No effect of glutamine supplementation and hyperoxia on oxidative metabolism and performance during high intensity exercise

Glutamine supplementation, hyperoxia and exercise performance

Keywords: Glutamine, tricarboxylic acid cycle intermediates, near-infrared spectroscopy, oxygen consumption, muscle deoxygenation.

Dr Simon Marwood
Health & Biology
Liverpool Hope University
marwoos@hope.ac.uk

Dr Joanna Bowtell
Sport & Exercise Science
London South Bank University
bowteljl@lsbu.ac.uk
Abstract
Glutamine enhances the exercise-induced expansion of the tricarboxylic acid intermediate pool. The aim of the present study was to determine whether oral glutamine, alone or in combination with hyperoxia, influenced oxidative metabolism and cycle time-trial performance. 8 participants consumed either placebo or 0.125g.kg body mass\(^{-1}\) of glutamine in 5 ml.kg body mass\(^{-1}\) placebo 1 h prior to exercise in normoxic (control & glutamine respectively) or hyperoxic (FiO\(_2\)=50%; hyperoxia & hyperoxia and glutamine respectively) conditions. Participants then cycled for 6 min at 70%\(\dot{V}O_2\)\(\text{max}\) immediately before completing a brief high intensity time-trial (~ 4min) where a pre-determined volume of work was completed as fast as possible. The increment in pulmonary oxygen uptake during the performance test (\(\Delta\dot{V}O_2\), p=0.02) and exercise performance \{243 ± 7 (control) vs 242 ± 3 (glutamine) vs 231 ± 3 (hyperoxia) vs 228 ± 5 (hyperoxia and glutamine) s, p<0.01\} were significantly improved in hyperoxic conditions. There was some evidence that glutamine ingestion increased \(\Delta\dot{V}O_2\) in normoxia, but not hyperoxia (interaction drink/FiO\(_2\), p=0.04) however there was no main effect or impact on performance. Overall the present data show no effect of glutamine ingestion either alone or in combination with hyperoxia, and thus no limiting effect of the tricarboxylic acid intermediate pool size, on oxidative metabolism and performance during maximal exercise.


Introduction

At the onset of exercise there is an increase in the tricarboxylic acid (TCA) intermediate pool size which has been suggested to facilitate increased oxidative ATP resynthesis (Sahlin, Katz, & Broberg, 1990; Wagenmakers, 1998). Conversely dissociation between the TCA intermediate pool size and oxidative energy provision during exercise has been consistently demonstrated during sub-maximal exercise (Bruce et al., 2001; Gibala, Gonzalez-Alonso & Saltin, 2002a; Gibala, Peirce, Constantin-Teodosiu & Greenhaff, 2002b; Dawson, Howarth, Tarnopolsky, Wong & Gibala, 2003; Howarth, LeBlanc, Heigenhauser & Gibala, 2004; Timmons, Constantin-Teodosiu, Poucher & Greenhaff, 2004; Dawson, Baker, Greenhaff & Gibala, 2005; Bangsbo, Gibala, Howart & Krstrup, 2006). However, Gibala, MacLean, Graham & Saltin, (1998) demonstrate that as exercise intensity (and hence TCA cycle flux) increases there is a concomitant (though non-linear) increase in the TCA intermediate pool size. Therefore it seems likely that only during maximal intensity exercise, once maximal TCA intermediate concentration has been reached, will the TCA intermediate pool size be limiting to TCA cycle flux and thus oxidative metabolism, (i.e. unchanging TCA intermediate pool size during requirement for increased TCA cycle flux).

