performance were 0.5%, 1.5%, and 2.7% for small, moderate, and large, respectively. The outcome was deemed clear if the odds ratio was >66 , given that the pretest metric was different from the posttest metric. We have also included magnitude-based qualitative statements for each outcome. For comparison of the broken bronco tests 1 and 2, the between-subject variation was 2.5% (calculated 15 from pre-test performance data) with a smallest worthwhile effect of 0.5% (0.2 times the between-subject variability based on Cohen's effect sizes) (Hopkins, Marshall, Batterham, & Hanin, 2009).

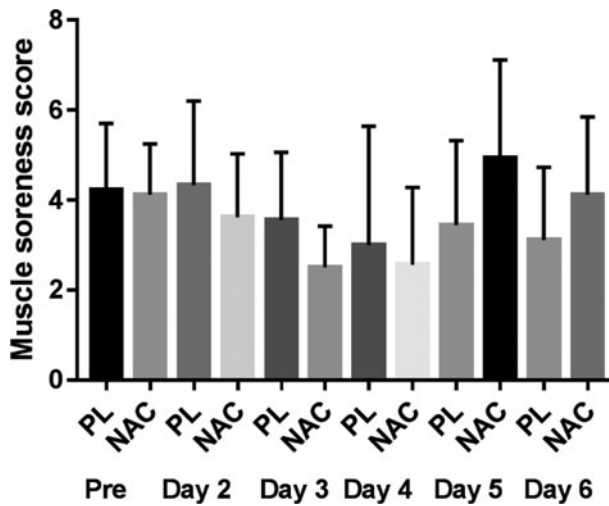


Figure 2. Daily muscle soreness scores and standard deviation for placebo (PL) and intervention (NAC). NAC = N-acetylcysteine.

Results

There were trivial differences in muscle soreness on NAC compared with placebo at baseline ($4 \pm 39\%$). From baseline to days 2–4 NAC was most likely harmful ($107 \pm 83\%$) and very likely harmful ($74 \pm 56\%$) between days 2 and 4 and days 5 and 6. Our clinical inference statements (likely beneficial/harmful) were based on the odds ratio of benefit to harm of > 66 (see Figure 2). During the initial days of supplementation, muscle soreness decreased for both groups; however, this decrease was 19% larger for those on NAC compared to placebo (PLA). During the study period, participants completed an identical amount of training and intensity; however, the amount of game time performed differed slightly between the two groups (NAC = 54 ± 20 min vs. PLA = 45 ± 24 min). The muscle soreness count and standard deviation were as follows: control baseline soreness: 4.2 ± 1.5 ; average soreness days 2–4: 3.6 ± 1.4 ; average soreness days 5–6: 3.3 ± 1.6 ; intervention baseline soreness: 4.1 ± 1.1 ; average soreness days 2–4: 2.9 ± 1.0 ; average soreness score day 5–6: 4.5 ± 1.7 .

The mean baseline performance measures (YYIRT-L1 scores) between the NAC and placebo group were similar, as the block design ensured athletes were allocated ranked according to pretesting fitness scores. The overall change in the performance effect of NAC compared to placebo on both total time to complete broken broncos 1 and 2 and the fastest shuttle time during each broken bronco compared to baseline performance measures were unclear (see Table 1). However, when the performance effect of NAC on the fastest shuttle time for broken bronco 1 was compared to the fastest shuttle time for broken bronco 2, NAC produced a likely

Table 1. Mean difference in performance (%) on total run time and fastest shuttle run time of NAC supplementation compared with placebo.

	BB1 vs. Pre	BB2 vs. Pre	BB1 vs. BB2
Time to complete broken bronco test	$-1.1 \pm 5.3\%$ (unclear)	$0.1 \pm 6.6\%$ (unclear)	$2.6 \pm 4.2\%$ (unclear)
Fastest shuttle time	$-4.6 \pm 6.7\%$ (unclear)	$1.8 \pm 7.3\%$ (unclear)	$4.4 \pm 4.5\%$ (likely beneficial)

Data are expressed as mean percent effect of the change \pm 90% CL; qualitative clinical inference is shown in parentheses. For comparisons between both broken bronco 1 and 2 (BB1 and BB2) and Pre (YYIRT-L1), the qualitative clinical inference statement is based on threshold chances of harm and benefit of 0.5% and 25%. NAC = N-acetylcysteine.

