

JEPonline
Journal of Exercise Physiologyonline

**Official Journal of The American
Society of Exercise Physiologists (ASEP)**

ISSN 1097-9751

An International Electronic Journal

Volume 7 Number 5 2004

Neuroendocrinology and Immune Function

MUCOSAL IgA RESPONSE TO INTENSE INTERMITTENT EXERCISE IN HEALTHY MALE AND FEMALE ADULTS

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ABSTRACT

MUCOSAL IgA RESPONSE TO INTENSE INTERMITTENT EXERCISE IN HEALTHY MALE AND FEMALE ADULTS. **Hermann-J. Engels, Marianne M. Fahlman, Amy L. Morgan, Lance R. Formolo.** **JEPonline.** 2004;7(5):21-26. The primary purpose of this study was to compare the secretory immunoglobulin A (SIgA) response to intense intermittent exercise in healthy male and female adults. A secondary goal was to determine if the acute perturbations in immune function induced by strenuous exercise were associated with a high incidence of signs and symptoms of upper respiratory tract infection (URTI) in the weeks following the test. Thirty-five recreationally active adults (19 females, 16 males) performed three successive 30 s. Wingate leg cycling tests (0.075 kp/kg), separated each by 3 min of recovery. Timed unstimulated whole saliva was collected at rest before and after completion of the exercise protocol. SIgA secretion rate (S-SIgA) and the concentration of SIgA relative to total protein (SIgA:protein) were determined from measurements of raw SIgA and protein using a standard enzyme-linked immunosorbent assay. Moreover, each subject completed a study log indicating signs and symptoms of URTI for 3 weeks following the test. Results indicate that S-SIgA (52.7 ± 28.0 ; 35.8 ± 21.1 $\mu\text{g}/\text{min}$), SIgA:protein ratio (28.7 ± 17.9 ; 17.1 ± 11.4 $\mu\text{g SIgA}/\text{mg protein}$), and saliva flow rates (415.7 ± 197.9 ; 320.3 ± 209.5 $\mu\text{L}/\text{min}$) were lower after compared to before exercise ($p < 0.05$) and that there was no difference in response patterns between male and female study groups ($p > 0.05$). The exercise-induced suppression of SIgA was not followed by URTI in 33 of 35 subjects. The present data show that intense intermittent exercise results in similar changes in SIgA in healthy male and female adults. In general, these acute exercise induced effects on SIgA seem inconsequential in view of susceptibility for URTI.

Key Words: Secretory Immunoglobulin A, Exercise, Gender, Upper Respiratory Tract Infection

INTRODUCTION

The effect of exercise on mucosal immunity and upper respiratory tract infection (URTI) risk has attracted considerable research attention (1,2). It is well known that the mucosal immune system provides resistance to URTI primarily through the secretion of immunoglobulin A (SIgA) (1,3). SIgA has been shown to impede bacterial and viral adherence to mucosal surfaces and, therefore, limit colonization of these surfaces by

pathogens (3,4). Levels of SIgA can readily be obtained non-invasively from a person's saliva (5) and they have become widely accepted as a key biological indicator of changes in the integrity of the human mucosal immune system with exercise and other types of stressors (6,7).

Previous studies have established that exercise induced perturbations in salivary SIgA can vary with a number of factors such as type of exercise, training status and fitness level (1). Although several researchers observed an important effect of gender on SIgA levels both at rest before exercise (8) and immediately following acute strenuous exercise (9), Nieman et al. (10) recently pointed out that a systematic examination of the role of gender on the SIgA response with exercise so far has not received adequate research attention.

Repetitive bouts of intense exercise are a regular part of many recreational and competitive physical conditioning programs. Previous studies have shown that this type of exercise results in acute reductions of mucosal SIgA levels, either expressed as the amount of SIgA appearing per minute or the SIgA/protein ratio (11,12). While a number of early studies suggest that exercise induced changes in SIgA may be an important means to affect a person's susceptibility for URTI (12,13), more recent attempts to relate SIgA changes with both acute and chronic exercise to incidences of URTI have met with mixed results (8,10,11).

Therefore, the purpose of this study was to (a) compare the acute mucosal immune response (salivary SIgA) to intense intermittent exercise in healthy male and female adults, and (b) determine if the acute perturbations in immune function induced by this strenuous exercise bout are associated with a high incidence in clinical sign and symptoms of URTI in the weeks following the test.

METHODS

Subjects

Thirty-five adults (19 females, 16 males) served as subjects in this study. Prior to testing, all subjects provided a written informed consent and all research procedures were approved by the Institutional Human Investigation Committee. Only healthy, recreationally active adults who had no signs and symptoms of recent URTI were allowed to take part in the study. The basic physical characteristics of the study participants are summarized in Table 1. Prior to experimental testing, subjects reported to the laboratory for a preliminary evaluation including a medical history/health status screen, resting 12-lead ECG review by a board certified cardiologist, and assessment of signs and symptoms of URTI for the last two weeks.

Table 1. Subject Characteristics.