Dichloroacetate infusion results in near-maximal activation of the pyruvate dehydrogenase complex and stockpiling of acetyl-units. During the transition to subsequent moderate intensity exercise, dichloroacetate infusion has consistently been shown to enhance the rate of increase of oxidative metabolism as indicated by a
reduction in phosphocreatine degradation and lactate accumulation (Timmons et al. 1996; Timmons, Poucher, Constantin-Teodosiu, Macdonald & Greenhaff, 1997; Timmons et al. 1998a Timmons, Gustafsson, Sundberg, Jansson & Greenhaff, 1998b; Howlett, Heigenhauser, Hultman, Hollidge-Horvat & Spriet, 1999a; Parolin et al. 2000; Roberts, Loxham, Poucher, Constantin-Teodosiu & Greenhaff, 2002). However during the transition to high intensity exercise dichloroacetate infusion appears to have no effect on oxidative metabolism (Savasi, Evans, Heigenhauser & Spriet, 2002; Howlett, Heigenhauser & Spriet, 1999b). Furthermore, whilst dichloroacetate infusion reduced TCA intermediate content at rest (Constantin-Teodosiu et al, 1999) the majority of studies show no effect of prior dichloroacetate infusion on the TCA intermediate pool during exercise (Gibala et al. 2002b; Timmons et al. 2004). The study by Bangsbo et al. (2006) is the only study to demonstrate manipulation (reduction) of the TCA intermediate pool during exercise following dichloroacetate infusion; after 15 s of high intensity exercise the TCA intermediate pool was reduced following dichloroacetate infusion, compared to saline, with no effect on oxidative metabolism. Importantly however, this effect on the TCA intermediate was not maintained after 3 min of exercise. Taken together, studies utilising dichloroacetate infusion prior to high intensity exercise therefore show a limitation downstream of the pyruvate dehydrogenase complex, hence implicating the TCA intermediate and / or oxygen delivery as limiting factors during high intensity exercise. Surprisingly there is a paucity of data relating to the possible role of the TCA intermediate in limiting oxidative metabolism during high intensity exercise. However, in contrast to the study by Bangsbo et al.
The rate of oxidative ATP production and power output were enhanced during severe intensity finger flexion exercise when 6 g.day\(^{-1}\) of a mixture containing 55 g.l\(^{-1}\) of malate (the TCA intermediate making the largest contribution to the increase in TCA intermediate during exercise (Gibala, Tarnopolsky, & Graham, 1997) was consumed for 15 days (Bendahan et al. 2002).

Glutamine ingestion enhances the exercise-induced increase in the TCA intermediate pool following 10 min of cycle exercise at 70\% \(\dot{V}O_2\)\(\text{max}\) (Bruce et al. 2001), though this had no effect on substrate level phosphorylation after 10 min of exercise. However no previous study has investigated the effects of glutamine ingestion during high intensity, whole body exercise. Therefore the first aim of the present study was to determine whether glutamine ingestion (via an enhanced TCA intermediate pool expansion) improves oxidative metabolism and performance during maximal aerobic exercise.

Relieving a limitation at the level of the TCA cycle may only expose other limitations (e.g. oxygen delivery, enzyme activation), which prevent enhancement of oxidative metabolism (Tschakovsky & Hughson, 1999; Gurd et al. 2006). We therefore hypothesised that any glutamine-mediated enhancement of TCA cycle flux, and hence NADH & FADH production, would exacerbate the oxygen delivery limitation found during high intensity exercise (Linossier, Karlsson, Fagraeus & Saltin, 1974; Adams & Welch, 1980; Knight et al. 1993; Hogan, Richardson & Haseler, 1999; Richardson et al. 1999a; Richardson, Leigh, Wagner & Noyszewski, 1999b; Linossier et al. 2000). Therefore a second aim of this experiment was to
compare the separate and combined effects of glutamine supplementation and hyperoxia on performance and oxidative metabolism during maximal aerobic exercise.

**Method**

**Participants**

Eight trained cyclists (age: 36.0 ± 4 yrs; $\dot{V}o_2$ max: 4.6 ± 0.2 l.min\(^{-1}\); WorkMax: 381 ± 46 W; mass: 80.4 ± 4 kg) completed the four-trial study, which was approved by the local university ethical committee.