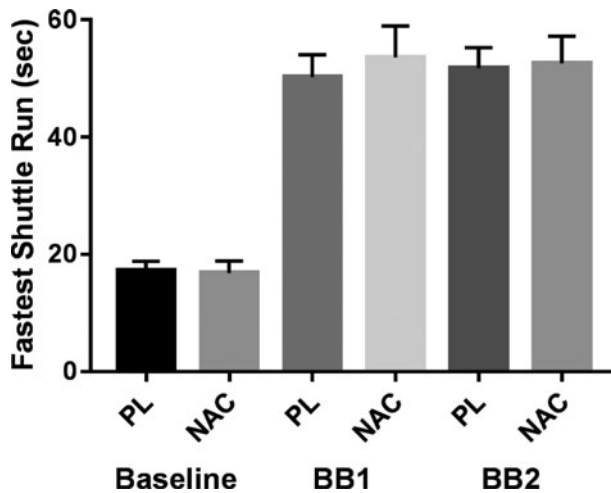


Figure 3. Fastest shuttle run time (seconds) and standard deviation. Baseline data (YYIRT-L1), BB1 broken bronco day 5, BB2 broken bronco day 6. Lower run time equates to better performance.

beneficial performance increase of $2.4\% \pm 4.8\%$ compared to placebo (see Table 1). The run time, and standard deviation, for the bronco broken is as follows: control group, test 1: 340 ± 30 min, test 2: 335 ± 24 min; intervention group, test 1: 346 ± 44 min, test 2: 335 ± 34 min. The fastest shuttle runs for the tests and standard deviation conducted on days 5 and 6 are as follows: control group, test 1: 50.3 ± 3.8 min total, test 2: 51.8 ± 3.5 min total; intervention group, test 1: 53.6 ± 5.3 min total, test 2: 52.6 ± 5.3 min total (see Figure 3).

All players reported 100% compliance to supplements ($n = 17$). NAC was well tolerated over the duration of the six-day supplementation period. One participant in the NAC group reported an episode of tiredness; however, one participant in the placebo group also reported an episode of tiredness.

Discussion

Supplementation with NAC for three to four days increased muscle soreness at days 2–4 and days 5–6, despite adjustments for player game time. NAC has no clear effect on the overall performance of a one-off high-intensity exercise session but is likely to improve sprint performance when these high-intensity exercise sessions are performed back to back. Supplementation with 1 g oral NAC produces no adverse side effects and is a tolerable dose for use among elite athletes.

The use of repeated sprint ability incorporating change in direction tests has been shown to correlate well with sporting ability in team sports, such as basketball and soccer (Nikolaidis, Dellal, Torres-Luque, & Ingebrigtsen, 2015; Padulo et al., 2016). The ability for a rugby player to repeatedly sprint and change direction is an important performance indicator; NAC may assist in reducing fatigue and subsequently improving athletic performance.

To our knowledge, our study is one of the first to show a potentially negative effect of acute NAC supplementation on muscle soreness scores. A number of previous studies have failed to delineate this link between muscle soreness and NAC supplementation (Childs, Jacobs, Kaminski, Halliwell, & Leeuwenburgh, 2001; Cobley et al., 2011; Silva et al., 2008). Skeletal muscle damage is the primary cause of muscle soreness, and ROS produced during exercise have been proven to play a causal role in muscle damage and fatigue through a

number of mechanisms: decreasing respiratory control of mitochondria, oxidizing ion-transport systems, losing structural integrity of sarcoplasmic reticulum, increasing lipid oxidation, distorting signal transduction pathways, and causing cellular dysfunction (Cleak & Eston, 1992; Padulo et al., 2016; Silva et al., 2008). It seems possible that NAC supplementation in an acute nature may have been effective in attenuating such harmful metabolic responses to exercise-induced ROS and thus reducing skeletal muscle damage and muscle soreness (Braakhuis & Hopkins, 2015). We are unable to explain why supplementation with NAC produced a likely harmful effect on muscle soreness, but there may be some possibility that those on NAC were able to work harder during the broken bronco exercise tests on days 5 and 6 of supplementation and consequently induced greater muscle damage and soreness. Further investigation of the effect of NAC supplementation on markers of cellular damage such as creatine kinase (CK) and lactate dehydrogenase (LDH) would be required to support this theory.

