Chronic glutamine supplementation increases nasal but not salivary IgA during 9 days of interval training

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Krieger, James W., Michelle Crowe, and Sally E. Blank. Chronic glutamine supplementation increases nasal but not salivary IgA during 9 days of interval training. J Appl Physiol 97: 585–591, 2004. First published April 23, 2004; 10.1152/japplphysiol.00971.2003.—Oral glutamine supplementation during and after exercise abolishes exercise-induced decreases in plasma glutamine concentration but does not affect secretory IgA (sIgA) salivary output. Whether chronic glutamine supplementation during high-intensity interval training influences salivary and nasal sIgA concentration is unknown. The purpose of this study was examine the effects of chronic glutamine supplementation on sIgA during intense running training. Runners (n = 13, body mass 69.9 ± 2.8 kg, peak whole body oxygen uptake 55.5 ± 2 ml·kg⁻¹·min⁻¹, age 29.1 ± 2.8 yr) participated in twice-daily interval training for 9–9.5 days, followed by recovery (5–7 days). Oral glutamine supplement (0.1 g/kg) or placebo was given four times daily for the first 14 days. After an overnight fast, venous blood, nasal washes, and stimulated saliva were collected at baseline (T1), midtraining (T2), posttraining (T3), and after recovery (T4). Mood states were assessed by using Profile of Mood States (POMS) inventories. We found that glutamine concentration in resting subjects decreased from T1 to T4 (P < 0.05) and was not altered by supplementation. Salivary IgA concentration and output were unchanged by training or supplementation. Mean nasal IgA across the study period was greater in runners receiving glutamine (264.7 ± 35.0 μg/mg protein) vs. placebo (172.4 ± 33.7 μg/mg protein; P < 0.05). POMS analyses indicated that vigor was lower at T3 vs. T1 (P < 0.05) and fatigue was higher at T2 vs. T1 and T4 (P < 0.05). We conclude that chronic glutamine supplementation during interval training results in higher nasal IgA than placebo but does not affect salivary IgA concentration or output.

upper respiratory tract infection; immune indexes; glutamine homeostasis

EPISTEMOLOGICAL AND ANECDOTAL evidence suggest that athletes engaged in high-volume and/or high-intensity training are at an increased risk for upper respiratory tract infections (URTI) compared with athletes engaged in more moderate forms of training (21). The mechanisms behind these clinical manifestations are not clear but may result from training-related changes in immune indexes, including decreased salivary IgA concentration and secretion rates (12, 22–24, 35, 36).

Newsholme (29) proposed that decreased availability of glutamine to immune cells may be a key factor behind some of the changes in an athlete’s immune system. Glutamine is an important fuel for immune cells and intestinal mucosal cells (38). Lymphocytes and macrophages utilize glutamine at high rates and are dependent on glutamine for replication (29). Clinical evidence also exists for improved immune indexes and reduced infection rates when glutamine supplementation is provided to trauma, cancer, and postoperative patients with low plasma glutamine concentration (8). Although physical training does not typically predispose athletes to extensive periods of reduced plasma glutamine concentration as observed in clinical populations, Newsholme postulated that when plasma glutamine concentration decreases below a physiologically normal range of 0.5–0.9 mM (3), limited glutamine availability may impair certain immune cell functions and, in turn, increase an individual’s susceptibility to infections, such as URTI.

Plasma glutamine concentration can decrease in response to chronic, intense interval training (17) and as a result of overtraining (18, 25, 31, 33). Plasma concentrations of <0.5 mM have been observed in resting athletes during intense training (17, 18). Furthermore, increased incidence of infection was observed in athletes with decreased plasma glutamine concentration (18), although this outcome is not consistently reported (25). Controversial evidence exists for the efficacy of glutamine supplementation on immune indexes and infection incidence in athletes engaged in intense exercise. In two literature reviews of glutamine supplementation, exercise, and immune indexes, it was concluded that changes in plasma glutamine concentration most likely do not play a role in changes in immune indexes, including salivary IgA concentration, and that glutamine supplementation would not beneficial to athletes (16, 30). However, it should be noted that all research to date has only involved acute supplementation during and after a single bout of exercise.

