N-Acetylcysteine’s Attenuation of Fatigue After Repeated Bouts of Intermittent Exercise: Practical Implications for Tournament Situations

James N. Cobley, Chris McGlory, James P. Morton, and Graeme L. Close

Production of reactive oxygen species (ROS) during muscle contractions is associated with muscle fatigue and damage in the short term and adaptive responses in the long term. When adaptation is inconsequential acute antioxidant supplementation may be able to attenuate muscle fatigue and damage to enhance performance. This study aimed to determine the effects of acute oral N-acetylcysteine (NAC) supplementation on Yo-Yo Intermittent Recovery Test Level 1 (YIRT-L1) performance after repeated bouts of damaging intermittent exercise. In a pair-matched design, 12 recreationally trained men engaged in 6 d of either NAC ($n = 6$) or placebo ($n = 6$) supplementation. After a treatment-loading day, participants completed 3 testing sessions, on alternating days, consisting of a preexercise isokinetic dynamometry (IKD) test, a damaging intermittent-exercise protocol, YIRT-L1, and a postexercise IKD test. Another IKD test was completed on the 2 intervening d. NAC treatment resulted in a significant preservation of YIRT-L1 performance ($p \leq .0005$). IKD performance significantly deteriorated over time at all contraction speeds, and this deterioration was not influenced by treatment group. Plasma creatine kinase values increased significantly over time ($p = .002$) and were significantly greater in the NAC group than in the placebo group ($p = .029$). NAC induced mild gastrointestinal side effects. NAC supplementation may be a useful strategy to enhance performance during short-term competitive situations when adaption is inconsequential. Titration studies to elucidate a treatment dose that enhances performance without inducing side effects are now required.

**Keywords**: NAC, DOMS, free radical, ROS, eccentric, soreness

Transient accumulation of reactive oxygen species (ROS) during muscle contractions is associated with muscle fatigue and damage in the short term and the promotion of adaptive responses in the long term (Ferreira & Reid, 2008; Powers, Durate, Kavazis, & Talbert, 2010). ROS can activate signal-transduction pathways to induct a stress-resistance response that protects against some of the toxic outcomes of ROS generation (Powers et al., 2010). This response involves the up-regulation of antioxidant enzymes and heat-shock proteins (Powers & Jackson, 2008). Reports of diminished adaptation to exercise training with long-term antioxidant supplementation have confirmed that ROS can function as essential signaling biomolecules in vivo (Gomez-Cabrera, Borrás, Pallardó, Sastre, Ji, & Viña, 2005; Gomez-Cabrera et al., 2008; Ristow et al., 2009). It is therefore apparent that chronic antioxidant supplementation is ill advised when training adaptation is desired (Powers et al., 2010). There are, however, scenarios in which training adaptation is inconsequential, and ameliorating the negative short-term effects of ROS is essential, such as during competitive tournament situations that are characterized by short recovery intervals between demanding exercise bouts. It follows that acute antioxidant supplementation may be beneficial in these situations, although this hypothesis has yet to be fully explored.

N-acetylcysteine (NAC) is a promising candidate to attenuate fatigue and muscle damage during successive bouts of damaging high-intensity contractions. NAC may act in several ways to influence cellular redox state. NAC deacetylation releases cysteine, which can be used to support glutathione synthesis, a process rate-limited by cysteine availability (Ferreira & Reid, 2008). Glutathione is an abundant cellular thiol that can serve as a substrate for the hydrogen peroxide scavenger glutathione peroxidize and recycle vitamins C and E (Ferreira & Reid, 2008). In addition, NAC can scavenge several reactive species directly and inhibit S-thiolation of redox-sensitive enzymes and proteins that may preserve their function during contractions (Lee, West, Phillips, & Britz-Mckibbin, 2010).

