Acute Postexercise Effects of Concentric and Eccentric Exercise on Glucose Tolerance

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Impaired glucose tolerance was shown to be present 48 hr following muscle-damaging eccentric exercise. We examined the acute effect of concentric and muscle-damaging eccentric exercise, matched for intensity, on the responses to a 2-hr 75-g oral glucose tolerance test (OGTT). Ten men (27 ± 9 years, 178 ± 7 cm, 75 ± 11 kg, VO₂max: 52.3 ± 7.3 ml·kg⁻¹·min⁻¹) underwent three OGTTs after an overnight 12 hr fast: rest (control), 40-min (5 × 8-min with 2-min interbout rest) of concentric (level running, 0%, CON) or eccentric exercise (downhill running, −12%, ECC). Running intensity was matched at 60% of maximal metabolic equivalent. Maximal isometric force of m. quadriceps femoris of both legs was measured before and after the running protocols. Downhill running speed was higher (level: 9.7 ± 2.1, downhill: 13.8 ± 3.2 km·hr⁻¹, p < .01). Running protocols had similar VO₂max (p = .59), heart rates (p = .20) and respiratory exchange ratio values (p = .74) indicating matched intensity and metabolic demands. Downhill running resulted in higher isometric force deficits (level: 3.0 ± 6.7, downhill: 17.1 ± 7.3%, p < .01). During OGTTs, area-under-the-curve for plasma glucose (control: 724 ± 97, CON: 710 ± 77, ECC: 726 ± 72 mmol·L⁻¹·120 min, p = .86) and insulin (control: 24995 ± 11229, CON: 23319 ± 10417, ECC: 21842 ± 10171 pmol·L⁻¹·120 min, p = .48), peak glucose (control: 8.1 ± 1.3, CON: 7.7 ± 1.2, ECC: 7.7 ± 1.1 mmol·L⁻¹, p = .63) and peak insulin levels (control: 361 ± 188, CON: 322 ± 179, ECC: 299 ± 152 pmol·L⁻¹, p = .30) were similar. It was concluded that glucose tolerance and the insulin response to an OGTT were not changed immediately by muscle-damaging eccentric exercise.

Keywords: muscle damage, glucose uptake, oral glucose tolerance test, insulin resistance, downhill running

Unaccustomed eccentric exercise of skeletal muscles (i.e., lengthening muscle actions) results in muscle damage. Established indicators of muscle damage, such as the inability to produce voluntary maximal isometric force (Behrens et al., 2012; Vila-Châ et al., 2012) and ultrastructural changes (Féasson et al., 2002; Lauritzen et al., 2009) can be observed immediately after the exercise, but others develop over time, such as muscle soreness and the elevation of blood creatine kinase. The delayed response of elevated blood creatine kinase clearly indicates a change in membrane properties enabling the leakage of intracellular creatine kinase from the muscle (Armstrong et al., 1991). Such eccentric exercise-induced change in membrane properties may have implications as well for transmembrane substrate transport. This has indeed been shown for glucose handling, as eccentric exercise increased pancreatic insulin secretion in response to 10 mMol glucose (King et al., 1993), decreased noninsulin mediated glucose uptake (Ide et al., 1996), and decreased glucose transport 4 (GLUT4) protein (Asp et al., 1995). Sherman et al. (1992) and Green et al. (2010) showed transient insulin resistance, i.e., a temporary decreased glucose tolerance in response to insulin, to an oral glucose load 48 hr after unaccustomed damaging eccentric exercise. In support of the transient insulin resistance is also the observation of lower muscle glycogen replenishment three days following eccentric exercise (Doyle et al., 1993).

