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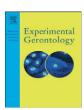
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### The effect of fasting on indicators of muscle damage

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#### ABSTRACT

Many studies have tested the consumption of foods and supplements to reduce exercise-induced muscle damage, but fasting itself is also worthy of investigation due to reports of beneficial effects of caloric restriction and/or intermittent fasting on inflammation and oxidative stress. This preliminary investigation compared indicators of exercise-induced muscle damage between upper-body untrained participants (N=29, 22 yrs old (SD=3.34), 12 women) who completed 8 h water-only fasts or ate a controlled diet in the 8 h prior to five consecutive laboratory sessions. All sessions were conducted in the afternoon hours (i.e., post meridiem) and the women completed the first session while in the follicular phase of their menstrual cycles. Measures of muscle pain, resting elbow extension, upper arm girth, isometric strength, myoglobin (Mb), total nitric oxide (NO), interleukin 1beta (IL1b), and tumor necrosis factor alpha (TNFa) were collected before and after eccentric contractions of the non-dominant elbow flexors were completed. The fasting group's loss of elbow extension was less than the post-prandial group (p<.05, eta²=.10), but the groups did not change differently across time for any other outcome measures. However, significantly higher NO (p<.05, eta²=.22) and lower TNFa (p<.001, eta²=.53) were detected in the fasting group than the post-prandial group regardless of time. These results suggest intermittent fasting does not robustly inhibit the signs and symptoms of exercise-induced muscle damage, but such fasting may generally affect common indirect markers of muscle damage.

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#### 1. Introduction

A myriad of dietary interventions for exercise-induced muscle damage have been investigated. In these studies, participants are often consuming foods or supplements of interest or placebos during a controlled diet. However, the effects of fasting on exercise-induced muscle damage are worthy of investigation.

Increasing evidence supports a strong relationship between energy metabolism and immune function (Matarese and La Cava, 2004). For example, numerous studies have shown that a high-fat meal increases markers of inflammation and/or oxidative stress — even in healthy humans (Derosa et al., 2009; Nappo et al., 2002; Tsai et al., 2004). In contrast, overweight adult asthmatics reduction of caloric input on alternate days over eight weeks was associated with decreased oxidative stress and inflammatory markers (Johnson et al., 2007). Also, in healthy adults, two months of a one-meal per day diet induced peripheral blood mononuclear cells to produce lower levels of cytokines than a three-meal per

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tially affected (Dixit et al., 2011). The results of these fasting studies are intriguing, but fasting interventions for months require participants with a high level of motivation. Accordingly, short-term fasting interventions would be more useful.

Unfortunately, studies of the effects of short-term fasting on inflam-

day diet, but serum levels of inflammatory mediators were not differen-

of such short-term fasting in preparation for surgical procedures have produced mixed results. In one study, patients who consumed only water for 6 h had a larger decrease in post-cholecystecomy or inguinal herniorrhaphy [please note the corrected spelling here] C-reactive protein levels than patients who consumed carbohydrate drinks while fasting from solid foods for 6 h. (Perrone et al., 2011). In the other study, a 3-day calorie restricted diet followed by a 1-day fast was associated with lower numbers of circulating leukocytes and less tumor necrosis factor alpha (TNFa) production after kidney donation, but higher serum levels of interleukin-8 (van Ginhoven et al., 2011). Thus, studies of both short- and long-term fasting have detected beneficial effects on markers of inflammation and/or oxidative stress.

The objective of this preliminary study was to test the effects of a controlled diet and intermittent fasting on exercise-induced muscle damage. Based on the literature showing beneficial effects of fasting

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on markers of inflammation and oxidative status, we hypothesized that fasting for 8 h prior would produce lower indicators of muscle damage than eating a controlled diet 8 h prior. Support for or against the hypothesis will clarify the importance of controlling diets to reduce variability in studies of exercise-induced muscle damage, which has been noted by many researchers (Beaton et al., 2002; Chen, 2006; Gulbin and Gaffney, 2002; Hubal et al., 2007; Dannecker, in press).

#### 2. Methods

#### 2.1. Experimental approach to the problem

The objective of this preliminary study was to test the effects of fasting and a controlled diet during the 8 h prior to data collection on each day of a 5-day investigation of exercise-induced muscle damage. We focused on the 8 h prior because such a duration is similar to the reviewed pre-surgical studies and an 8-hour fast could be easily administered by skipping breakfast and/or lunch. The typical signs and symptoms of exercise-induced muscle damage were measured along with circulating levels of muscle proteins, inflammation, and oxidative status before and after isokinetic eccentric contractions of the non-dominant elbow flexors were completed.