In terms of NAC's potential to improve exercise performance, this study was unable to demonstrate a clear effect of 1 g NAC on total time to complete a broken bronco exercise protocol, and we believe this lack of ergogenic effect was due to the low dosage of NAC supplemented. We did, however, show a likely beneficial effect of NAC on elite athletes' sprint performance during back-to-back high-intensity exercise testing sessions. Previous works also using sport-specific exercise protocols have reported similar evidence to suggest a beneficial effect of NAC in improving performance when athletes are exercising in a state of fatigue. Slattery (Matuszczak et al., 2005) observed an improvement in performance during repeated short sprints bouts (5, 10, 15 s) with 1.2 g oral NAC during a cycle ergometer race simulation, with the greatest performance enhancement observed at the latter stages of the race simulation test. Cogley et al. (2011) gave their participants a higher dose of 50 mg/kg/day and observed an increase in YYIRT-L1 performance over time, with the greatest performance enhancement seen on the last testing session (three sessions in total). This current evidence, along with our findings, suggests that there may be some benefit in elite athletes taking a one-off or acute dosage of NAC supplementation before periods of anticipated high energy turnover with limited recovery time, such as during tournaments, competitions, or back-to-back hard training sessions.

Although a pattern of NAC enhancing recovery and performance during fatiguing exercise is emerging, we are still unsure of the exact mechanisms by which NAC produces these beneficial effects. The most likely mechanism is that NAC is effective in providing cysteine for glutathione biosynthesis, an important nonenzymatic antioxidant that then works to reduce ROS accumulation and thus the risk of muscle damage and fatigue during unaccustomed, high-intensity exercise (Ferreira & Reid, 2008). NAC can also act directly within cells and myocytes to reduce reactive radicals (Medved et al., 2004). Previous research also suggests that NAC is effective in attenuating the decline in muscle Na⁺/K⁺ pump activity during exercise, preventing the oxidation of contractile proteins and altering the expression of redox-sensitive enzymes and proteins (Cogley et al., 2011; McKenna et al., 2006; Slattery et al., 2014). We believe that NAC was effective in alleviating muscle damage for the semi-elite athletes in our study, resulting in greater ability of the athletes to recover and back up sprint performance after the first broken bronco testing session. The ability and extent to which NAC may enhance recovery and performance for semi-elite athletes during exercise sessions with a high turnaround rate remains inconclusive; therefore, further studies using sport-specific exercise protocols with back-to-back testing sessions of fatiguing exercise are encouraged to provide further evidence to support the current findings.

The most common side effects to NAC include diarrhea, nausea, vomiting, and headache, and our study did not result in any of these. We were not surprised by this finding as a systematic review of NAC supplementation by Natural Medicines reported that NAC is generally well tolerated in doses of 1.2–2.6 g per day (Cleak & Eston, 1992). Other studies using similar doses also report good tolerance of oral NAC among their study participants (Corn & Barstow, 2011; Kelly, Wicker, Barstow, & Harms, 2009; Kerksick et al., 2013; Michailidis et al., 2013; Slattery et al., 2014).

We appreciate a number of limitations in our study design. The most predominant limitation to our study is the dose. NAC was supplemented in such a small dose that it was unlikely that we would be able to detect a clear performance benefit. As previously mentioned, we were limited to using a highest dose of 1 g NAC per day; however, we believe that we may have possibly seen a greater performance effect with NAC if the dosage were higher.

The bioavailability of oral NAC is low (6%–10%), and NAC and cysteine concentrations typically peak within one to two hours after ingestion, with the half-life for plasma concentration decay at ~2.3–2.4 hours (Corn & Barstow, 2011; Ferreira & Reid, 2008; Holdiness, 1991). Based on this, the NAC supplement should ideally be taken one hour prior to performing the exercise test, rather than using NAC as a recovery modality. The players were instructed to take their final dose of NAC one to two hours prior to the broken bronco test; however, on the remaining days the supplement was likely consumed in one dose at one time point during the day.

For this study, subjective muscle soreness was only measured for one day after the first broken bronco test, and not at all after the second broken bronco test. Following unaccustomed, high-intensity exercise, muscle soreness and pain peaks within 24–72 hours post exercise and is defined as delayed-onset muscle soreness (DOMS) (Cheung, Hume, & Maxwell, 2003). Based on this theory, we believe that the muscle soreness reported in this study is likely to be a result of the participants' usual training routine, and not attributable to the broken bronco testing sessions. If the period of muscle soreness monitoring was extended by 3–4 days, then there is a possibility that we may have observed a beneficial effect of NAC on recovery and DOMS 1–3 days after broken bronco testing sessions. Measuring blood indicators of muscle damage such as CK and LDH, or taking muscle biopsies, would have also been useful to support and explain the link between NAC and muscle soreness (or damage).

Overall, our results suggest the dose of 1 g daily for six days to be insufficient to improve performance; however, it may reduce muscle soreness in athletes undertaking general training and improve the maximal sprint time. In our opinion, future studies should use NAC for a few days only, using a larger dose, and investigate the effect on a one-off maximal intermittent exercise bout.