The effect of chronic, high-dose glutamine supplementation on the immune system of human athletes during overload training has not been investigated. Unlike acute exercise, which may only marginally affect glutamine homeostasis for a short period of time, repetitive and intense training may repeatedly challenge glutamine homeostasis and adversely affect certain immune cell functions (29). Intense exercise may induce small transient decrements in plasma glutamine concentration, which are manifested by a greater decline in glutamine availability to mucosal tissues (29). Repetitive reductions in glutamine supply to IgA-producing lymphoid cells could affect their ability to produce IgA and increase susceptibility to infection. Under such conditions, chronic glutamine supplementation would, theoretically, help maintain glutamine homeostasis and secretory IgA concentration. No studies, to date, have attempted to utilize chronic glutamine supplementation to prevent the decrease in secretory IgA associated with intense training. In addition, only the effects of intense exercise on salivary IgA have been reported in the literature. However,
some pathogens, such as rhinovirus, only infect nasal mucosa (14). Thus investigation of the effects of supplementation and intense training on nasal IgA is warranted.

The purpose of this study was to determine whether chronic, high-dose glutamine supplementation would affect salivary and nasal IgA during a 9-day, intense interval training program. We hypothesized that supplementation would attenuate training-induced decreases in plasma glutamine and secretory IgA concentrations.

METHODS

Subject recruitment and cohorts. Thirteen healthy runners (4 women and 9 men) were recruited by advertisement within the local community. Inclusion criteria required subjects to (1) be between the ages of 18 and 49 yr, 2) currently run a minimum of 20 miles/wk, and 3) have a peak whole body oxygen uptake (V\textsubscript{O\textsubscript{2peak}}) of at least 52.5 ml·kg\textsuperscript{-1}·min\textsuperscript{-1} for men or 41.0 ml·kg\textsuperscript{-1}·min\textsuperscript{-1} for women. These values are classified as “superior” according to Cooper’s aerobic fitness classifications (5). Exclusion criteria included the following: self-reported respiratory illness within 7 days before training; prescription/nonprescription drug use; smoking; obesity; use of dietary supplements other than a multivitamin; illegal drug use; food/caffeine intake <8 h before testing; alcohol intake <8 h before testing; injury that impeded training; illness; diabetes; pregnancy; any heart, respiratory, or liver condition that contraindicated intense exercise training; and any other health condition that contraindicated intense exercise training. Washington State University’s Institutional Review Board approved the study, and written consent was obtained before data collection. Subjects were compensated $100 on successful completion of the study. The subjects were randomly assigned to receive glutamine (n = 6) or placebo (n = 7). A male subject from the placebo group withdrew after the second testing day due to self-diagnosed URTI. Because this subject completed two testing days, his data were included in the final analysis.

Testing and training. During the week before the commencement of the study, subjects were given an orientation to the testing and training procedures. Testing was conducted at the Exercise Science Human Physiology Laboratories at Washington State University. Subjects were tested for body mass, body composition, and V\textsubscript{O\textsubscript{2peak}} during treadmill running. The treadmill protocol was performed according to a modification of a protocol described by Fry et al. (10). Briefly, subjects walked or ran on the treadmill at a self-selected speed and grade as a warm-up for a self-selected period. Subjects then ran for 4 min at 12 km/h and a 1% incline. After a 3-min rest, subjects ran for 4 min at 15 km/h and a 1% incline. After another 3-min rest, subjects ran to volitional exhaustion at 18 km/h and a 1% incline. V\textsubscript{O\textsubscript{2peak}} was measured using an open-circuitry, online gas-analysis system (Sensormedics, Loma Linda, CA). Body mass was determined by a standard laboratory scale. Bioelectrical impedance (Omron, Vernon Hills, IL) was used to assess subject body composition. Heart rate was monitored every 30 s telemetrically (Polar, Woodbury, NY).