**Preliminary testing**

The pre-experimental procedures were employed to replicate the protocol of Bruce *et al.* (2001) in which oral glutamine was demonstrated to enhance the exercise-induced expansion of the TCA intermediate pool. Full details of preliminary testing and pre-experimental procedures can be found elsewhere (Marwood & Bowtell, 2007). In brief, a submaximal test and a maximal ramp test to determine $\dot{V}o_2$ max, were completed. An incremental maximum workload (WorkMax) test was also completed to individually determine the volume of work for the time trial (Jeukendrup, Saris, Brouns, & Kester, 1996). Prior to the main trials, a familiarisation trial was performed to reduce any possible learning effect across the four trials. A separate unpublished study utilising the present exercise protocol examined performance across three identical trials; there was no significant improvement in performance across trials. In addition, the 95% limits of agreement
between adjacent trials reduced from 15.6 s / 27.9 W (mean performance: 222 s / 377 W) between trials 1 & 2 to 9.25 s / 17.0 W (mean performance: 222 s / 378 W) between trials 2 & 3, suggesting a reduction in the 95% limits of agreement between adjacent trials to ~4% of overall performance after a single familiarisation trial. Therefore we were confident that performance during the experimental trials was reliable and without a learning effect.

**Pre-experimental procedures**

**Participants** were instructed to consume their habitual diet and refrain from strenuous physical activity in the 48 h prior to each experiment. On the evening before the experiment (day 1), participants completed 30 min cycling at 70% \( V_o_2 \)max. The workload was then doubled and 3 * 50 s bursts of exercise were completed, separated by 2 min of rest. Participants then cycled for a further 45 min at 70% \( V_o_2 \)max. This also ensured that blood lactate concentration was low at the end of exercise to minimise glycogen resynthesis from lactate during recovery. The glycogen depleting protocol was designed to deplete both type I and type II muscle fibres of glycogen as validated by Vollestad et al. (1992). Participants were free to drink water throughout exercise. Following the glycogen depleting exercise, participants consumed a prescribed diet (identical for each trial), based on their habitual diet, but which provided only 30% carbohydrate. This ensured that only limited muscle glycogen resynthesis occurred before the 2nd day of the experiment, and that the magnitude of resynthesis, and hence pyruvate availability, were similar for each trial. This design was employed to replicate the protocol of Bruce et al.
(2001) in which oral glutamine was demonstrated to enhance the exercise-induced expansion of the TCA intermediate pool.

Experimental Design

Participants completed four main trials: placebo & normoxia (CON), glutamine & normoxia (GLN), placebo and hyperoxia (HYP) and hyperoxia and glutamine (HPG). Trials were allocated in a systematic rotation fashion with participants blind to the condition. Each trial took place over the course of two days and trials were separated by 10 – 14 days.

Experimental protocol

Each experimental trial was completed across 2 days. On the evening of day 1, participants undertook a glycogen depletion protocol (see above). On the morning of day 2, participants arrived at the laboratory following an overnight fast and rested in the supine position. A cannula was inserted into an antecubital vein and a resting blood sample was obtained. Participants then consumed a drink containing either 5ml.kg body wt⁻¹ of placebo or 0.125g.kg body wt⁻¹ glutamine in 5ml.kg body wt⁻¹ of placebo and rested for 1 h before exercise commenced. Ten min before exercise, participants positioned themselves on the ergometer and inspired either normoxic (room) air (FiO₂ = 21%) or a hyperoxic gas mixture containing 50% oxygen and balanced nitrogen (FiO₂ = 50%). Exercise commenced from rest and consisted of cycling for 6 min at 70% Vo₂ max immediately before completing a fixed-work time-trial (equal to 4 min at 95%Wmax). Participants received verbal
encouragement to perform maximally and were provided with standardised information relating to their progress in the time trial. Participants were informed of the completion of each 10 kJ until 20 kJ remaining where they were informed of each kJ completed until the finish. Following 30 min of stationary recovery from exercise, participants cycled for a further 5 min at 100 W, after which a tourniquet was immediately inflated (around the thigh interrogated by near infrared spectroscopy, see below) to 260mmHg for 1 minute and then quickly deflated.