Several authors have reported that acute NAC administration delays fatigue during submaximal endurance-type exercise in humans (Lee et al., 2010; Matuszczak et al., 2005; McKenna et al., 2006; Medved, Brown, Bjorksten, & McKenna, 2004; Reid, Stokie, Koch, Khawli,
& Leis, 1994; Travaline, Sudarshan, Roy, Cordova, Leyenson, & Criner, 1997). For instance, intravenous NAC infusion pre- and during cycling exercise-capacity tests prolongs time to exhaustion by ~25% (McKenna et al., 2006; Medved, Brown, Bjorksten, Murphy, et al., 2004). Analogous results have been reported after oral NAC supplementation (Lee et al., 2010; Matuszczak et al., 2005), suggesting that the findings were not an artifact of intravenous administration. Although definitive causal mechanisms are lacking, NAC may enhance potassium (K⁺) homeostasis, inhibit the oxidation of sarcoplasmic reticulum calcium ATPase, and prevent the oxidation of contractile proteins to attenuate fatigue during submaximal contractions (McKenna et al., 2006; Powers & Jackson, 2008). Conversely, NAC has failed to enhance high-intensity intermittent-exercise performance in untrained humans (Matuszczak et al., 2005; Medved, Brown, Bjorksten, Leppik, Sostaric, & McKenna, 2003). This observation could limit the use of NAC. Although the severity of the exercise may have prevented the realization of treatment effects in untrained individuals, the possibility that NAC is ineffective during this form of contractile activity cannot be excluded. Further work with moderately trained individuals may help clarify this issue.

Contractions, especially those of an eccentric nature (Nikolaidis, Jamurtas, Paschalis, Fatouros, Koutedakis, & Kouretas, 2008), often invoke muscle damage, which stimulates postexercise (48–96 hr) ROS production as a result of the respiratory burst of phagocytes (Close, Ashton, Mc Ardle, & MacLaren, 2005; Pizza, Peterson, Baas, & Koh, 2005). ROS generation during this period can further depress muscle function but is associated with the long-term restoration of muscle function (Close et al., 2006). Acute antioxidant supplementation could prevent further decrements in muscle function during this period. To our knowledge, no study has determined the effects of acute NAC supplementation on muscle function after repeated bouts of damaging contractions. Nevertheless, no effect of exogenous antioxidants, notably vitamin C, on muscle function, as determined by isokinetic dynamometry (IKD), has been observed at any time point (0–96 hr) after damaging contractions (Close et al., 2006; Thompson et al. 2003; Thompson et al., 2001). This could reflect a need to use different antioxidants or markers of muscle function. It could equally reflect a need to perform repeated bouts of damaging contraction to realize treatment effects. Determining the influence of acute NAC supplementation on markers of muscle function after repeated bouts of exercise could help resolve some of these issues.

The aim of this study was to determine the effects of acute NAC supplementation on biomarkers of muscle function and fatigue after repeated bouts of damaging high-intensity intermittent contractions. We hypothesized a preservation of Yo-Yo Intermittent Recovery Test Level 1 (YIRT-L1) and IKD performance together with a reduction in creatine kinase (CK) accumulation with NAC supplementation compared with placebo.

### Methods

#### Subjects

Using Minitab version 15.0 (Minitab Inc., USA), we estimated that a sample size of 10 would enable the detection of a practically significant treatment effect of 60 m in YIRT-L1 performance between testing Sessions 1 and 3 with a statistical power of 90%. In accordance with statistical guidelines (Batterham & Atkinson, 2005), the standard deviation associated with mean test–retest YIRT-L1 scores (24 m; Krustup et al., 2003) was used. Fourteen recreationally trained male subjects were recruited to allow for subject attrition. For this study’s purposes, recreationally trained was defined as participating in physical activity of an intermittent nature at least three times per week for at least 12 months. During the course of the study, 2 subjects dropped out for personal reasons; hence, 12 recreationally trained men (age 24.7 ± 4.2 years, height 172.1 ± 4.9 cm, weight 70.1 ± 6.9 kg) participated. Prospective subjects were excluded if they smoked or engaged in any course of supplementation or medication (e.g., antioxidant supplementation) that may have interfered with the study’s results. Institutional ethical approval was granted.