Training took place on outdoor or indoor tracks according to a modification of protocol of Fry et al. (10). Subjects participated in 9–9.5 days of twice a day interval training, beginning on day 1, the day of initial testing. Subjects performed a warm-up at a self-selected pace for a self-selected time. Morning sessions were conducted between 6 and 9 AM and included 15 × 1-min periods separated by 2 min of recovery, where subjects were permitted to walk briskly. Afternoon sessions were conducted between 4 and 8 PM and involved 10 × 1-min run periods separated by 1 min of recovery. Subjects ran at a pace approximate to the speed of the final stage that they reached during the preliminary treadmill test. If subjects were not able to maintain the required pace, the distance was reduced by 25 m until the subject was able to maintain pace. Heart rates were monitored telemetrically via Polar Vantage XL heart rate monitors. All training sessions were supervised. A 96% compliance rate was obtained. Reasons for absences from training included participation in races on the day of training and complaints of muscle pain from training. The training period was followed by a 5-day recovery period during which subjects returned to their normal daily exercise or physical activities.

Subject testing. Testing was performed on day 1 (T1), days 6 and 7 (T2), day 11 (T3), and day 16 or day 18 (T4). Subjects arrived at the laboratory between 6 and 8 AM after an overnight fast. Subjects were requested to not brush their teeth before they came to the laboratory and to have not consumed food or beverage (with the exception of water) or exercised for at least 8 h prior. Subjects provided blood, nasal wash, and stimulated saliva samples, and each subject filled out a Profile of Mood States (POMS) questionnaire (26). Total mood disturbance, a composite mood assessment, was determined according to Morgan et al. (27). At T4, two of the subjects failed to comply with the no-exercise requirement before testing. Samples were collected from these subjects 3 h postexercise. The values for these subjects were not greater than one standard deviation from the mean of the group, and, therefore, their data were included in the analysis.

Blood. The blood samples (±15 ml) were obtained via venipuncture of an antecubital vein. The blood was collected into heparinized vacutainers. Hematocrit was measured by microcentrifugation. Hemoglobin concentration was determined using the cyanmethemoglobin technique. Plasma volume changes were estimated according to Dill and Costill (7).

Diet. Three-day dietary food records were obtained for days 1–3 or 3–5 and for days 12–14. Diets were analyzed for average daily caloric, protein, carbohydrate, and fat content using Diet Analysis Plus (ESHA Research, Salem, OR).

Supplementation. Subjects received 0.1 g/kg of L-glutamine (Experimental and Applied Sciences, Golden, CO) mixed with sugar-free lemonade (Safeway, Pleasanton, CA) or a placebo (sugar-free lemonade only) four times daily for 14 days beginning on the first day of training. Subjects were blinded to which treatment they received. The supplement or placebo was mixed in ~300 ml of water. Supplement and placebo were identical in appearance and taste when mixed. Subjects consumed the drinks immediately after preparation. Subjects were instructed to consume no protein for 30 min to avoid competition of other amino acids. During the training period, the first dose was provided immediately after the morning session. The last dose was provided midway between the morning and afternoon session. The last dose was provided immediately after the afternoon session. The last dose was provided in the evening. During the recovery period, subjects were given their supplement packets ahead of time with instructions on how to prepare the drink. They were also given a sheet on which to record the times when they consumed the supplement. A 97.9% compliance rate was achieved.

Plasma glutamine and total protein determination. Plasma samples deproteinized with ice-cold 10% perchloric acid and neutralized with KOH were analyzed for glutamine by enzymatic determination according to the manufacturer’s instructions (Sigma Aldrich, St. Louis, MO). The detection range for this assay is 0.14–1.4 mM L-glutamine. Salivary and nasal total protein levels were analyzed spectrophotometrically according to Bradford (1). The technicians performing all the biological assays were blinded to the treatments that the subjects received.

