THE INFLUENCE OF ACETAMINOPHEN ON SPRINT INTERVAL TREADMILL RUNNING: A RANDOMIZED CROSSOVER TRIAL

Laura L. Park[1], Catherine E. Baker[2], Alvin Sum[1], and Lawrence D. Hayes[3]

[1]School of Human Sciences, London Metropolitan University, London, UK
[2]English Institute of Sport, Bisham Abbey National Sports Centre, Buckinghamshire, UK
[3]Department of Medical and Sport Sciences, University of Cumbria, Lancaster, UK

Original scientific paper
UDC: 615:796.422

Abstract:

Although considerable research concerning the efficacy of analgesics in sport exists, there is a paucity of data concerning effects of acute acetaminophen (ACT) ingestion on sprint interval running exercise. This investigation concerned the effect of acute ACT ingestion on eight 30 s maximal treadmill sprints on a non-motorized treadmill, interspersed with two-minute rests in males (N=8, age 26±3 years, body height 174±7 cm, body mass 71±8 kg) in a placebo-controlled, randomized crossover design. A time x condition repeated measures analysis of variance (ANOVA) determined ACT ingestion did not influence mean power output, peak power output, peak vertical ground reaction force, peak oxygen uptake, or total distance completed ($p>.05$). Perceived pain was reduced by 8-15% during the final three sprints following ACT ingestion ($p<.05$). Data presented here suggest ACT may reduce exercise-induced pain during the latter stages of sprint interval treadmill running, without influencing performance.

Key words: *fatigue, pain, perception, power output, sprint intervals*

Introduction

Acetaminophen (ACT) is a commonly used over-the-counter analgesic to reduce musculoskeletal pain in sub-elite athletes (Garcin, et al., 2005; Lily, 2010; McDonald & Molloy, 2012). Although the primary mechanism of action for ACT is poorly understood, it exhibits both analgesic and antipyretic properties (Blough & Wu, 2011). ACT is thought to act similarly to ibuprofen as a cyclooxygenase inhibitor without influencing inflammation or oedema, whilst modulating afferent and efferent pain pathways (Bonnefont, Alloui, Chapuy, Clottes, & Eschalie, 2003; Boutaud, Aronoff, Richardson, Marnett, & Oates, 2002; Pickering, et al., 2006).

Although limited research exists regarding the role of ACT in exercise performance, acute ACT ingestion has been reported to improve time to exhaustion during running and cycling performed in the heat (Burtscher, et al., 2013; Mauger, et al., 2014). These studies provided initial evidence that ACT ingestion may be used as an ergogenic aid due to its antipyretic properties. Foster and colleagues (2014) explored the analgesic influence of ACT during sprint interval cycling (Foster, Taylor, Chrismas, Watkins, & Mauger, 2014). Participants completed eight 30 s Wingate Anaerobic Tests, 30 minutes after ingesting 1.5 g of ACT or a placebo (PLA). The authors indicated a significant improvement in mean power output in the ACT condition compared to PLA. This was attributed to increased mean power output during the final three sprints, accompanied by significantly slower power diminution. No significant differences were observed for pain perception, peak power output, or heart rate between ACT and PLA conditions. The authors suggested ACT permitted participants to tolerate increased muscular pain associated with this type of exercise. Therefore, these authors suggested untrained cyclists may rely on afferent feedback to calculate an appropriate pacing strategy.

Stocchero et al. (2014) explored metabolic differences between intense running and cycling exercise and observed serum creatine kinase (CK) was greater after intense running than after intense cycling. Moreover, Nieman et al. (2014) observed that after three days of intensified training, runners experienced a greater relative increase in pro-inflammatory cytokines than did cyclists. In addition, Kolkhorst, Londeree, and Thomas (1994) observed post-running muscular soreness was greater and lasted longer than following cycling. This intimates potential for a greater muscle damage

following running compared to cycling, and therefore the possibility that ACT may improve running performance to a greater extent than cycling performance requires exploration.