#### Experimental Design

In a between-subjects design, subjects were pair-matched according to the greatest preliminary YIRT-L1 score (see preliminary measurements) and assigned to a treatment group (NAC, N = 6 YIRT-L1: 1,506.7 ± 379.2 m; placebo, n = 6 YIRT-L1: 1,466.7 ± 395.1 m) in a random double-blind fashion. The experimental preparation was consumed in the form of a 500-ml drink that contained 375 ml H₂O, 125 ml sugar-free cordial, and 2 g glucose dextrose powder mixed with 50 mg/kg of powdered NAC (Myprotein Inc., Manchester, UK). Blind tasting sessions performed during pilot work with people who did not undertake any experimental trials revealed that without added cordial and dextrose powder the NAC condition was easily detectable and unpalatable. The placebo preparation lacked NAC but was otherwise identical to the experimental preparation. Because of the short half-life of orally ingested NAC, a 500-ml drink was consumed 1 hr before and immediately after each testing session (and at corresponding time points on the loading day) during the 6-day treatment period to enhance NAC bioavailability (Lee et al., 2010). Analogous treatment strategies have proven effective in arresting fatigue (Matuszczak et al., 2005; McKenna et al., 2006; Medved, Brown, Bjorksten, Murphy, et al., 2004). Side-effect prevalence was assessed using a subjective 0–10 side-effects scale that was administered daily by an experimenter who was unblinded for ethical reasons. After a treatment-loading day subjects were required to report to the laboratory on five consecutive occasions to complete alternate testing and sampling sessions. The composition of each sampling and testing session is illustrated in Figure 1. Subjects refrained from caffeine,
alcohol, recovery interventions (e.g., ice baths), and unprescribed exercise for the 48 hr preceding and during the study. All experimental sessions were performed at a similar time of day and under consistent ambient conditions to eliminate extraneous chronobiological and environmental effects, respectively. Dietary intake was recorded during the first 2 experimental days using a 48-hr food diary that was subsequently photocopied and repeated during the remaining 4 experimental days.

**Preliminary Measurements**

After a standardized warm-up of 5 min at 10 km/hr on a motorized treadmill (HP Cosmos, Germany) subjects completed a progressive shuttle protocol to estimate maximal oxygen uptake (VO$_{2\text{max}}$; Leger & Lambert, 1982; Ramsbottom, Brewer, & Williams, 1988). Saliently this ensured that running speeds during the Loughborough Intermittent Shuttle Test (LIST) were tailored to individual VO$_{2\text{max}}$ values, thus ensuring that exercise
intensity was similar between individuals and hence treatment groups. Although precision is sacrificed when estimating VO2max with this approach, it did have the advantage of incorporating rapid acceleration–deceleration actions that enabled LIST intensity to be more accurately prescribed. To eliminate learning effects, two muscle-function and YIRT-L1 familiarization sessions were performed. The greatest YIRT-L1 familiarization score attained represented each subject’s baseline score to enable the calculation of the deterioration in YIRT-L1 performance during the experiment. Subjects completed a 15-min LIST block only to ensure that no significant muscle damage was invoked before commencement of the study.