Saliva collection. Saliva flow was stimulated by chewing a single Parafilm (5 cm²) section for 1 min, which typically elicits 1–3 ml/min of flow (6). Subjects were encouraged to allow the saliva to accumulate in the mouth until the urge to swallow occurred. Without expecting, the subjects allowed the saliva to flow into the collection tube and repeated the entire process until time elapsed. The sample was immediately placed on ice and then centrifuged to remove cellular debris. The supernatant fluid was frozen at ~80°C for later analysis of IgA and protein concentration.

Nasal wash. Nasal washes were collected as follows. The subject’s head was tilted back at an angle of ~70° from vertical. While the
subject closed the glottis, a rubber bulb syringe containing ~7 ml of sterile PBS was inserted into a nostril. The subject then tilted the head forward to allow the wash to drip into a sterile cup. The wash sample was immediately placed on ice and then centrifuged to remove cellular debris. The supernatant fluid was frozen at −80°C for later analysis of IgA and protein concentration.

IgA. Nasal wash and saliva samples were analyzed for IgA concentrations by using an enzyme-linked immunosorbent assay. Briefly, 96-well polystyrene plates were coated with goat anti-human IgA (α-chain specific, Sigma Chemical) diluted in 0.05 M carbonate buffer and incubated overnight at 4°C. The residual fluid was gently removed, and 1% bovine serum albumin in PBS was added to the wells as a blocking agent. The plate was incubated for 1 h at 37°C. After the fluid was gently removed, human IgA standards (Sigma Chemical) and saliva and nasal samples (diluted 1:500) were added to the wells. The plate was incubated for 1 h at 37°C and then washed with PBS-Tween 20. After residual fluid was gently removed, peroxidase conjugate anti-human IgA (Sigma Chemical) was added to each well and the plate incubated for 1 h at 37°C. The plate was washed, and the fluid was gently removed. The substrate, o-phenylenediamine in 0.05 M phosphate-citrate buffer and 0.03% H2O2, was added before a 30-min incubation at 37°C. The reaction was stopped with 2.5 M HCl, and absorbance was read at 490 nm (Molecular Devices, Sunnyvale, CA).

Statistics. Subject demographic data between groups, cohorts, and gender were compared by using an independent t-test. In cases of unequal variances, an Aspin-Welch unequal variance t-test was used. All other data were modeled using a linear mixed model estimated by the restricted maximum likelihood algorithm as determined by Hurvich and Tsai’s information corrected criterion (16a). For salivary, nasal, glutamine, and POMS data, baseline values were included in the model as a covariate. If the covariate was not significant, it was removed from the model. Because of the low sample size and statistical power, gender was not included as a factor in any mixed-model analyses. The normality-of-residuals assumption required by the restricted maximum likelihood algorithm was checked using a one-sample Kolmogorov-Smirnov test on the residuals and via visual inspection of a histogram of the residuals. All data satisfied the normality-of-residuals assumption.

If significant interactions were present, post hoc analyses on simple main effects within each factor level were done using multiple t-tests with a Sidak adjustment. If no significant interactions existed, post hoc analyses on main effects were done using multiple t-tests with a Sidak adjustment. Main effects for salivary IgA, salivary IgA-to-protein ratio, salivary IgA output, nasal IgA-to-protein ratio, and plasma glutamine, were declared significant at a one-tailed critical α of 0.05. All interactions, and all other main effects, were tested by using the null hypothesis and were declared significant at a two-tailed α of 0.05. Spearman’s rank correlations were determined between plasma glutamine and IgA measures, plasma glutamine and POMS variables, POMS variables and IgA measures, nasal IgA-to-protein ratio and salivary IgA output, and plasma glutamine and dietary protein intake. Separate correlations were performed for variables where a significant effect of treatment existed for the placebo group and glutamine group. Otherwise, correlations were conducted using data from all subjects. All analyses were performed using NCSS 2000 (Kaysville, UT) and SPSS 12.0 (Chicago, IL). All data are reported as means ± SE.