In general, nondamaging dynamic exercise is known to induce a short-term increase in insulin action in skeletal muscle (Wojtaszewski et al., 2002). The immediate response of damage-inducing eccentric exercise to an oral glucose load has not been established. Therefore, the aim of the current study was to examine the acute effects of eccentric exercise (i.e., downhill running) on insulin responses and whole body glucose tolerance from an oral glucose challenge. An ability for normal or increased glucose tolerance immediately post exercise may provide a window of opportunity to minimize reduced muscle glycogen levels following damaging exercise. However, our observations will provide evidence whether impaired glucose tolerance is immediately present after muscle-damaging eccentric exercise.
Methods

Participants

Ten male participants (27 ± 9 years, 178 ± 7 cm, 75 ± 11 kg, VO₂max : 52.3 ± 7.3 ml·kg⁻¹·min⁻¹) volunteered for the study. Participants were routinely undertaking physical exercise and had no activities in the last 3 months with uncustomed eccentric contractions of the quadriceps muscles (e.g., hill running). All participants were healthy, free from musculoskeletal injury and provided written informed consent. Approval for the study was obtained from the Research Ethics Committee of the University of Chichester with protocols performed in accordance with the 1964 Declaration of Helsinki.

Experimental Design

Participants visited the laboratory for five sessions on different days. Details of all procedures will be described below. See Figure 1 for the timeline of experimental sessions and measurements. In brief, in the first visit, participants were familiarized for the production of voluntary maximal isometric contractions of the m. quadriceps femoris of both legs followed by determination of the relationship between level (gradient 0%) running speed at submaximal intensities and energy cost and a maximal oxygen uptake test. In the second visit, the individual resting metabolic equivalent (1-MET) in a fasted state was determined followed by administration of a 2 hr oral glucose tolerance test (OGTT) with measurement of glucose and insulin at 15-min intervals. In visit 2, fasting glucose and insulin were 4.3 mmol·L⁻¹ and 47.3 pmol·L⁻¹, respectively. In the third visit, we determined the relationship between downhill (gradient -12%) running speed and energy cost. In the fourth and fifth visit, a bout of level running (i.e., concentric exercise, 5 × 8-min bouts with 2 min rest) and downhill running (i.e., eccentric exercise, 5 × 8-min bouts with 2 min rest) at 60% of maximal metabolic equivalent was immediately followed by measurement of voluntary maximal isometric force with subsequent OGTT (approximately 15 min following running). All testing was in the morning with visit 2, 4, and 5 (with measurement of OGTT) following an overnight fast.

Force Measurements

Maximal isometric force of the m. quadriceps femoris was assessed with participants seated on a custom-built chair. Upper body movement during contractions was restricted using velcro straps placed around hip and waist. A cuff was positioned around the ankle of the participants (proximal to the fibular notch and medial malleolus) and attached via a steel chain to an s-beam load cell (RS 250kg, Tedea Huntleigh, Cardiff, UK). Hip and knee angles were kept at 90° flexion with participants instructed to keep both arms crossed in front of the chest during contractions. In addition, participants received standardized instructions (Gandevia, 2001) including strong verbal encouragement. Participants performed three maximal isometric contractions of about 3–4 s with 2 min recovery between contractions. Isometric force was recorded on computer with a sampling frequency of 1000Hz using Chart 4 V4.1.2 (AD Instruments, Oxford, UK) and displayed 1.5 m in front of the participants. Maximal isometric force was quantified as the highest mean value over a time period of 0.5 s.

Maximum Oxygen Uptake

Maximal oxygen uptake was established during an incremental exercise test on a motorized treadmill (HP Cosmos Pulsar, Bodycare Products, UK). Expired air samples were collected using Douglas Bags (Plysu Protection Systems Limited, Milton Keynes, UK). Starting speed was 9 km·hr⁻¹ on a gradient of 1%; gradient increased by 1%-min⁻¹ during the first five minutes followed by speed increases of by 0.1 km·hr⁻¹ every 5 seconds until volitional exhaustion. Expired air was collected in separate bags for the last 3-min of the test. The last collection bag was only analyzed when collection time and expired volume was greater than 30 s and 65 L, respectively. Expired and inspired fractions of oxygen and carbon dioxide were recorded using calibrated gas analyzers (Series 1400 gas analyzer, Servomex, Crowborough, UK) and