Although considerable research exists concerning the efficacy of analgesics in sport, there is a paucity of data concerning the effect of acute ACT ingestion on sprint interval running performance. Consequently, the purpose of this study was to investigate whether an acute dose of ACT would improve performance during sprint interval running exercise.

Materials and methods

Participants

Following an *a priori* power calculation, eight recreationally active male participants (N=8, age 26±3 years, body height 174±7 cm, body mass 71±8 kg), who participated in regular exercise (4±2 sessions·wk^{-1}), were recruited for the present study. Prior to study commencement, participants were required to provide written informed consent and complete a Physical Activity Readiness Questionnaire (PAR-Q). Prior to experimental trials, participants were given a verbal and written explanation of the protocol and the opportunity to familiarize themselves with the laboratory and experimental conditions on a calibrated WOODWAY®Force 3.0 treadmill. Ethical approval was granted by the London Metropolitan University research ethics review panel.

Experimental procedures

Following three initial familiarization sessions, participants reported to the laboratory on two separate occasions (separated by a minimum of 48 h) and completed testing at the same time of day to ameliorate the influence of diurnal variation (Hayes, Bickerstaff, & Baker, 2010). Upon arrival at the laboratory, participants orally ingested either 1.5 g ACT or placebo (PLA) taste-matched solution administered in a randomized, double-blinded, crossover design. Thirty minutes post-ingestion, participants completed a standardized 5 min warm-up involving walking at a moderate pace interspersed with two 10 to 15 second all-out sprints. A recovery period of 5 minutes was allowed between the warm-up and the test. Participants performed eight 30-second maximal sprints, separated by two-minute active rests to allow time for substantial recovery, and to prevent substantial lactate clearance, in order to facilitate an increase in pain and fatigue (Mendez-Villanueva, Hamer, & Bishop, 2007). For each stage, participants were provided with a 5 s countdown and verbal encouragement throughout. Participants did not receive any feedback (visual or verbal) concerning sprint performance (distance covered, time remaining, power output). All sprints were performed on a non-motorized treadmill as previously described (Delextrat, Baliqi, & Clarke, 2013). Subjects were equipped with a harness around their waist, connected by a non-elastic tether to a horizontal load cell attached to the vertical strut of the treadmill which was locked during sprinting. For each participant, the gauge was adjusted to ensure the tether was horizontal during sprinting. This device was used to measure horizontal force (N). Treadmill speed was monitored by two optical speed photomicrosensors mounted on the rear shaft of the treadmill belt, while vertical force (N) was recorded by four individual vertical load cells mounted onto the underside of the belt. Power (W) was computed from instantaneous force and speed data. Data were collected at a sampling rate of 75 Hz by the XPV7 PCB interface. Peak power output (W), mean power output (W), peak vertical ground reaction (GRF_V [kg]) and distance completed (m) were collected and calculated at 200 Hz sample rate throughout the test using the WOODWAY®Force 3.0 software package. Intra-class correlations have been previously reported as r=.89, .94, and .97 for peak power output, mean power output, and distance covered, respectively, during 30 s sprints on a non-motorized treadmill (Gonzalez, et al., 2013).

Oxygen uptake

Oxygen uptake (ml·kg·min^{-1}) was determined by open circuit spirometry using Quark PFT (COSMED, Italy). Expiratory airflow was achieved using a volume transducer connected to an oxygen analyser. Prior each test, the Quark PFT was calibrated according to the manufacturers' guidelines. After a 60 minute warm-up period, the carbon dioxide and oxygen sensors were calibrated against room air in addition to a reference gas of a known composition (5% carbon dioxide, 15% oxygen, and 80% nitrogen) with volume calibrated using a 3 L pump. Oxygen uptake (VO_2) carbon dioxide uptake (VCO_2) respiratory exchange ratio, and minute ventilation were displayed continuously. Breath-by-breath data were sampled and transferred to a PC for real-time display. The recorded data were saved to the internal database until analysis. The coefficient of variation for VO_2 determination using online systems has previously been determined as <3% (Foss & Hallen, 2005; Hayes, et al., 2015).