Muscle Function

After a standardized warm-up, the dominant-limb concentric quadriceps was determined using an IKD (Biodex Medical Systems, Shirley, NY). Once the subject was seated, his lateral femoral condyle was aligned to the axis of rotation of the dynamometer, and the actuator was attached proximal to the lateral malleolus. The chair settings required to produce this position were recorded and repeated in subsequent trials. Range-of-motion assessments were performed to minimize injury risk. Gravity corrections were conducted to negate the extraneous influence of limb mass on torque development. Concentric quadriceps torque was determined at 60, 180, and 300 rad/s). Three maximal repetitions were performed at each speed, with the greatest value attained being recorded. Subjects received no quantitative performance feedback, but strong verbal encouragement was provided throughout. IKD tests were performed daily to provide a baseline measure of the decline in muscle function between testing days. They were conducted postexercise on testing days to determine the impact of exercise on muscle function. Muscle soreness was determined using the previously validated Visual Analog Scale (VAS; Price, McGrath, Rafii, & Buckingham, 1983). The VAS consists of a 12-cm line that has two end points labeled no pain and intolerable pain. Subjects were required to mark a point on the VAS scale that corresponded to their perception of total muscle soreness after performing a 90° squat. The VAS score was the distance in centimeters from the no-pain mark.

Intermittent-Exercise Bout

A 60-min LIST was completed in a well-ventilated indoor runway. The LIST test was selected to provide an intermittent exercise stimulus capable of inducing muscle damage (Thompson, Nicholas, & Williams, 1999; Nicholas, Nutall, & Williams, 2000). The LIST consists of successive cycles of cruising at 95% VO2max (60 m), jogging at 55% VO2max (60 m), walking (60 m), and maximally sprinting (20 m) between two pairs of timing lights (TC timing system, Brower Timing Systems, Draper, USA) placed 20 m apart in time with audio beeps for 15 min (Nicholas, Nutall, & Williams, 2000). Twenty-meter-sprint time was recorded on a handheld device that measured the elapsed time between the breaking of the infrared beams separating each pair of timing lights. Heart rate (HR) was recorded after every sprint using wireless telemetry (Polar, Kempele, Finland). Two 60-s and one 180-s recovery periods were allotted at 15, 45, and 30 min, respectively. Rating of perceived exertion (RPE) on a 6–20 Borg scale was determined every 15 min (Borg, 1973). Water was consumed ad libitum throughout the LIST. The amount consumed was recorded and repeated during subsequent trials. Capillary blood was extracted from a fingertip site and analyzed for lactate using a portable device (Lactate Pro, Arkary Factory Inc., Japan) pre- and post-LIST. The device was calibrated according to the manufacturer’s instructions before each testing session.

YIRT-L1

A YIRT-L1 was performed to obtain a valid, reliable, and intermittent sport-specific marker of the ability to perform repeated bouts of high-intensity exercise (see Krustup et al., 2003). Briefly, the YIRT-L1 involves the performance of consecutive 2 × 20-m shuttles separated by 10-s recovery intervals. Running velocity is dictated by audio beeps and increased by 0.5 km/hr throughout the test until volitional exhaustion ensues (demarcated by an inability to run in time with the audio beeps). Blood lactate and RPE were determined immediately post-YIRT-L1.

Blood Sampling

Duplicate venous blood samples were drawn from a prominent superficial forearm vein pre- and postexercise on testing days and preexercise only on sampling days. After sterilization of the skin surface with an alcoholic swab a tourniquet was applied to induce vasodilation. A sample of 6 ml of venous blood was drawn into a lithium heparin Vacutainer using a butterfly needle. Samples were analyzed for hemoglobin and hematocrit using an automated system (Hemocue AB, Änglehom, Sweden) and a Hawksley reader (Gelman Hawksley Ltd., Lansing, UK), respectively. This basic hematological analysis was performed to correct for changes in plasma volume postexercise according to the method of Dill and Costill (1974). Samples were centrifuged immediately at 3,000 revolutions/min for 15 min at 4°C. Plasma was dispensed into three 2-ml aliquots and stored at –80°C for subsequent biochemical analysis. Plasma CK concentration was determined using a commercially available kit (Daytona RX, Randox Laboratories Ltd., Crumlin, UK). This CK-NAC kit involves spectrophotometric measurement of nicotinamide adenine dinucleotide phosphate and uses NAC as a reducing agent to optimize the assay.