Pulmonary gas exchange & near infrared spectroscopy

Breath by breath pulmonary oxygen uptake ($\dot{V}O_2$) was measured throughout exercise; participants wore a nose-clip and breathed through a mouthpiece connected to a low inertia turbine volume transducer (Interface associates, USA) and mass spectrometer system (CaSE QP9000, Morgan Medical, UK) tuned to measure oxygen, carbon dioxide, nitrogen and argon. Prior to each exercise test, the turbine was calibrated using a precision 3-litre calibration syringe (Hans Rudolph Inc., USA). The system was calibrated prior to each trial using gases of known concentration spanning the range of anticipated fractional gas concentrations during each trial (normoxia: 15% $O_2$; hyperoxia: 40% $O_2$). The inlet port of the mouthpiece was connected to a 250L Douglas bag which was continuously filled with a gas mixture containing 50% oxygen and balanced nitrogen from a pressurised cylinder. In the normoxic trials the Douglas bag was by-passed and participants breathed room air. Measurement of $\dot{V}O_2$ in hyperoxia is technically difficult due to potential problems with contamination with ambient air. However, open circuit
systems such as that used in the present study appear to circumvent such problems and have been shown to be valid measures of $\dot{V}O_2$ in hyperoxia (Prieur et al. 1998). The present device utilises standard algorithms (Beaver, Lamarra & Wasserman, 1981) which have been utilised in previous studies measuring $\dot{V}O_2$ in hyperoxia (Bell, Paterson, Kowalchuk & Cunningham, 1999; Wilkerson, Berger & Jones, 2006). Hence we were confident that our measurement of $\dot{V}O_2$ in hyperoxia was valid.

Continuous, non-invasive measurements of muscle deoxygenation via the deoxyhaemoglobin signal (Hb) were made via near infrared spectroscopy (NIRO 500, Hamamatsu, Japan) throughout rest and exercise periods (see Marwood & Bowtell, 2007 for full details of these procedures). Muscle deoxyhaemoglobin data were normalised to the physiological range which inflation and release of a cuff (see above) around the interrogated thigh produced (%Hb), (Marwood & Bowtell, 2007).

**Blood analysis**

Venous blood samples (12 ml) were taken at rest (prior to placebo / glutamine ingestion), 30 min post ingestion, at the onset of submaximal exercise, at the onset and after 2 min and at termination of the time trial and after 3, 6, 10, 15, 20 min of recovery from the time trial. Samples were immediately centrifuged at 13,000 rpm for 2 min, the supernatant collected, snap frozen in liquid nitrogen and stored at -80°C and later analysed for lactate and glucose by an automated colorimetric assay.
(Cobas Mira, ABX Diagnostics) and for glutamine using standard colorimetric assays (Bergmeyer, 1974).

Data analysis

$\dot{V}O_2$ and $%Hb$ data are expressed as the increment from the mean value during the final minute of submaximal exercise ($\Delta\dot{V}O_2$ & $\Delta%Hb$). $\Delta\dot{V}O_2$ & $\Delta%Hb$ data are also normalised against the increment in power output relative to submaximal exercise ($\Delta\dot{V}O_2/\Delta W$ and $\Delta%Hb/\Delta W$).

Statistics

Values are presented as mean ± standard error of the mean (SE) with an n of 8 for near infrared spectroscopy data and performance, 7 for pulmonary variables and 6 for blood variables (due to technical problems with pulmonary gas and blood sampling). Data from the first 6 min of exercise have been presented elsewhere (Marwood & Bowtell, 2007).

Time course dependent data were analysed by a 3 way ANOVA for repeated measures {drink (glutamine vs placebo) by inspired oxygen fraction ($FiO_2$: hyperoxia vs normoxia) by time}. All other data were analysed by a 2 way ANOVA for repeated measures {drink (glutamine vs placebo) by $FiO_2$ (hyperoxia vs normoxia)}. The specific location of any effect was identified using a pairwise analysis (t-test) corrected by a Sidak-based Holm step-down procedure for multiple comparisons.
Results

Time trial

The average volume of work to be completed during the performance test was 86.8 ± 10.4 kJ. Average time-trial power output was higher (5.7 ± 2.1%) during hyperoxic conditions (average of two hyperoxic trials versus two normoxic trials) but glutamine supplementation had no effect, \{358 ± 20 (control) vs 357 ± 17 (glutamine) vs 374 ± 18 (hyperoxia) vs 380 ± 20 (hyperoxia and glutamine) W, main effect FiO$_2$, p=0.002, figure 1\}. Time to complete the time-trial was 243 ± 7 (control) vs 242 ± 3 (glutamine) vs 231 ± 3 (hyperoxia) vs 228 ± 5 (hyperoxia and glutamine) s (main effect FiO$_2$, p=0.002).