Declaration of interest

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of the article.

About the authors

Kate M Rhodes, MHS, is a registered dietitian with an interest in sports nutrition.

Dane F Baker, MSc, is a dietitian employed with high performance sport New Zealand and works with elite athletes.

Brett T Smith, PhD, is an exercise physiologist with years of experience with elite sport, particularly rowing and rugby.

Andrea J Braakhuis, PhD, is a registered dietitian with a background and research interest in sports nutrition.

Funding

This study was funded by the University of Auckland Internal Staff funding, including the purchase of the dietary supplement.

References

- Atkinson MJ, Sinha A, Hass SL, Colman SS, Kumar RN, Brod M, et al. 2004. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. *Health Qual Life Outcomes*. 26:12. doi:10.1186/1477-7525-2-12.
- Bailey SJ, Winyard PG, Blackwell JR, Vanhatalo, Lansley KE, DiMenna FJ, et al. 2011. Influence of N-acetylcysteine administration on pulmonary O₂ uptake kinetics and exercise tolerance in humans. *Respir Physiol Neurobiol*. 175(1):121–9. doi:10.1016/j.resp.2010.10.002. PMID:20937413.
- Braakhuis AJ, Hopkins WG. 2015. Impact of dietary antioxidants on sport performance: a review. *Sports Med*. 45(7):939–55. doi:10.1007/s40279-015-0323-x. PMID:25790792.
- Cheung K, Hume PA, Maxwell L. 2003. Delayed onset muscle soreness. *Sports Med*. 33:145–64. doi:10.2165/00007256-200333020-00005. PMID:12617692.
- Childs A, Jacobs C, Kaminski T, Halliwell B, Leeuwenburgh C. 2001. Supplementation with vitamin C and N-acetyl-cysteine increases oxidative stress in humans after an acute muscle injury induced by eccentric exercise. *Free Radical Biol Med*. 31:745–53. doi:10.1016/S0891-5849(01)00640-2.
- Cleak M, Eston R. 1992. Delayed onset muscle soreness: mechanisms and management. *J Sports Sci*. 10:325–41. doi:10.1080/02640419208729932. PMID:1518094.
- Cobley JN, McGlory C, Morton JP, Close GL. 2011. N-Acetylcysteine's attenuation of fatigue after repeated bouts of intermittent exercise: practical implications for tournament situations. *Int J Sport Nutr Exerc Metab*. 21:451–61. doi:10.1123/ijsnem.21.6.451. PMID:22089305.
- Corn SD, Barstow TJ. 2011. Effects of oral N-acetylcysteine on fatigue, critical power, and W' in exercising humans. *Respir Physiol Neurobiol*. 178(2):261–8. doi:10.1016/j.resp.2011.06.020. PMID:21740986.
- Currell K, Jeukendrup AE. 2008. Validity, reliability and sensitivity of measures of sporting performance. *Sports Med*. 38:297–316. doi:10.2165/00007256-200838040-00003. PMID:18348590.
- Ferreira LF, Reid MB. 2008. Muscle-derived ROS and thiol regulation in muscle fatigue. *J Appl Physiol*. 104:853–60. doi:10.1152/jappphysiol.00953.2007. PMID:18006866.
- Holdiness MR. 1991. Clinical pharmacokinetics of N-acetylcysteine. *Clin Pharmacokinet*. 20(2):123–34. doi:10.2165/00003088-199120020-00004. PMID:2029805.
- Hopkins W. n.d. ParallelGroupsTrial.xls. from <http://sportssci.org>. Retrieved October 5, 2015.
- Hopkins W, Marshall S, Batterham A, Hanin J. 2009. Progressive statistics for studies in sports medicine and exercise science. *Med Sci Sports Exerc*. 41:3. doi:10.1249/MSS.0b013e31818cb278. PMID:19092709.
- Hopkins WG. 2006. Sample sizes for magnitude-based inferences about clinical, practical or mechanistic significance. *Med Sci Sports Exerc*. 38:5. doi:10.1249/00005768-200605001-03080.
- Kelly MK, Wicker RJ, Barstow TJ, Harms CA. 2009. Effects of N-acetylcysteine on respiratory muscle fatigue during heavy exercise. *Respir Physiol Neurobiol*. 165:67–72. doi:10.1016/j.resp.2008.10.008. PMID:18992854.
- Kerksick CM, Roberts MD, Dalbo VJ, Kreider RB, Willoughby DS. 2013. Changes in skeletal muscle proteolytic gene expression after prophylactic supplementation of EGCG and NAC and eccentric damage. *Food and Chemical Toxicol*. 61:47–52. doi:10.1016/j.fct.2013.01.026.