Figure 1 — Experimental design and measurements during the 5 visits. MVCs, maximal voluntary contractions; OGTT, oral glucose tolerance test; VO₂max, maximum oxygen uptake.
volumes were measured using a Harvard dry gas meter (Harvard Apparatus Ltd., Edenbridge, UK). A finger prick capillary blood sample was taken 4 min after the end of the protocol and plasma lactate concentration measured. Participants attained VO₂max if at least two of the following criteria were met: 1) plateau in VO₂ of < 2.1 ml·kg⁻¹·min⁻¹ between the last two air collections, 2) plasma lactate > 8 mmol·L⁻¹, or a respiratory exchange ratio (RER) ≥ 1.15 (Howley et al., 1995). All participants achieved VO₂max. Participants VO₂max was converted in MET (i.e., maxMET) to allow intensity matching of achieved V·O₂max. Exercise intensity for the level and downhill running was set at 60%maxMET. Exercise intensity for the level and downhill running that would provide identical intensity based on MET values. Exercise intensity for the level and downhill running was set at 60%maxMET.

**Level and Downhill Running at Matched Intensity**

For all participants, the relationship between running speed (8, 9, 10 and 11 km·hr⁻¹, 5-min bouts with 2 min rest) and energy cost was determined for level (i.e., concentric exercise, CON) and downhill (i.e., eccentric exercise, ECC) running. This linear relationship was used to calculate the speed for level and downhill running that would provide identical intensity based on MET values. The major finding of this study was that matched-intensity level and downhill running session were not different (CON: 582 ± 144, ECC: 615 ± 129N). Downhill running resulting in higher isometric force deficits (CON: 3.0 ± 6.7, ECC: 17.1 ± 7.3%, p < .01). Figures 2A and 2B show the relationship between blood glucose and blood insulin, respectively, as a function of time. During OGTTs, area-under-the-curve for plasma glucose (control: 724 ± 97, CON: 710 ± 77, ECC: 726 ± 72 mmol·L⁻¹·120 min, p = .86) and insulin (control: 24995 ± 11229, CON: 23319 ± 10417, ECC: 21842 ± 10171 pmol·L⁻¹·120 min, p = .48), peak glucose (control: 8.1 ± 1.3, CON: 7.7 ± 1.2, ECC: 7.7 ± 1.1 mmol·L⁻¹, p = .63) and peak insulin levels (control: 361 ± 188, CON: 322 ± 179, ECC: 299 ± 152 pmol·L⁻¹, p = .30) were similar.

**Oral Glucose Tolerance Test—Glucose and Insulin Measurements**

Participants consumed 75-g of glucose dissolved in water (Trutol 75, NERL Diagnostics, East Providence, RI, USA) with finger prick capillary samples taken every 15 min for 120 min. Participants remained rested in a seated position throughout the test. No lysing agent was used in the YSI analyzer, so blood plasma glucose was measured (YSI 2300 Stat Plus, Yellow Springs Instruments Co. Inc., Yellow Springs, USA). Subsequently, the sample was centrifuged (C2 Series, Centurion Scientific, Chichester, UK) at 5000 rpm for 5-min. This provided ~90 μL of plasma. Blood plasma was pipetted from the separation and frozen (−20 °C) for insulin analysis. Plasma insulin samples were measured in triplicate (~25 μL of plasma for each measurement) using a human 96-well insulin enzyme-linked immunosorbent assay (IBL international, Hamburg, Germany). The assay worked on the sandwich principle with the microtiter wells precoated with the antibody. The intensity of the color developed was proportional to the concentration of insulin with absorbance values of each well determined at 450nm with a microtiter plate reader (Tecan GENios, Männedorf, Switzerland). Multichannel pipettes were calibrated to volumes pipeted during the assay of: 25 μL, 50 μL, and 400 μL with coefficients of variation for pipette error calculated as 3.52%, 1.77%, and 1.46%, respectively.