Pulmonary gas exchange

Average $\dot{V}O_2$ in the final minute of steady state exercise was 3.48 ± 0.17 (control), 3.68 ± 0.14 (glutamine), 3.65 ± 0.10 (hyperoxia) 3.43 ± 0.19 (hyperoxia and glutamine) l.min$^{-1}$.

$\Delta \dot{V}O_2$ was higher in hyperoxia compared to normoxia (main effect FiO$_2$, p=0.02; figure 2). There was also a significant drink / FiO$_2$ interaction (p=0.04) showing that the effect of glutamine was different in hyperoxia compared to normoxia. Subsequent pairwise analysis revealed that $\Delta \dot{V}O_2$ was higher in the hyperoxia trial...
versus control, but that following glutamine ingestion $\Delta \dot{V}o_2$ was no higher in the hyperoxic condition compared to normoxia. These effects remained when $\Delta \dot{V}o_2$ was normalised for the increment in power output (figure 3).

**Near infrared spectroscopy**

$\Delta \%Hb$ & $\Delta \%Hb /\Delta W$ increased throughout exercise with no effect of glutamine ingestion or hyperoxia (main effect time, p<0.001; figures 4, 5).

**Plasma Glutamine**

At rest, plasma glutamine concentration was not different between trials {537 ± 43 (control) vs 651 ± 64 (glutamine) vs 570 ± 35 (hyperoxia) vs 565 ± 48 (hyperoxia and glutamine) $\mu$mol.l$^{-1}$}. Glutamine ingestion resulted in a 94% and 96% increase in plasma glutamine concentration 30 min post-consumption compared to pre-ingestion but was unchanged in placebo trials {537 ± 46 (control) vs 1261 ± 91 (glutamine) vs 633 ± 44 (hyperoxia) vs 1108 ± 64 (hyperoxia and glutamine) $\mu$mol.l$^{-1}$, main effect drink, p<0.001, figure 6}. Immediately prior to exercise, plasma glutamine concentration remained slightly elevated above pre-ingestion in the glutamine trials but was not different to the placebo trials. In the placebo trials plasma glutamine concentration was not different from rest at any time and there was no difference in plasma glutamine concentration between the two placebo-trials (control vs hyperoxia) or between the two glutamine-trials (glutamine vs hyperoxia and glutamine) at any time.
Plasma lactate

Plasma lactate concentration was not significantly different between trials and this remained the case when the data were re-calculated as the change from rest or normalised against power output (figure 7). There was no difference in peak plasma lactate concentration \(12.2 \pm 1.8\) (control) vs 10.6 ± 1.0 vs (glutamine) vs 10.2 ± 1.4 (hyperoxia) vs 10.6 ± 1.1 (hyperoxia and glutamine) mmol.l\(^{-1}\), figure 7 but the time to the peak measured lactate concentration following the termination of exercise was significantly longer following glutamine supplementation \(1.5 \pm 0.7\) (control) vs 4.0 ± 1.0 vs (glutamine) vs 2.6 ± 0.5 (hyperoxia) vs 5.0 ± 1.0 (hyperoxia and glutamine) min, main effect drink, p<0.001; figure 7).

Discussion

This is the first study to assess oxidative metabolism and performance during high intensity exercise following augmentation of the normal exercise-induced expansion of the TCA intermediate pool. Exercise was also conducted in hyperoxic conditions in order to blunt the anticipated oxygen delivery limitation found during high intensity exercise and thus maximise any potential effect of glutamine ingestion on oxidative metabolism. The main finding of the present study was that time-trial performance was unaffected by glutamine ingestion, whether in normoxia or hyperoxia. In contrast performance was enhanced by ~ 6% in hyperoxia, with a concomitant significant increase in \(\Delta \dot{V}o_2\). Hyperoxia has previously been shown to result in enhanced performance during high intensity exercise (Linnarsson, et al. 1974; Adams & Welch, 1980; Knight et al. 1993; Hogan et al. 1999; Richardson et
Glutamine ingestion conferred no main effect on any measured parameter. However, there was a drink/FiO₂ interaction effect for both Δ\(\dot{V}o_2\) and Δ\(\dot{V}o_2/\Delta W\), whereby in the placebo trials Δ\(\dot{V}o_2\) and Δ\(\dot{V}o_2/\Delta W\) were higher in hyperoxia than normoxia, but hyperoxia had no further effect in glutamine trials. Therefore the augmentation of Δ\(\dot{V}o_2\) and Δ\(\dot{V}o_2/\Delta W\) by hyperoxia was not apparent in the glutamine-supplemented trials, suggesting a beneficial effect of glutamine ingestion in normoxic conditions. However, there was no main effect of glutamine ingestion on these parameters, nor muscle deoxygenation or plasma lactate concentration. Therefore the weight of the evidence suggests that there was no effect of glutamine ingestion on oxidative metabolism or exercise performance.