	N	Age (years)	Weight (kg)	Height (cm)
<i>Females</i>	19	23.7±5.6	60.3±9.7	166.2±5.2
<i>Males</i>	16	25.7±6.4	76.3±8.6	175.4±3.8

Exercise Protocol

The experimental, intermittent exercise protocol consisted of three successive 30 s standard Wingate tests (load = 0.075 kp/kg body weight) (14), separated each by 3 min of seated recovery. Before each experimental test, subjects completed a standard warm-up procedure and were instructed to give a maximal effort throughout each high intensity 30 s. exercise bout. To control for diurnal effects associated with both salivary (15,16) and performance measures (17), laboratory based exercise evaluations were always carried out during the same hours of the day (afternoon).

Tests were conducted using a stationary, friction-loaded leg cycle ergometer (Model 818, Monark, Varberg, Sweden) with the height of the seat adjusted for leg length. Pedal revolutions were counted using an infrared optical sensor array fitted to the cycle ergometer and interfaced with a microcomputer for analysis of mechanical power output (SMI OptoSensor 2000TM, SMI PowerTM Software program, Sport Medicine Industries, St. Cloud, MN). Individual peak and mean mechanical power output (W/kg) performance data were recorded as the highest mechanical power output produced during a single five s period of each 30 s test and the arithmetic average of the total power output generated during a 30 s test period, respectively

(14).

Salivary Immunoglobulin A

After the subjects had carefully rinsed out their mouths, unstimulated whole saliva was collected into test tubes for 4 min prior to and, again 5 min after completion of the intermittent exercise protocol. Samples were measured for volume (to the nearest 0.1 mL) and then stored at -70°C until subsequent analysis in one batch. Total salivary protein was determined using a commercially available diagnostic kit based on Bradford's standard assay (Bradford; Bio-rad Total Protein Assay Kit, Bio-rad Laboratories, Hercules, CA). SIgA secretion rate (S-SIgA) and the concentration of SIgA relative to total protein (SIgA:protein) were determined from measurements of raw SIgA and protein using a standard enzyme-linked immunosorbent assay (11). The rationale to report salivary immune data as both S-SIgA, indicating the total amount of SIgA appearing on the mucosal surface per minute, and the SIgA/protein ratio, which adjusts for exercise induced changes in saliva volume that may happen due to drying of oral surfaces as a result of exercise, was based on expert recommendations (1,2) and in recognition that there is still considerable debate regarding which method to express SIgA data may be most appropriate (10).

URTI Signs and Symptoms

Study participants were provided with standardized weekly logs in which they were asked to indicate the incidence and duration of signs and symptoms of URTI (including sore throat, runny nose, and cough) not related to allergies over a three week time period immediately following the laboratory exercise test. Since the incidence of URTI exhibits regional geographic seasonality (18), and to be able to directly compare findings to a previous study from this lab (11), data collection was performed over a two months time period during the summer (June and July).

Statistical Analyses

Saliva derived data (S-SIgA, SIgA:protein, saliva flow rate) was analyzed using a 2×2 (gender \times time) ANOVA and Wingate performance data was analyzed using a 2×3 (gender \times test) repeated measures ANOVA. In cases where the 2×3 ANOVA revealed a significant main effect, a Tukey post-hoc test was used to identify the source of the difference. The Wingate performance data was analyzed using repeated measures ANOVA. When the ANOVA showed significant main effects, a Tukey post-hoc test was used to identify the source of the difference. All statistical analyses were performed using SPSS (version 10.5) for Windows NT (Chicago, IL).

RESULTS

Experimental findings revealed significant reductions in the SIgA secretion rate (52.7 ± 28.0 ; 35.8 ± 21.1 $\mu\text{g}/\text{min}$) and the SIgA:protein ratio (28.7 ± 17.9 ; 17.1 ± 11.4 μg SIgA/mg protein) from before to after completion of the intermittent exercise protocol ($p < 0.05$). These changes were accompanied by pronounced decreases in the saliva flow rate (before exercise: 415.7 ± 197.9 $\mu\text{L}/\text{min}$; after exercise: 320.3 ± 209.5 $\mu\text{L}/\text{min}$) ($p < 0.05$). On the other hand, although males on average showed somewhat greater exercise induced changes compared to females, findings indicated no significant gender-specific differences in the observed patterns for SIgA secretion rate, SIgA:protein ratio, and saliva flow rate ($p > 0.05$). Pre- and post exercise saliva data by gender are summarized in Table 2 for S-SIgA, SIgA:protein ratio and saliva flow rate, respectively.

A review of completed standardized weekly sign and symptoms logs revealed that only two incidences of URTI occurred in the three weeks following the test. The reported incidences (1 male, 1 female) lasted two and three days, respectively, and both occurred during the first week after completion of the laboratory exercise test.

Performance data indicated a significant decrease in peak and mean mechanical power output (W/kg) among consecutive Wingate tests ($p < 0.05$). As expected (14), the observed mean and peak power output values (W/kg) were lower in the female relative to the male study group ($p < 0.05$) (Table 3).

Table 2. S-IgA ($\mu\text{g}/\text{min}$), IgA:protein ratio (μg IgA/mg protein), and saliva flow rate ($\mu\text{L}/\text{min}$) in females and males before and after intense intermittent exercise.