Pain scale

Participants were asked to provide pain perception ratings following each sprint (Cook, O'Connor, Eubanks, Smith, & Lee, 2007). A ten-point scale accompanied with verbal, written and visual descriptions was used. This was chosen given high intra-class correlations (r=.88-.98) suggest this scale is a reliable measure of pain perception during exercise (Cook, et al., 2007). Standardized

verbal instruction of the correct use of the scale was provided prior to each experimental procedure.

Statistical analysis

Data were analyzed using IBM SPSS statistics version 21.0 (IBM Corp, NY, USA). Parametric assumptions were checked using numerical methods: checking studentized residual, Shapiro-Wilk test and Mauchly's Test of sphericity. Following confirmation of parametricity, mean differences in mean power output, peak power output, GRFv, peak VO_2, distance completed, and perceived pain between the two experimental conditions (ACT and PLA) were assessed using a two-way (condition x sprint) analysis of variance (ANOVA) with repeated measures and *posteriori* Sidak. The difference in distance completed over the eight bouts was analysed using a paired samples *t*-test. Alpha was set *a priori* at $p<.05$ and 95% confidence intervals (CI) and effect sizes (ES) are displayed where appropriate. Data are presented as mean±standard deviation (SD).

Results

No main effect of condition (p=.83; ES=.01), or interaction between condition and bout (p=.22; ES=.17) was observed for peak power output between ACT (1008±418 W, 95% CI=909-1108 W) and PLA (983±374 W, 95% CI=894-1072 W) conditions (Figure 1:A). No significant main effect (p=.64; ES=.03), or interaction effect (p=.21; ES=.17) was observed for mean power output between ACT (320±119 W, 95% CI=292-3486 W) and PLA (323±119 W, 95% CI=295-351 W) conditions (Figure 1:B). No significant main effect (p=.31; ES=.15) was found for pain perception between ACT (5.97±2.35, 95% CI=5.41-6.53) and PLA (6.24±2.78, 95% CI=5.58-6.91) conditions. A significant interaction effect existed between condition and sprint number ($p<.001$; ES=.61). Posteriori Sidak adjustment revealed that pain perception was significantly reduced during sprint six (8.6±1.4 compared to 7.4±1.4), seven (8.9±1.4 compared to 7.7±1.5), and eight (9.3±0.9 compared to 8.6±1.1) during the ACT condition compared to the PLA condition (Figure 1:C).

No significant main effect (p=.42; ES=.10) was observed for peak GRFv between ACT (178±27 kg, 95% CI=172-185 kg) and PLA (185±60 kg, 95% CI=171-200 kg) conditions. No effect of condition (p=.47; ES=.08) was observed for peak VO_2 between ACT (48±7 ml·kg·min^{-1}, 95% CI=46-50 ml·kg·min^{-1}) and PLA (49±8 ml·kg·min^{-1}, 95% CI=47-51 ml·kg·min^{-1}) conditions (Figure 1:D). Paired-samples *t*-test revealed no significant difference in distance completed between ACT (664±109 m, 95% CI=580-748 m) and PLA (657±111 m, 95% CI=572-742 m) conditions (p=.31).