RESULTS

Physical and physiological characteristics. Subject physical and physiological characteristics were as follows: men: n = 9, body mass 73.5 ± 2.9 kg, VO2 peak 57.8 ± 2.3 ml·kg−1·min−1, age 29.3 ± 3.8 yr; women: n = 4, body mass 61.6 ± 3.8 kg, VO2 peak 50.3 ± 2.6 ml·kg−1·min−1, age 28.5 ± 4.4 yr. There were no significant treatment or group differences in body mass, height, VO2 peak, age, body fat percent, lean body mass, or fat mass. Height, body mass, and lean body mass were significantly higher in men than women (P < 0.05). There were no significant gender differences for any other variable. There was no significant effect of treatment on changes in plasma volume (P = 0.08). There was a significant effect of time (P = 0.001). The percent change in plasma volume from baseline at T4 (3.6 ± 1.6%) was significantly less than at T2 (13.6 ± 2.9%; P = 0.048) and T3 (18.4 ± 4.3%; P = 0.001).

Table 1. Dietary intake

<table>
<thead>
<tr>
<th>Kilocalories</th>
<th>Glutamine</th>
<th>Placebo</th>
<th>For treatment</th>
<th>For time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kilocalories</td>
<td>2,262 ± 174</td>
<td>2,569 ± 348</td>
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<td>Protein, g</td>
<td>2,627 ± 264</td>
<td>2,688 ± 327</td>
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<td>0.60</td>
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<td>Carbohydrates, g</td>
<td>80.2 ± 8.6</td>
<td>111 ± 11.4</td>
<td>0.95</td>
<td>0.32</td>
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<tr>
<td>Fat, g</td>
<td>97.0 ± 14.2</td>
<td>104 ± 8.1</td>
<td>0.51</td>
<td>0.47</td>
</tr>
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</table>

Values are means ± SE. Record 1 represents the food record for days 1–3 or 3–5. Record 2 represents the food record for days 12–14.
Training heart rate. There was no significant difference between glutamine and placebo groups in heart rate, expressed as a percentage of age-predicted maximum heart rate, at each training session (89.7 ± 0.4 and 89.3 ± 0.5% for placebo and glutamine groups, respectively, \( P = 0.80 \)). Heart rate in the afternoon and evening sessions was higher than the heart rate in the morning sessions (90.3 ± 0.4 and 88.7 ± 0.4%, respectively; \( P = 0.0 \)), and heart rate steadily decreased from 92.8 ± 0.6% on the first full day of training to 87.6 ± 1.2% on the last day of training.

Plasma glutamine concentration and diet. There was no significant effect of treatment (\( P = 0.14 \)) on plasma glutamine concentration (Fig. 1). There was a significant effect of time (\( P = 0.043; \) Fig. 1). Post hoc analysis did not reveal any significant differences among days. The training and glutamine supplementation protocols did not significantly change caloric intake (\( P = 0.21 \) and \( P = 0.62 \), respectively; Table 1), protein intake (\( P = 0.60 \) and \( P = 0.16 \), respectively; Table 1), carbohydrate intake (\( P = 0.32 \) and \( P = 0.95 \), respectively; Table 1), or fat intake (\( P = 0.47 \) and \( P = 0.51 \), respectively; Table 1).

Salivary and nasal IgA. The treatment and training protocols did not significantly alter salivary flow rate (\( P = 0.67 \) and \( P = 0.47 \), respectively; Fig. 2), salivary IgA concentration (\( P = 0.41 \) and \( P = 0.10 \), respectively; Fig. 3A), salivary IgA output (\( P = 0.17 \) and \( P = 0.48 \), respectively; Fig. 3C), and salivary protein concentration (\( P = 0.53 \) and \( P = 0.23 \), respectively; Fig. 4). There was a significant time \( \times \) treatment interaction for salivary IgA relative to total salivary protein (\( P = 0.021 \); Fig. 3B). Post hoc analysis revealed that, in the placebo group, salivary IgA-to-protein ratio was significantly greater at T2 compared with T1 (\( P = 0.022 \); Fig. 3B) and T3 (\( P = 0.044 \); Fig. 3B).
Fig. 4. Salivary protein concentration in the G and P groups. Values are means ± SE; n = 6 per group, with the exception of T1 and T2, where n = 7 in the P group.