Glutamine ingestion was utilised as it has previously been demonstrated to result in an enhancement of the exercise-induced increase in the TCA intermediate pool size at the onset of exercise (Bruce et al. 2001). The present experimental protocol was designed to replicate as closely as possible that of Bruce et al. (2001) whilst inserting a period of high intensity exercise. The study by Bruce et al. (2001) demonstrated a glutamine-induced enhanced expansion of the TCA intermediate
pool after 10 min of exercise at 70% $\dot{V}o_{2}\max$. The present study, in addition to employing identical pre-exercise procedures, utilised the same exercise duration but divided into 6 min of exercise at 70% $\dot{V}o_{2}\max$ and a ~4 min time trial. **TCA intermediate** pool size is increased 4-fold after only 5 min of cycle exercise at 70% $\dot{V}o_{2}\max$ (Gibala et al. 1997) but decreases between 10 and 15 min exercise (Gibala et al. 2002a). Hence the present protocol was designed to maximise **TCA intermediate** pool size throughout the period of the time-trial. However a limitation of the present study is a lack of muscle **TCA intermediate** data, and no previous study has determined whether the glutamine-induced expansion of **TCA intermediate** pool is evident during higher intensity exercise. Examination of figure 6 shows a marked (94-96%) increase in plasma glutamine concentration 30 min post-ingestion, which persisted up to the onset of exercise (19% higher than pre-ingestion). This suggests that as shown previously (Hankard et al. 1995; Bruce et al. 2001), a substantial amount of the ingested glutamine escaped utilisation by the splanchnic bed. Elevated plasma glutamine concentration stimulates muscle glutamine uptake via the human muscle glutamine transporter, system N$^m$ (Ahmed, Maxwell, Taylor, & Rennie, 1993). Therefore the decrease in plasma glutamine concentration from 30 min post-ingestion to the onset of exercise suggests that a significant amount of glutamine entered the muscle (Varnier, Leese, Thompson, & Rennie, 1995). Hence it is likely that in the present study glutamine ingestion resulted in an enhancement of the exercise-induced expansion of the **TCA intermediate** pool as in the Bruce et al. (2001) study. Therefore the present results
suggest that the size of the TCA intermediate pool does not limit oxidative metabolism or performance during maximal aerobic performance.

The lack of any effect of hyperoxia on plasma lactate concentration during maximal exercise was perhaps not surprising since a number of previous studies have found similar results (Linnarsson et al. 1974; Adams & Welch, 1980; Knight et al. 1993; Hogan et al. 1999; Linossier et al. 2000; Savasi et al. 2002) suggesting that whilst exercise performance is enhanced in hyperoxia, fatigue occurs at the same intracellular concentrations of potential fatiguing metabolites (H⁺, AMP, IMP, Pi). Conversely, in the present study when plasma lactate concentration was normalised for power output, there still remained no differences in plasma lactate concentration between trials. However, plasma lactate concentration reflects the balance between efflux of lactate from the muscle and removal of lactate from the circulation by non-exercising muscle and the liver. Therefore, conclusions with regard to oxidative metabolism based on alterations in plasma lactate concentrations should be treated with caution. Indeed, the later peak plasma lactate concentration following glutamine ingestion in the present study demonstrates the many factors that may influence plasma lactate concentration (indeed it is possible that glutamine interferes with either the passive or active export of lactate from the muscle, via monocarboxylate transporter 1; Fei et al. 2000). Furthermore, the reduction in lactate concentration in hyperoxia observed in previous studies during submaximal exercise is likely due to a reduction in muscle glycogenolysis (Stellingwerff et al. 2005; Stellingwerff, LeBlanc, Hollidge, Heigenhauser & Spriet, 2006). However
the glycogen depletion protocol employed in the present study may have reduced muscle glycogenolysis during exercise, thus blunting this effect (Hargreaves, McConell & Proietto, 1995).