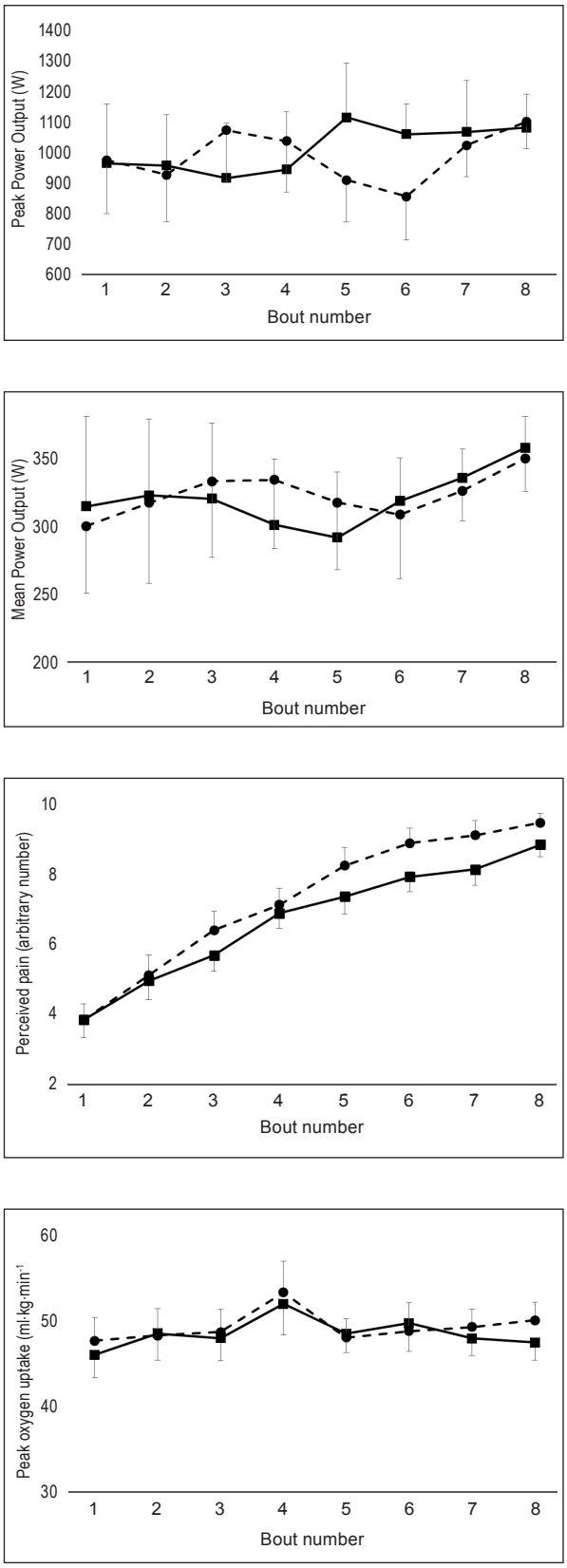

Figure 1. **A:** *Peak power output during 8 x 30 s treadmill sprints.* **B:** *Mean power output during 8 x 30 s treadmill sprints.* **C:** *Peak oxygen uptake observed during each 30 s treadmill sprint.* **D:** *Perceived pain after 8 x 30 s treadmill sprints. Data are presented as mean±standard error for clarity. Acetaminophen: solid line. Placebo: dashed line. *denotes a significant difference between groups (p<.05).*

Discussion

The main finding of the present study was that ACT ingestion did not improve sprint internal treadmill running performance. However, pain perception was reduced during sprint six, seven, and eight using the ACT condition compared to the PLA condition. This suggests ACT may be used to reduce exercise-induced pain in the latter stages of sprint interval training.

Results of the present study differ from those concerning cycling performance, where a significant change was observed for peak power output and mean power output accompanied by unaltered pain perception (Foster, et al., 2014). These findings in combination with the present investigation indicate ACT ingestion may be used to either improve performance, or minimise pain perception during repeated sprint exercise at a given exercise intensity. Findings from the present investigation indicate that exercise-induced pain did not significantly influence sprint interval performance, as pain perception decreased without significant alteration in performance parameters. A possible explanation for this is that muscle fatigue does not only occur in the working muscle, but is a conscious awareness of physical activity in which exercise-induced neuromuscular pain is one factor amongst a multitude of factors that influence central drive (Bundle & Weyand, 2012; Noakes, 2012; St Clair Gibson, et al., 2003).

Amann, Proctor, Sebranek, Pegelow, and Dempsey (2009) previously demonstrated that complete removal of pain with an opioid analgesic enabled participants to experience higher tolerance to peripheral neuromuscular fatigue during initial stages of exercise, but at a cost of increased diminution in mean power output during the final stages, resulting in no net increase in performance. This occurred as a result of participants adopting a more aggressive approach to their pacing strategy, resulting in greater levels of end-exercise peripheral neuromuscular fatigue. Therefore, it appears a degree of afferent neuromuscular feedback is required to maintain an appropriate pacing strategy and not induce premature fatigue (Amann, et al., 2009).