Variable	Pre-Exercise		Post-Exercise	
	Males	Females	Males	Females
S-IgA ($\mu\text{g}/\text{min}$)	54.9 \pm 26.8	50.9 \pm 29.7	33.6 \pm 22.1 ^a	37.7 \pm 20.6 ^a
IgA:protein ratio	29.0 \pm 11.8	28.6 \pm 21.9	14.6 \pm 8.5 ^a	18.5 \pm 13.2 ^a
Saliva flow rate ($\mu\text{l}/\text{min}$)	398.1 \pm 186.7	430.5 \pm 210.8	298.1 \pm 181.1 ^a	338.9 \pm 233.6 ^a

Values are mean \pm SD. ^a $p < 0.05$ compared to pre-exercise. Data indicates no significant effect of gender ($p > 0.05$).

Table 3. Mean and peak mechanical power output (W/kg) in females and males during intense intermittent exercise.

Gender	Wingate I		Wingate II		Wingate III	
	Mean	Peak	Mean	Peak	Mean	Peak
Females ^c	6.11 \pm 0.77 ^a	8.31 \pm 0.73 ^b	5.20 \pm 0.77 ^a	7.12 \pm 0.82 ^b	4.56 \pm 0.84 ^a	6.25 \pm 0.99 ^b
Males	7.25 \pm 0.87 ^a	9.88 \pm 0.78 ^b	6.23 \pm 1.00 ^a	8.97 \pm 0.86 ^b	5.38 \pm 1.04 ^a	7.73 \pm 1.11 ^b

Values are mean \pm SD. ^aSignificant difference in mean power value compared to other two Wingate tests ($p < 0.05$). ^bSignificant difference in peak power value compared to other two Wingate tests ($p < 0.05$). ^cSignificant effect of gender for both mean and peak mechanical power output ($p < 0.05$).

DISCUSSION

It is widely recognized that salivary SIgA levels are an important measure of mucosal immunity and resistance to URTI (4), and that they can readily be altered by both acute and chronic exercise (1,2). The present investigation substantiates earlier findings (11,12) indicating that intense intermittent exercise results in pronounced decreases in the secretion of SIgA (-32.1%), the SIgA:protein ratio (-40.2%), and saliva flow rate (-22.9%). To our knowledge, this is the first study to show that the salivary SIgA response following this common training exercise is similar in healthy male and female adults.

Nieman et al. (10) recently also found no gender difference in SIgA response patterns to a competitive long distance race in experienced marathon runners. In contrast, Gleeson et al. (8) noted a gender difference in mean pre-training SIgA levels at rest before and a similar trend after swim training sessions over a 7-month training period in elite swimmers. Similarly, Schouten and colleagues (9), in young healthy Dutch adults, observed that while pre-exercise resting levels of SIgA were not different between males and females, following a graded maximal oxygen uptake treadmill test, they were acutely increased in males but suppressed in females. It is interesting to note that similar discrepancies regarding the effects of gender on SIgA are also readily apparent among studies that examined other types of laboratory stress tasks (7,19).

Collectively, the inconsistencies in SIgA findings among available studies may be related to both known and yet unknown factors. In addition to exercise (i.e., type, duration, intensity, volume), training status (e.g., athletes vs. non-athletes), and fitness level, it is widely recognized that salivary SIgA levels can be affected by nutritional status, various psychological and environmental factors, and the specific techniques used for saliva collection, storage, and chemical analysis (1,10,20). Moreover, important circadian rhythms (15,16) and the different methods commonly used to express SIgA data can make a comparison of findings among studies difficult at times (10,11). Clearly, whether or not gender is an important variable affecting the SIgA response warrants further inquiry. In designing future studies, it is important to take into account that there is already a lengthy list of factors that have been shown to affect SIgA levels under a variety of experimental conditions.

Although decreases in salivary IgA after intense exercise are widely regarded as a possibly important mechanism contributing to the risk of URTI (1,2), only two of the 35 participants (5.7%) in this study experienced clinical signs and symptoms consistent with URTI in the three weeks following the controlled exercise evaluation. These observations are in close agreement with recent findings of a 3.8% (1/26) rate in moderately to highly active females who were evaluated using the same intense intermittent exercise protocol and 3-week URTI follow-up duration (11). On the other hand, both rates are low compared to the

17.2% (16/93) URTI incidence rate observed by Nieman et al. (10) over a 15-day period following a competitive marathon race. Of note is that none of the above exercise studies was conducted during time periods when incidences of URTI would usually be found to be rather high due to seasonal effects (18). While previous research has often revealed promising associations between both resting SIgA levels and post-exercise SIgA changes on one hand, and the occurrences of URTI on the other (1,2), more studies are needed to help clarify the strength of this relationship and to further establish its causative nature.

In conclusion, the present study found a pronounced reduction in SIgA levels following intense intermittent exercise and showed that the response pattern was similar in healthy adult males and females. The observed incidence of URTI signs and symptoms in the weeks following this strenuous exercise bout was low, though, and suggests that the acute exercise induced effects on SIgA were inconsequential in view of subsequent susceptibility for URTI.

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