Fig. 3B). Salivary IgA-to-protein ratio was also significantly greater at T2 in the placebo compared with the glutamine group (P = 0.011; Fig. 3B). There was no significant effect of time on nasal IgA relative to protein (P = 0.48, Fig. 5). There was a significant treatment effect on nasal IgA per protein content, with the overall mean lower in the placebo group (264.7 ± 35.0 vs. 172.4 ± 33.7 μg/mg, P = 0.047; Fig. 5).

POMS. Measures of vigor, fatigue, and composite mood were significantly changed during the training protocol (Table 2). Post hoc analysis revealed that vigor was significantly reduced at T3 compared with T1 (P = 0.024). Fatigue was significantly increased at T2 compared with T1 (P = 0.013) and T4 (P = 0.014). Total mood disturbance was significantly increased at T2 (P = 0.003) and T3 (P = 0.01) compared with T4. Measures of anger, depression, confusion, and tension were not significantly altered by treatment or time (Table 2).

Correlational analyses. Statistically weak associations were observed between IgA measures and POMS indexes, indicating that POMS scores could not be used as markers of changes in secretory IgA with training. A significant correlation was observed for salivary flow rate and vigor (P = 0.01, r = 0.34).

DISCUSSION

Plasma glutamine concentration decreased significantly with training, which is consistent with Keast et al. (17), who reported a significant decrease in plasma glutamine concentration in five military recruits during a 9.5-day, twice-per-day interval training protocol. The mechanisms behind the reduction in plasma glutamine concentration in response to overload training are not currently known but may include renal uptake and glutamine concentration returns to baseline within 90–120 min (40). The lack of a significant effect of supplementation in this study can be attributed to the time span of exercise-induced acidosis (34).

Plasma glutamine concentration was highly variable with a range of 0.18–0.80 mM and independent of glutamine supplementation. The variability did not reflect differences in training intensity, because some subjects with low plasma glutamine concentrations had the lowest percentage of maximum heart rate during exercise. It is also unlikely that diet directly influenced glutamine concentration because protein intake did not change over the course of the study. The diets were, however, self-reported, and precise determination of protein intake was not possible.

Glutamine supplementation four times per day would be expected to increase the average daily concentration of plasma glutamine. An oral dosage of 0.1 g/kg increases plasma glutamine concentration by 50% within 30 min after administration, and glutamine concentration returns to baseline within 90–120 min (40). The lack of a significant effect of supplementation in this study can be attributed to the time span of least 8 h between the last daily glutamine dose and the early morning blood draw in fasted subjects.

Nasal IgA concentration relative to total protein was significantly increased by chronic glutamine supplementation during training. Covariate analyses indicated that this effect was independent of baseline group differences. It is not clear why chronic glutamine supplementation would selectively increase nasal IgA concentration but have no effect on salivary IgA content. Differences may be due to collection of unstimulated

<table>
<thead>
<tr>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
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<tbody>
<tr>
<td>Confusion</td>
<td>4.9 ± 1.0</td>
<td>6.4 ± 1.5</td>
<td>6.0 ± 1.1</td>
</tr>
<tr>
<td>Tension</td>
<td>6.0 ± 1.0</td>
<td>6.4 ± 1.1</td>
<td>5.3 ± 0.9</td>
</tr>
<tr>
<td>Depression</td>
<td>3.9 ± 1.2</td>
<td>3.7 ± 1.2</td>
<td>2.3 ± 1.0</td>
</tr>
<tr>
<td>Anger</td>
<td>4.4 ± 0.8</td>
<td>3.3 ± 0.9</td>
<td>3.5 ± 1.2</td>
</tr>
<tr>
<td>Vigor*</td>
<td>19.7 ± 1.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16.8 ± 1.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15.8 ± 1.7&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fatigue*</td>
<td>6.1 ± 0.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.8 ± 1.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10.8 ± 1.5&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>Composite*</td>
<td>105.6 ± 3.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>114.8 ± 5.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>112.1 ± 4.7&lt;sup&gt;b&lt;/sup&gt;</td>
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</table>