#### 2.2. Participants

Participants (N=29, 22 yrs old (SD=3.34), 12 women) provided written informed consent to participate in a six-session protocol that was approved by the University of Missouri's Health Science Institutional Review Board. Of these participants, 10 (24 years old (SD=1.50), 5 women) were recruited for this preliminary study and assigned to the post-prandial group. The fasting group was composed of 19 participants (21 years old (SD = 5.09), 7 women), who had previously completed afternoon sessions after daily 8-h water only fasts as part of an investigation of sex differences in muscle damage using the same methodology. The restrictions for participation were the following: (a) had not engaged in upper body strength training on a regular basis (i.e., two times per week) for consecutive weeks within the previous six months, (b) were not currently experiencing arm pain, (c) had no history of upper arm injury within the previous six months, and (d) no chronic pain conditions. In addition, participants were screened for potential risk factors to the exercise protocol (e.g., excessive swelling, loss of range or motion, exertional rhabdomyolysis). Furthermore, participants were restricted from the following behaviors: smoking 3 h prior to a session, caffeine for 3 h prior to a session, and performing self-care behaviors for musculoskeletal pain (e.g., taking analgesics) throughout the study period. Only one of the 5 women in the fasting group and only one of the 7 women in the post-prandial group were consuming oral contraceptives.

#### 2.3. Procedures

A familiarization session was held to determine the participants' heights and weights and to acclimate the participants to the sensory tests and arm girth and elbow joint angle measures. After the familiarization session, participants visited the laboratory during afternoon hours (i.e., post meridiem) for five consecutive days. The participants in the fasting group consumed only water for eight hours before each of the five sessions. The participants in the post-prandial group consumed only a supplied meal at 4–5 h before each of the five sessions. The supplied meal consisted of 810–860 kcal, 250–320 fat kcal, 28–35 g fat, 10–13 g sat fat, 40–45 mg cholesterol, 6–7 g fiber, 101–104 g carbohydrate, and 32–34 g protein, which reflects a typical lunch for males between the ages of 20–29 years of age (U.S. Department of Agriculture et al., 2010). Also, the first session was scheduled when women were in the follicular phase of their menstrual cycles (Cole et al., 2009).

At the beginning of the first session, participants were seated and asked to complete questionnaires regarding their adherence to the study restrictions. Next, non-dominant upper arm muscle pain during rest and movement and pressure pain thresholds were collected. Then, after participants had been seated for about 15 min, 10 mL of blood was collected from venous access on the dominant arm. Subsequently, non-dominant upper arm girth and resting elbow extension were measured before participants were positioned in a muscle testing apparatus (Biodex System 3; Biodex Medical Systems, Shirley, NY). While seated in the muscle testing apparatus, a 5-repetition maximal isometric strength test was completed and ratings of perceived exertion and muscle pain during the test were collected.

Following the isometric strength test, an eccentric strength test was completed. Next, the participants performed 3 sets of 12 maximal eccentric contractions to induce temporary muscle damage. All of the eccentric contractions were completed at a velocity of 90°/s through the participants' active range of motion with a rest period of 60 s in between each set.

During the next hour, participants were instructed to continue their adherence to the pre-session restrictions, but they were allowed to sit quietly outside the laboratory if they desired. After the 1-h delay, arm muscle pain, pressure pain thresholds, arm girth, resting elbow extension, and 10 mL of blood were collected again in the same manner as before the eccentric exercise. Finally, the session was terminated and participants were reminded of the schedule and restrictions for the subsequent sessions, which included avoiding any self-care behaviors for musculo-skeletal pain (e.g., ice or heat application, stretching, massage, etc.).

Participants returned to the laboratory at one, two, three, and four days after the eccentric exercise with all of these follow-up sessions held in the afternoon hours. During the follow-up sessions, participants' adherence to the study restrictions were checked by questionnaire again and arm muscle pain, pressure pain thresholds, arm girth, resting elbow extension, and 10 mL of blood were collected again.

#### 2.4. Measures

#### 2.4.1. Height and weight

The height and weight of participants were measured using an upright platform and balance beam scale (Health O Meter Professional; Sunbeam Products, Inc.; Boca Raton, FL). Based upon the ratio of height and weight, body mass index (BMI;  $kg/m^2$ ) was calculated.

#### 2.4.2. Exercise behavior

The exercise behavior of participants during a typical week was assessed by the Leisure-Time Exercise Questionnaire (LTEQ) (Godin and Shepard, 1985). The LTEQ is composed of three items that assess the frequency of performing strenuous, moderate, and mild exercise during leisure-time. The correlation between the LTEQ's total weighted score and maximal oxygen intake was r = .56 (p<.05), which was the highest correlation among 10 other self-report measures of exercise behavior (Jacobs et al., 1993).

#### 2.4.3. Numeric muscle pain ratings

Ratings of non-dominant arm muscle pain intensity were assessed before and after the eccentric exercise with 0–100 numeric scales. More specifically, these ratings were collected while the non-dominant arm was (1) stationary at approximately 90° of elbow flexion, (2) moving through active range of motion without applied load, and (3) completing the isometric strength test. The anchors of the pain intensity rating scale were "no pain" and "most intense pain sensation imaginable." The anchors of the pain unpleasantness rating scale were "no unpleasantness" and "most unpleasant imaginable." Numeric pain scales have been found to be reliable and valid (Jensen and Karoly, 2001).

#### 2.4.4. Pressure pain threshold

Pressure pain threshold (PPT) was defined as the point at which a pressure stimulus first became painful. The pressure stimulus was applied on the belly of the biceps brachii at 25% of the distance from the

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