**Statistical Analysis**

Maximal voluntary isometric force was analyzed with a two-way ANOVA with repeated measures on time. Area under the curve (AUC) for insulin and glucose were calculated using the trapezoid method (GraphPad Prism, V5.04) and expressed as pmol·L⁻¹·120 min and mmol·L⁻¹·120 min, respectively. Differences between AUC for glucose and insulin were analyzed with an one-way ANOVA and Bonferroni post hoc analysis. At the end of each 8-min bout during the level and downhill running protocol (i.e., 5 recordings), oxygen consumption, heart rate, and respiratory exchange ratio were averaged and analyzed with a paired sample t test. Physiological data of one subject was excluded due to abnormal high ventilatory equivalent values (>50) during the downhill running session. Data normality assumptions were assessed using Kolmogorov-Smirnov test. Statistical significance was determined with an alpha level of p < .05. All statistical analyses were completed using SPSS 12.0 (SPSS, Chicago, IL). Data are presented as means± SD except otherwise indicated.

**Results**

Downhill running speed was 42% higher (CON: 9.7 ± 2.1, ECC: 13.8 ± 3.2 km·hr⁻¹, p < .01). Running protocols had similar VO₂ (CON: 2.28 ± 0.51, ECC: 2.20 ± 0.34 L·min⁻¹, n = 9, p = .59), respiratory exchange ratio (CON: 0.89 ± 0.03, ECC: 0.89 ± 0.05, n = 9, p = .79) and heart rates (CON: 143 ± 16; ECC: 147 ± 19 b·min⁻¹, n = 9, p = .20) indicating matched intensity and metabolic demands. The baseline values for isometric force before the matched-intensity level and downhill running session were not different (CON: 582 ± 144, ECC: 615 ± 129N). Downhill running resulting in higher isometric force deficits (CON: 3.0 ± 6.7, ECC: 17.1 ± 7.3%, p < .01). Figures 2A and 2B show the relationship between blood glucose and blood insulin, respectively, as a function of time. During OGTTs, area-under-the-curve for plasma glucose (control: 724 ± 97, CON: 710 ± 77, ECC: 726 ± 72 mmol·L⁻¹·120 min, p = .86) and insulin (control: 24995 ± 11229, CON: 23319 ± 10417, ECC: 21842 ± 10171 pmol·L⁻¹·120 min, p = .48), peak glucose (control: 8.1 ± 1.3, CON: 7.7 ± 1.2, ECC: 7.7 ± 1.1 mmol·L⁻¹, p = .63) and peak insulin levels (control: 361 ± 188, CON: 322 ± 179, ECC: 299 ± 152 pmol·L⁻¹, p = .30) were similar.

**Discussion**

The major finding of this study was that matched-intensity concentric exercise (i.e., level running) and eccentric exercise (i.e., downhill running) did not alter the glucose and insulin responses from an OGTT immediately following exercise compared with the resting condition. Because the oxygen demands of downhill running were lower than level running at similar speeds, matching of the intensity of the level and downhill running provided higher downhill running speeds. Downhill running at this speed resulted in substantial isometric force deficits of the m. quadriceps femoris (17.1%), which were comparable...
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To other studies (~22%, males and females, 5 × 8 min bouts at 11.3 km·hr⁻¹ and −12% gradient) (Eston et al., 2000); (21%, males, 30 min downhill run at 12.4 km·hr⁻¹ and -15% gradient) (Chen et al., 2007); (17%, females, 6 × 5 min bouts at 13 km·hr⁻¹ and −12% gradient) (Green et al. 2010). For both running protocols, the force deficits were measured immediately postexercise, suggesting that fatigue from the exercise may have caused some of the force deficits. However, our protocol of concentric exercise did not have an effect on the ability to produce maximal force suggesting that the force deficits by eccentric exercise can be considered to be primarily due to muscle damage. It needs to be noted, however, that we do not know the effects of fatigue by concentric exercise at the running speeds at which the downhill running protocol was completed.