That we report no significant differences between the ACT and PLA conditions for peak GRFv is likely due to participants exceeding velocities of 6 $m \cdot s^{-1}$ for both ACT and PLA conditions. During velocities greater than 6 $m \cdot s^{-1}$, peak GRFv remains relatively constant on a non-motorized treadmill despite any increase in running velocity (Brughelli, Cronin, & Chouachi, 2010) and therefore our findings are in line with previous studies (Brughelli, et al., 2010).

That improved power profiles were observed following ACT ingestion by previous investigations (Foster, et al., 2014) but not in the present study is puzzling. However, a possible explanation may be that sprint interval cycling results in greater peripheral neuromuscular fatigue than does repeated sprint exercise running (Rampinini, et al., 2014). Moreover, Rampinini and colleagues (2014) reported rating of perceived exertion (RPE) to be higher during repeated sprint cycling compared to repeated sprint running. We therefore propose that ACT may have a greater ergogenic potential during activities where peripheral neuromuscular fatigue (and therefore RPE) is higher such as cycling and resistance exercise. However, further research is required to test this hypothesis.

In conclusion, the present study was the first to investigate the effects of 1.5 g ACT ingestion on sprint interval treadmill running. Results presented here suggest that sprint interval treadmill running performance was not influenced by ACT ingestion; however, pain perception was decreased during the final stages of exercise. Future research may wish to investigate events where peripheral neuromuscular fatigue is high as ACT may have more potential as an ergogenic aid.

References

Amann, M., Proctor, L., Sebranek, J., Pegelow, D., & Dempsey, J. (2009). Opioid-mediated muscle afferents inhibit central motor drive and limit peripheral muscle fatigue development in humans. *Journal of Physiology, 587*, 271-283.

Blough, E., & Wu, M. (2011). Acetaminophen: Beyond pain and fever relieving. *Frontiers in Pharmacology, 2*, 72.

Bonnefont, J., Alloui, A., Chapuy, E., Clottes, E., & Eschalie, A. (2003). Orally administered paracetamol does not act locally in the rat formalin test. *Anaesthesiology, 99*, 976-981.

Boutaud, O., Aronoff, D., Richardson, J., Marnett, L., & Oates, J. (2002). Determinants of the cellular specificity of acetaminophen as an inhibitor of prostaglandin H(2) synthase. *Proceedings of the National Academy of Sciences, 99*, 7130-7135.

Brughelli, M., Cronin, J., & Chouachi, A. (2010). Effects of running velocity on running kinetics and kinematics. *Journal of Strength & Conditioning Research, 25*, 933-939.

Bundle, M.W., & Weyand, P.G. (2012). Sprint exercise performance: Does metabolic power matter? *Exercise and Sport Sciences Reviews, 40*, 174-182.

Burtscher, M., Gatterer, H., Philippe, M., Krüsmann, P., Kernbeiss, S., Frontul, V., et al. (2013). Effects of a single low-dose acetaminophen on body temperature and running performance in the heat: A pilot project. *International Journal of Physiology, Pathophysiology and Pharmacology, 5*, 190-193.

Cook, D., O'Connor, P., Eubanks, S., Smith, J., & Lee, M. (1997). Naturally occurring muscle pain during exercise: Assessment and experimental evidence. *Medicine and Science in Sports and Exercise, 8*, 999-1012.

Delextrat, A., Baliqi, F., & Clarke, N. (2013). Repeated sprint ability and stride kinematics are altered following an official match in national-level basketball players. *Journal of Sports Medicine and Physical Fitness, 53*, 112-118.

Foss, O., & Hallen, J. (2005). Validity and stability of a computerized metabolic system with mixing chamber. *International Journal of Sports Medicine, 26*, 569-575.

Foster, J., Taylor, L., Chrismas, B.C., Watkins, S.L., & Mauger, A.R. (2014). The influence of acetaminophen on repeated sprint cycling performance. *European Journal of Applied Physiology, 114*, 41-48.