Summary
The main finding of the present study was that glutamine ingestion, previously shown to result in an enhancement of the exercise-induced increase in the TCA intermediate pool size (Bruce et al. 2001), has no effect on performance during high intensity exercise. In addition, despite some evidence to the contrary (i.e. hyperoxia did not increase ΔVo₂ and ΔVo₂/ΔW following glutamine ingestion, figures 2 and 3) on balance glutamine ingestion did not enhance pulmonary oxygen or muscle deoxygenation kinetics during the time trial. In accordance with previous studies demonstrating no effect of the TCA intermediate pool size on oxidative metabolism during submaximal exercise (Bruce et al. 2001; Gibala et al. 2002a,b; Dawson et al. 2003; Howarth et al. 2004; Timmons et al. 2004; Dawson et al. 2005) and intense (Bangsbo et al. 2006) exercise, the present results show no effect of glutamine ingestion, and thus no limiting effect of the TCA intermediate pool size, on oxidative metabolism and performance during maximal aerobic exercise.
Figure 1. Power output during the time-trial. Values are mean ± SE. There was a main effect of time (p<0.001) and of FiO₂ (p=0.002). + different to 1st minute of the time-trial (all trials, main effect time: pairwise analysis, p<0.05); # different to previous time point (all trials, main effect time: pairwise analysis, p<0.05). $ hyperoxia vs normoxia (main effect FiO₂, pairwise analysis, p<0.05).

Figure 2. ΔVo₂ during the time-trial. Values are mean ± SE. There was a main effect of time (p<0.001) and of FiO₂ (p=0.02). There was also a significant drink / FiO₂ interaction (p=0.04). + different to 1st minute of the time-trial (all trials, main effect time: pairwise analysis, p<0.05); # different to previous time point (all trials, main effect time: pairwise analysis, p<0.05). $ HYP vs CON (interaction drink / FiO₂: pairwise analysis, p<0.05).

Figure 3. ΔVo₂/ΔW during the time-trial. Values are mean ± SE. There was a main effect of time (p<0.01) and of FiO₂ (p<0.05). There was also a significant drink / FiO₂ interaction (p=0.02). + different to 1st minute of the time-trial (main effect time: pairwise analysis, p<0.05); $ HYP vs CON (interaction drink / FiO₂: pairwise analysis, p<0.05).

Figure 4. Δ%Hb during the time-trial. Values are mean ± SE. There was a main effect of time for all trials (p<0.001). # different to previous time point (main effect time: pairwise analysis, p<0.05).
Figure 5. $\Delta%Hb/\Delta W$ during the time-trial. Values are mean ± SE. There was a main effect of time for all trials (p<0.001). # different to previous time point (main effect time: pairwise analysis, p<0.05).

Figure 6. Plasma glutamine concentration at rest and during exercise. Plasma glutamine concentration was higher following glutamine supplementation compared to placebo (main effect drink, p<0.001). There was also a significant drink/time interaction (p<0.001). *glutamine vs placebo supplementation (interaction drink/time: pairwise analysis, p<0.05); # higher than resting concentrations (glutamine supplemented trials only; interaction drink/time: pairwise analysis, p<0.05); $ lower than at end of exercise (glutamine trials only; interaction drink / time: pairwise analysis, p<0.05).

Figure 7. Plasma lactate concentration during and following the time-trial. Values are mean ± SE. There was a main effect of time (p<0.001). + different to submaximal exercise (main effect time: pairwise analysis, p<0.05); # different to previous time point (main effect time: pairwise analysis, p<0.05); $ time to peak lactate concentration longer following glutamine supplementation (main effect drink, P<0.001).
References


Bangsbo, J., Gibala, M. J., Howarth, K. R. & Krstrup, P. (2006). Tricarboxylic acid cycle intermediates accumulate at the onset of intense exercise in man but are not essential for the increase in muscle oxygen uptake. *Pflugers Archives, 452* (6), 737-743


Figure 1

Figure 2
Figure 5

Figure 6
Figure 7