As far as we know, our study was the first to examine the response to an OGTT immediately following an intensity-matched protocol of concentric and eccentric exercise. Many studies have provided evidence for the delayed response of insulin resistance with increased glucose and insulin area-under-the-curves 48 hr after downhill running. Both studies used the OGTT as used in the current study. Using euglycemic–hyperinsulinemic clamps, insulin resistance was observed 48 hr after matched intensity (60%) downhill (~17% gradient) and level running in healthy untrained individuals (Kirwan et al. 1992). It should be noted, however, that studies using insulin clamps can provide direct measures of insulin sensitivity (and resistance) whereas studies using OGTTs provide information on glucose tolerance and insulin responses. An OGTT cannot provide information on whole body glucose clearance (Radziuk & Lickley, 1985), a well-established physiological concept that requires information on whole body glucose uptake rate and arterial plasma glucose concentration (Dela et al., 1999).

Insulin resistance will affect glucose transport into muscle cells. Glucose is transported across the sarcolemma of muscle cells by GLUT4, which is translocated from intracellular vesicles to the sarcolemma. GLUT4 translocation is sensitive for muscle contraction and insulin and essential for postexercise glycogen resynthesis. Eccentric exercise, however, is known to result in impaired glycogen resynthesis 10 days later (O’Reilly et al., 1987). The observation of normal protein GLUT4 levels immediately after eccentric exercise in white and red gastrocnemius muscle of male Wistar rats (Asp et al., 1995) may be in line with our observation of normal glucose tolerance responses. Interestingly, GLUT4 content was normal post marathon in well-trained individuals with decreased glycogen levels 2 days following the race suggesting other factors than GLUT4 levels to be involved in glycogen synthesis (Asp et al., 1997). However, this may indicate that after eccentric exercise, a window of opportunity exists for nutrient intake to facilitate glycogen resynthesis (Doyle et al., 1993). Our study was unique for examination of glucose tolerance immediately postexercise with most studies allowing some hours of recovery before establishing postexercise effects (Thong et al., 2002; Wojtaszewski et al., 2000). However, in our study, no improved glucose tolerance by nondamaging exercise was observed in contrast to previous work using euglycemic-hyperinsulinemic clamping (e.g., Thorell et al., 1999). Such contrasts may be due to differences in those techniques examining insulin sensitivity and in exercise protocols. Although previous work has clearly established reduced glucose tolerance 48 hr after muscle-damaging exercise, future work would focus on how long there is normal glucose tolerance and insulin responses following unaccustomed eccentric exercise. Widrick et al. (1992) showed similar muscle glycogen concentrations 6 hr after nondamaging and damaging exercise. Therefore, information on the time period of normal glucose tolerance after exercise would allow researchers to investigate whether a targeted nutrient intake following short-duration eccentric exercise can induce glycogen resynthesis before impairment of glucose tolerance by insulin and

![Figure 2](image-url)

Figure 2 — (A): Glucose and (B) insulin response to an oral glucose tolerance test at rest (control) and immediately after level running and downhill running. Data are mean ± SEM.
impaired muscle glycogen synthesis (Widrick et al., 1992). Limitations of the current study were that glucose tolerance and insulin responses were only investigated after muscle-damaging exercise in leg muscles, e.g., m. quadriceps femoris, a muscle group less susceptible for injury compared with elbow flexor muscles. In addition, an intensity was investigated that was relatively mild in causing muscle damage. However, it was concluded that unaccustomed damaging eccentric exercise (e.g., downhill treadmill running) does not immediately result in impaired glucose tolerance and insulin responses to an OGTT. This information may have implications for the supplementation practice of athletes in the recovery phase after having performed damage-inducing eccentric exercise.

References


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