Statistical Analysis

A mixed general linear model was employed to statistically determine the efficacy of NAC treatment. The
between-subjects factor was treatment group and the within-subject factor was dependent variables (e.g., YIRT-L1 scores) across time. If Mauchly’s test of sphericity indicated a minimum level of violation, as assessed by a Greenhouse–Geisser epsilon (ε) of ≥.75, data were corrected using the Huynh–Feldt ε. If Mauchly’s test of sphericity was violated (Greenhouse–Geisser ε of ≤.75) data were corrected using the Greenhouse–Geisser ε (Close et al., 2006). If any significant F values were observed, least-significant-difference tests were performed post hoc to determine where any significant differences occurred (Close et al., 2006). An alpha value of p ≤ .05 was used for all tests. All statistical analysis was performed with the Statistical Package for Social Sciences version 17.0 (SPSS, Woking, Surrey, UK). Data are presented as M and SD.

Results

**YIRT-L1 Performance**

Maximal HR (~190 beats/min) and RPE (~20) were observed at volitional exhaustion, confirming the maximal nature of the YIRT-L1. Maximal HR and RPE values were not influenced by treatment group (HR p = .058, RPE p = .661). Blood lactate concentration significantly increased postexercise (p = .006) irrespective of treatment group (p = .133). A divergence in YIRT-L1 performance occurred between testing Sessions 1 and 3 in NAC- and placebo-treated subjects, with performance being significantly increased across time in NAC-treated subjects and decreased in placebo-treated subjects (p ≤ .0005). YIRT-L1 performance was ~50% greater in NAC- than in placebo-treated subjects by testing Session 3. Analogous results were obtained when YIRT-L1 scores were expressed absolutely (see Figure 2).

**LIST Performance**

The physiologically demanding nature of the LIST was confirmed by blood lactate values increasing from preexercise values of ~0.8 mmol/L to ~4.0 mmol/L postexercise (time effect: p ≤ .0005). NAC supplementation did not influence blood lactate supplementation (p = 8.25; data not shown). HR values significantly increased across time (p = .002; data not shown) irrespective of treatment group (p = .618). RPE increased across time, but values were significantly lower in the NAC group (p = .038).

**IKD Performance**

Absolute muscle torque significantly decreased across time at 60 rad/s (p = .000), 180 rad/s (p = .000), and 300 rad/s (p = .003). This depression in muscle function was not influenced by treatment group 60 rad/s (p = .246), 180 rad/s (p = .520), and 300 rad/s (p = .898). Analogous results were obtained when muscle torque was observed when IKD scores were expressed relative to preexercise (testing Session 1 scores). Table 1 illustrates the depression in absolute and relative IKD scores across time.

**Plasma CK**

Plasma CK significantly increased across time (p = .002) in both groups, confirming the damaging nature of the experimental protocol. CK values were significantly greater (p = .029) in NAC-treated than placebo-treated subjects at 24, 50, and 72 hr postexercise. Although not statistically significant, a trend toward greater CK levels at 48 and 96 hr was also observed in NAC-treated compared with placebo-treated subjects (Figure 3).

**VAS**

VAS scores increased significantly across time (p ≤ .0005) irrespective of treatment group (p = .651; see Figure 4).

**Side Effects**

Acute oral NAC supplementation produced mild gastrointestinal side effects (Table 2).

Discussion

The main finding of this study was that acute oral NAC supplementation prevents the deterioration in YIRT-L1 performance of repeated bouts of damaging intermittent exercise. Indeed, YIRT-L1 performance diverged between the two groups over time, culminating in an enhancement and depression in YIRT-L1 performance during testing Session 3 in NAC- and placebo-treated subjects, respectively.