Values are means ± SE; n = 13 subjects for baseline (T1) and midtraining (T2), and n = 12 subjects for postraining (T3) and after recovery (T4). Group data are combined in this table. POMS, Profile of Mood States. *Significant main effect of time (P < 0.05). Within each variable, different letters are significantly different from each other as determined by Sidak post hoc analysis (P < 0.05).
nasal fluid samples vs. stimulated salivary samples. Stimulation by chewing increases epithelial cell transcytosis of IgA into salivary fluid (32) and may have masked the effects of chronic glutamine supplementation on basal IgA secretion in nonstimulated samples.

To our knowledge, we are the first to report an effect of glutamine supplementation on nasal IgA during training. It is possible, because of the low power of the test, that this effect occurred by random chance. However, this result seems unlikely given that 83% of the subjects receiving chronic glutamine supplementation demonstrated an increase in nasal IgA per protein between T1 and T3, whereas 63% of the placebo group had a decrease in this variable during the same period. Increasing the sample size would increase the power of the test. Because of the large variability in nasal IgA concentration, a sample size of at least 32 subjects per group would be required to attain a statistical power of at least 0.80.

Investigation of nasal IgA in athletic populations at increased risk for URI T is warranted because some viruses that cause URI T, such as rhinovirus, only infect nasal mucosa (14). The relationship between nasal IgA and infection risk is not as well studied. Intranasal treatment with nasal IgA reduced the risk of respiratory syncytial virus in rhesus monkeys (39). Lindberg and Berglund (20) observed that intranasal treatment with IgA did not reduce risk of URI T symptoms in world-class canoeists over a 17-day period. There are no studies to date that include direct evaluation of the relationship between endogenous nasal IgA and URI T risk.

Supplementation had no effect on salivary IgA concentration or salivary IgA output. These findings are consistent with Krzywkowski et al. (19), who reported that glutamine supplementation provided during and after an acute bout of cycle ergometer exercise failed to prevent the postexercise decrease in salivary IgA. The results of the present investigation conflict with other studies in which decreases in salivary IgA concentration have been observed (2, 13, 21, 35). The disparity may relate to the duration of the training period used in protocols. The present study included a training period of ~9 days, which may not have provided a sufficient stimulus to reduce early morning salivary IgA in resting subjects. Others have observed decreases in salivary IgA concentration after longer training periods. Gleeson et al. (13) observed that preexercise salivary IgA concentration in elite swimmers decreased by 4.1% per month during 7 mo of training. Tharp and Barnes (35) reported that salivary IgA concentration in elite swimmers were significantly lower during 1 mo of heavy training vs. 1 mo of light or moderate training. Others have reported decreases in secretory IgA (2) and salivary IgA-to-protein ratio (21) after ~3 wk of strenuous training.

Salivary IgA-to-protein ratio increased at T2 in the placebo group and was greater at this time than values observed for the supplemented group. This can be attributed to the nonsignificant increase in salivary IgA at T2 in the placebo group ($P = 0.054$; Fig. 3A), with a concomitant lack of change in salivary protein (Fig. 4). The increase in salivary IgA concentration at T2 in the placebo group is most likely due to a reduced salivary flow rate, which also occurred at this time (Fig. 2).

Overload and overtraining are associated with mood disturbances (9, 10, 15, 27) and reduced secretory IgA concentrations and secretion rates (4, 11, 28). In the present study, vigor decreased and fatigue increased with interval training and returned to baseline after the recovery period. These observations are in agreement with the findings of others (15, 27, 37). Overall, correlational analyses failed to identify POMS scores as indicators of changes in secretory IgA during training.

In conclusion, chronic, high-dose glutamine supplementation during 9 days of interval training had no effect on salivary IgA concentration or output or plasma glutamine concentration in resting athletes. However, supplementation resulted in higher nasal IgA during training. The biological significance of this effect on nasal IgA (i.e., whether it helps reduce an athlete’s risk of URI T during intense periods of training) remains to be demonstrated.

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GRANTS

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