Garcin, M., Mille-Hamard, L., Billat, V., Imbenotte, M., Humbert, L., & Lhermitte, M. (2005). Use of acetaminophen in young subelite athletes. *Journal of Sports Medicine and Physical Fitness, 45*, 604-607.

Gonzalez, A.M., Wells, A.J., Hoffman, J.R., Stout, J.R., Fragala, M.S., Mangine, G.T., et al. (2013). Reliability of the Woodway Curve™ non-motorized treadmill for assessing anaerobic performance. *Journal of Sports Science and Medicine, 12*, 104-108.

Hayes, L.D., Bickerstaff, G.F., & Baker, J.S. (2010). Interactions of cortisol, testosterone and resistance training: Influence of circadian rhythms. *Chronobiology International, 27*, 675-705.

Hayes, L.D., Sculthorpe, N., Herbert, P., Baker, J.S., Spagna, R., & Grace, F.M. (2015). Six weeks of conditioning exercise increases total, but not free testosterone in lifelong sedentary aging men. *Aging Male, 18*, 195-200.

Kolkhorst F.W., Londeree, B.R., & Thomas, T.R. (1994). Effects of consecutive exercise days of jogging or cycling on the resting metabolic rate and nitrogen balance. *Journal of Sports Medicine and Physical Fitness, 34*, 343-350.

Lily, K.F. (2010). Athletes, NSAID, coxibs, and the gastrointestinal tract. *Current Sports Medicine Reports, 9*, 103-105.

Mauger, A., Taylor, L., Harding, C., Wright, B., Foster, J., & Castle, C. (2014). Acute acetaminophen (paracetamol) ingestion improves time to exhaustion during exercise in the heat. *Experimental Physiology, 99*, 164-171.

McDonald, D.D., & Molloy, B. (2012). Factors predicting older adults' use of exercise and acetaminophen for osteoarthritis pain. *Journal of the American Academy of Nurse Practitioners, 24*, 669-674.

Mendez-Villanueva, A., Hamer, P., & Bishop, D. (2007). Physical fitness and performance: Fatigue responses during repeated sprints matched for initial mechanical output. *Medicine and Science in Sports and Exercise, 39*, 2219-2225.

Nieman D.C., Luo, B., Dreau, D., Henson, D.A., Shanely, R.A., Dew, D., & Meaney, M.P. (2014). Immuno and imflammation responses to a 3-day period of intensified running versus cycling. *Brain, Behavior, and Immunity, 39*, 180-185.

Noakes, T. (2012). Fatigue is a brain-derived emotion that regulates the exercise behaviour to ensure the protection of whole body homeostasis. *Frontiers in Physiology, 3*, 82.

Pickering, G., Loriot, M., Libert, F., Eschalier, A., Beaune, P., & Dubray, C. (2006). Analgesic effect of acetaminophen in humans: First evidence of a central serotonergic mechanism. *Clinical Pharmacology & Therapeutics, 79*, 371-378.

Rampinini, E., Connolly, D.R., Ferioli, D., La Torre, A., Alberti, G., & Bosio, A. (2014). Peripheral neuromuscular fatigue induced by repeated-sprint exercise: Cycling vs running. *Journal of Sports Medicine and Physical Fitness*, Epub ahead of print.

St Clair Gibson, A., Baden, D., Lambert, M., Lambert, E., Harley, Y., Hampson, D., et al. (2003). The conscious perception of the sensation of fatigue. *Sports Medicine, 33*, 167-176.

Stocchero, C.M., Oses, J.P., Cunha, G.S., Martins, J.B., Brum, L.M., Zimmer, E.R., et al. (2014). Serum S100B level increases after running but not cycling exercise. *Applied Physiology, Nutrition and Metabolism, 39*, 340-344.

Submitted: May 14, 2015
Accepted: October 15, 2015

Correspondence to:
Lawrence D. Hayes, B.Sc (Hons), M.Sc., Ph.D.
Department of Medical and Sport Sciences
University of Cumbria
Bowerham Road, Lancaster
LA1 3DH, UK
E-mail: Lawrence.Hayes@Cumbria.ac.uk