Previous work has reported that acute intravenous NAC treatment pre- (125 mg/kg) and during (25 mg/kg) nondamaging high-intensity intermittent cycling exercise fails to prolong time to fatigue at 130% VO2max in untrained humans (Medved et al., 2003). Disparate protocols, treatment regimens, and subject training status confound any direct comparisons between the findings of the current study and that of Medved et al. (2003). Nevertheless, it is interesting to note that only trained individuals have consistently demonstrated performance enhancements after NAC treatment (McKenna et al., 2006; Medved, Brown, Bjorksten, Murphy, et al., 2004). A commonality of these studies, the current one included, is the incorporation of a fatiguing submaximal exercise protocol before the maximal work bout (Lee et al., 2010; McKenna et al., 2006; Medved, Brown, Bjorksten, Murphy, et al., 2004). It could be that submaximal fatiguing exercise is needed to precipitate treatment effects in trained individuals. Future studies are encouraged to address the question of whether submaximal fatiguing exercise is required to precipitate treatment effects.

We hypothesized that the efficacy of NAC in preserving muscle function would, in part, be contingent on arresting muscle damage. The fact that NAC significantly increased plasma CK levels is discordant with this hypothesis. Indeed, other groups have documented increased CK values after short-term...
antioxidant (vitamin C and NAC) supplementation in humans (Childs, Jacobs, Kaminski, Halliwell, & Leewenburgh, 2001). The physiological relevance of this finding is unclear because Childs et al. did not determine muscle function. In the current instance, it is conceivable that elevated CK levels with NAC were the biochemical manifestation of an ability to perform more work with NAC and hence induce greater muscle damage. Our results are compatible with the redox-brake hypothesis of Reid (2008), which postulates that the fatiguing actions of ROS during contractions act as a negative feedback signal to limit ROS toxicity (Reid, 2008). According to this hypothesis, attenuating ROS-mediated fatigue would be expected to increase the susceptibility of muscle to contraction-induced damage (Reid, 2008). It should, however, be noted that this increased susceptibility to exercise-induced muscle damage was not accompanied by a corresponding increase in the perception of muscle soreness and decrease in muscle-force production (IKD tests) in NAC-treated subjects. The results of the current study, along with those of previous investigations, indicate that NAC treatment increases the susceptibility

Figure 2 — A: Mean (SD) relative Yo-Yo Intermittent Recovery Test Level 1 (YIRT-L1) performance across time. B: Mean (SD) absolute YIRT-L1 performance across time. Note. NAC = N-acetylcysteine. *Denotes a significant treatment effect.
Table 1  Side-Effect Incidence and Severity by Treatment Group

<table>
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<tr>
<th>Side effect</th>
<th>No incidence (0)</th>
<th>Mild incidence (1–5)</th>
<th>Severe incidence (6–10)</th>
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<td>Sweating</td>
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<td>6</td>
<td>0</td>
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<tr>
<td>NAC placebo</td>
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<tr>
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<td>NAC placebo</td>
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<tr>
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<td>5</td>
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<td>NAC placebo</td>
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<tr>
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<td>0</td>
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<tr>
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<td>NAC placebo</td>
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Note. Incidence reflects number of cases. Severity reflects subject perception of the side effect on a 0–10 Likert scale with 0 indicating no incidence and 10 severe incidence.

Figure 3 — Mean (SD) plasma CK activity across time by treatment group. Note. NAC = N-acetylcystein; CK = creatine kinase. *Denotes a significant treatment–time interaction effect.

to contraction-induced damage but that this does not impair short-term muscle function. It is apparent that future work employing histological techniques and measures of oxidative stress that are influenced by NAC administration such as 3-methylhistidine is required to further elucidate the relationship between NAC supplementation and muscle damage.