- Matuszczak Y, Farid M, Jones J, Lansdowne S, Smith MA, Taylor AA, et al. 2005. Effects of N-acetylcysteine on glutathione oxidation and fatigue during handgrip exercise. *Muscle Nerve*. 32:633–8. doi:10.1002/mus.20385. PMID:16025522.
- Maughan RJ. 2009. The encyclopaedia of sports medicine: an IOC medical commission publication. The Olympic Textbook of Science in Sport. John Wiley & Sons.
- McKenna MJ, Medved I, Goodman CA, Brown MJ, Bjorksten AR, Murphy KT, et al. 2006. N-acetylcysteine attenuates the decline in muscle Na, K -pump activity and delays fatigue during prolonged exercise in humans. *J Physiol (Lond)*. 576(1):279–88. doi:10.1113/jphysiol.2006.115352. PMID:16840514.
- Medved I, Brown MJ, Bjorksten AR, Leppik JA, Sostaric S, McKenna MJ. 2003. N-acetylcysteine infusion alters blood redox status but not time to fatigue during intense exercise in humans. *J Appl Physiol*. 94:1572–82. doi:10.1152/jappphysiol.00884.2002. PMID:12496140.
- Medved I, Brown MJ, Bjorksten AR, McKenna MJ. 2004. Effects of intravenous N-acetylcysteine infusion on time to fatigue and potassium regulation during prolonged cycling exercise. *J Appl Physiol*. 96(1):211–7. doi:10.1152/jappphysiol.00458.2003. PMID:12959960.
- Medved I, Brown MJ, Bjorksten AR, Murphy KT, Petersen AC, Sostaric S, et al. 2004. N-acetylcysteine enhances muscle cysteine and glutathione availability and attenuates fatigue during prolonged exercise in endurance-trained individuals. *J Appl Physiol*. 97:1477–85. doi:10.1152/jappphysiol.00371.2004. PMID:15194675.
- Michailidis Y, Karagounis LG, Terzis G, Jamurtas AZ, Spengos K, Tsoukas D, et al. 2013. Thiol-based antioxidant supplementation alters human skeletal muscle signaling and attenuates its inflammatory response and recovery after intense eccentric exercise. *Am J Clin Nutr*. 98:233–45. doi:10.3945/ajcn.112.049163. PMID:23719546.
- Natural Medicines. N-acetyl cysteine. n.d. from <https://naturalmedicines-therapeuticresearch-com>. Retrieved June 29, 2015.
- Nikolaidis PT, Dellal A, Torres-Luque G, Ingebrigtsen J. 2015. Determinants of acceleration and maximum speed phase of repeated sprint ability in soccer players: a cross-sectional study. *Sci & Sports*. 30(1):e7–16. doi:10.1016/j.scispo.2014.05.003.
- Padulo J, Bragazzi NL, Nikolaidis PT, Iacono AD, Attene G, Pizzolato F, Dal Pupo J, Zagatto AM, Oggianu M, Migliaccio GM. 2016. Repeated Sprint Ability in Young Basketball Players: Multi-direction vs. One-Change of Direction (Part 1). *Frontiers in Physiol*. 7:133 doi:10.3389/fphys.2016.00133.
- Rhodes K, Braakhuis A. 2017. Performance and Side Effects of Supplementation with N-Acetylcysteine: A Systematic Review and Meta-Analysis. *Sports Medicine*. 47(8):1–8. doi:10.1007/s40279-017-0677-3. PMID:27251334.
- Sen C, Packer L, Hänninen O. 2000. *Handbook of oxidants and antioxidants in exercise*. Elsevier.
- Silva LA, Silveira PC, Pinho CA, Tuon T, Pizzol FD, Pinho RA. 2008. N-acetylcysteine supplementation and oxidative damage and inflammatory response after eccentric exercise. *Int J Sport Nutr*. 18:379.
- Slattery KM, Dascombe B, Wallace LK, Bentley DJ, Coutts A. 2014. Effect of N-acetylcysteine on cycling performance after intensified training. *Med Sci Sports Exerc*. 46:1114–23. doi:10.1249/MSS.0000000000000222. PMID:24576857.
- Zembron-Lacny A, Slowinska-Lisowska M, Szygula Z, Witkowski Z, Szyszka K. 2010. Modulatory effect of N-acetylcysteine on pro-antioxidant status and haematological response in healthy men. *J Physiol Biochem*. 66(1):15–21. doi:10.1007/s13105-010-0002-1. PMID:20354834.