The fact that acute NAC supplementation reverses fatigue implicates ROS in the etiology of muscle fatigue during contractions (Ferreira & Reid, 2008; Medved et al., 2006; McKenna et al., 2005; Medved, Brown, Bjornke, et al., 2004; Powers & Jackson, 2008; Reid et al., 1994; Travail et al., 1997). The applied nature of the current investigation means we are unable to link improvements in intermittent-exercise performance with acute NAC supplementation to a physiological mechanism. It should, however, be noted that taking serial muscle biopsies to reveal mechanistic insights would have been prohibitive in the current instance because of the confounding influence of the inflammatory response that accompanies serial biopsies. This reasoning does not apply to blood-borne redox markers; hence, the lack of these measurements represents a limitation of the current study. Nevertheless, in terms of potential mechanisms, recent work suggests that ROS oxidize sodium (Na⁺),K⁺ pumps to accelerate K⁺ loss, which is associated with impaired membrane potential and reduced contractility (McKenna et al., 2006). Consistent with this, NAC treatment can salvage Na⁺,K⁺ activity (McKenna et al., 2006). Sarcoplasmic reticum calcium ATPase is another redox-sensitive protein important to force production (Powers & Jackson, 2008). Specifically, ROS exposure
can inhibit the function of sarcoplasmic reticulum calcium ATPase by disrupting ATP binding and calcium uptake after ATP hydrolysis (Powers & Jackson, 2008; Scherer & Deamer, 1986; Xu, Zweier, & Becker, 1997). ROS may also interfere with calcium sensitivity during contractions via several mechanisms, notably through altering cross-bridge kinetics (reviewed in Smith & Reid, 2006). Fascinating insights may be derived from further research focusing on how NAC is able to attenuate muscle fatigue during contractions.

In an exercise setting, Matuszczak et al. (2005) were the first to adopt an oral NAC supplementation strategy in humans. They observed a 32% increase in time to fatigue during submaximal handgrip exercise after acute oral NAC ingestion (150 mg/kg dissolved in 100 ml saline). This supplementation strategy induced several mild side effects including erythema, conjunctivitis, pruritus, light-headedness, drowsiness, dysphoria, nausea, dyspepsia, and diarrhea (Matuszczak et al., 2005). The fact that none of these side effects were evident in placebo-treated subjects who ingested 100 ml saline (Matuszczak et al., 2005) supports the notion that reduced side-effect incidence in the current study was attributable to a decreased treatment dose that was consumed twice daily. Nevertheless, our strategy did induce mild gastrointestinal side effects. Despite the performance benefits of NAC, the occurrence of gastrointestinal side effects may limit its use in practical settings (Ferreira & Reid, 2008). Recent work by Mike Reid’s group indicates that a 70-mg/kg dose of orally ingested NAC does not cause significant adverse reactions (Ferreira, Campbell, & Reid, 2011). It will be necessary to confirm the findings of the current study with further titration studies and to conduct pharmacokinetic studies on high-dose oral NAC supplementation before this nutritional strategy can be recommended as a safe and effective means of enhancing athletic performance.

**Conclusion**

It has been demonstrated for the first time that acute oral NAC supplementation preserves YIRT-L1 performance after repeated bouts of intermittent damaging contractions at the expense of inducing mild gastrointestinal side effects. This novel finding supports the efficacy of acute oral NAC supplementation for performance preservation during demanding short-term (≤14-day) athletic events where adaptation is inconsequential. In light of the role of ROS in stimulating adaptive responses, chronic NAC supplementation may be ill advised. It is recommended that titration studies be performed to elucidate a supplementation strategy that enhances performance without inducing side effects.

**Acknowledgments**

We would like to thank all subjects for their sterling efforts during data collection. Christopher Thompson and Rebecca Lockhart are thanked for their valued assistance during data collection. Dr. Gordon Lowe is thanked for advice regarding laboratory analysis. Dr. Stuart Galloway is thanked for his critical reading of the manuscript.
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<td>20-m-sprint time</td>
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<td>3.45* (0.25)</td>
<td>3.51* (0.22)</td>
<td>3.61* (0.18)</td>
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<td>HR, beats/min</td>
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<td>154.6 (7.1)</td>
<td>156.7 (5.2)</td>
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Note. NAC = N-acetylcysteine.
*Significant treatment effect, p = .029.
References


