Insulin sensitivity not modulated 24 to 78 h after acute resistance exercise in type 2 diabetes patients

Resistance exercise is recommended as part of the exercise guidelines to prevent and manage type 2 diabetes (T2D), however, the frequency of exercise required to improve glycaemic control and insulin sensitivity is not clear. We recruited and tested 10 individuals with T2D by collecting a fasting blood sample immediately prior to, a whole-body moderate–high intensity resistance exercise session, and 24, 48 and 72 h afterwards. No changes to estimates of insulin sensitivity (HOMA2), glucose or insulin were observed using a repeated measures analysis of variance (p > 0.05). Further, there were no changes observed to markers of inflammation at 24 h following the resistance exercise session (p > 0.05). These findings suggest that insulin sensitivity is not acutely modified, positively or negatively, at 24, 48 or 72 h after a bout of resistance exercise. Nor are markers of inflammation altered during this time frame in a way that could cause transient insulin resistance.

Keywords: inflammation, resistance training, training frequency, type 2 diabetes

Introduction

Resistance exercise has become a focus for preventing and managing type 2 diabetes (T2D), as a consequence of studies reporting improvements to glucose levels and insulin sensitivity [1,2]. Insulin sensitivity or glucose tolerance is improved up to 24 h following a single resistance exercise session in T2D patients [3,4], with higher intensities providing increased benefits. Consequently, guidelines now advise the completion of resistance exercise [5]. However, the required frequency to maintain or augment these improvements remains unclear [6] and further research to elucidate this is required.

Therefore, the aim of this study was to investigate the insulin sensitivity and inflammatory cytokine response over 3 days following a single session of moderate–high intensity resistance exercise in middle-aged adults with T2D.

Materials and Methods

Participants

Ten inactive (not meeting physical activity guidelines) individuals with T2D (males N = 6, females N = 4) with a mean ± standard deviation age of 61.8 ± 7.2 years, height of 169.7 ± 7.7 cm and body mass of 86.8 ± 13.4 kg volunteered and provided written informed consent. Ethical approval was granted from the Human Research Ethics Committees of RMIT University and Austin Health. This study conformed to the principles of the Declaration of Helsinki. Inclusion criteria were: aged 40–69 years, at least 6 months of no resistance training and taking a stable dose of medications (if they were taking medications). Exclusion criteria included: recent coronary event or established heart disease, any medical condition that contraindicated resistance exercise, and unable to understand English or follow instructions.

Study Design

On their first visit to the exercise facility, participants’ height and body mass were measured and a fasting blood sample collected before consuming a standardized breakfast (toast and juice). They were then familiarized with the exercise equipment and completed one repetition maximum (1RM) testing on all exercises included in the resistance exercise session (bench press, 45° leg press, shoulder press, 45° calf raises and lateral pull down).

After a minimum 7-day wash-out period, participants returned and provided a fasting blood sample prior to consuming the standardized breakfast. Participants completed the resistance exercise session (3 sets of 10 repetitions for each of the five exercises at 45, 60 and 75% of 1RM) [7] and returned to provide a fasted blood sample on each of the next 3 days. Physical activity and diet were measured and assessed as previously reported [7].

Blood Analysis

Aliquots of serum and plasma were frozen at −80 °C for later analysis of glucose, insulin, adiponectin, leptin, interleukin-6 (IL)-6 and tumour necrosis factor-alpha (TNF)-α in duplicate. Glucose was analyzed using the YSI 2300 StatPlus (Yellow Springs, OH, USA; CV < 1%). Defined ELISA kits were used for analysis of insulin, adiponectin, leptin (Millipore Corporation, Billerica, MA, USA), IL-6 and TNF-α (R&D...
Figure 1. Response of fasting glucose (A), fasting insulin (B), HOMA2 insulin resistance (C) and HOMA2 insulin sensitivity (D) to a single session of resistance exercise. 0 h is immediately before resistance exercise and 24, 48 and 72 h are all following resistance exercise. Bars are means with the 95% confidence interval.

Systems, Minneapolis, MN, USA), respectively, with CVs of 8.1, 2.9, 2.8, 3.2 and 2.7%. The limits of detection for adiponectin, leptin, IL-6 and TNF-α were 1.56, 0.5 ng/ml and 0.7, 1.6 pg/ml, respectively. Insulin sensitivity (%S) and resistance (HOMA2-IR) were determined using the updated homeostasis modeling assessment (HOMA2) equations [8].

Statistical Analysis

All data were analyzed using SPSS version 18 for Windows (IBM, Armonk, NY, USA) with significance set at p = 0.05. Covariate outcomes, physical activity and nutritional content, were assessed by multivariate analysis of variance (MANOVA). Repeated measures analyses of variance (ANOVA) were conducted for primary outcomes; fasting glucose, fasting insulin, %S and HOMA2-IR to assess the response over 72 h. Repeated measures ANOVAS were also conducted for secondary outcomes; adiponectin, leptin, IL-6 and TNF-α to assess the response 24 h following exercise. Data are presented as means ± standard deviation or means [95% confidence intervals (CI)] unless otherwise stated. Effect sizes for primary outcomes were estimated to range between 0.35 and 0.5 from published literature [3,4] and were used for a priori power calculation. To achieve statistical significance at α = 0.05 with 80% power, 7–13 participants were required.

Missing data at 24 h after exercise (one blood sample was unable to be collected) and 72 h after exercise [no serum obtained due to technical difficulties (N = 1)] were substituted by bringing the last known value for that time-point forward [9]. Therefore, N = 9 for the secondary outcomes of markers of inflammation.

Results

Participants had been diagnosed with T2D for an average (range) of 7.5 (0.25–15.0) years, had good glycaemic control (HbA1c = 6.8 ± 0.6%) and glucose (7.6 ± 1.6 mmol l⁻¹), but insulin concentrations were high (137.9 ± 82.5 pmol l⁻¹). Nine individuals were taking oral hypoglycaemic medications, six metformin monotherapy, two metformin combined with a glitazone and one metformin and a glitazone. Additional medications were prescribed as follows: statins (N = 9), aspirin (N = 4), antihypertensives (N = 4), proton-pump inhibitors (N = 3), diuretic (N = 1), antidepressants (N = 1) and antiuricemic agents (N = 1). One individual was currently smoking, but refrained from smoking during the fasting period. There were no statistical differences in total energy consumption (p = 0.31) or physical activity (p = 0.19) during the follow-up period.

For the primary analysis, no statistically significant response for any variable was detected (p > 0.05; figure 1). No adiponectin was detected in one individual either pre- or postexercise. Leptin was detected in 100% of samples. Interleukin-6 was detected in 100% of samples pre-exercise but only 78% samples post-exercise. TNF-α was detected pre- and postexercise in three participants, only pre-exercise in one and postexercise in another. For the secondary analysis, there was no response to exercise (p > 0.05) in any variable (Table 1).
Conclusion
In contrast to previous findings [3,4] estimating insulin sensitivity up to 24 h after exercise, we did not find changes to insulin sensitivity 24–78 h following a single session of moderate–high intensity resistance exercise. The contrast in analysis methods for insulin sensitivity estimated using HOMA2 equations compared to others using oral glucose tolerance tests (OGTT) and the timing of completing the outcome measures may have contributed to these findings along with differences between the populations. However, recent suggestions that OGTT may not provide an accurate estimation of insulin sensitivity in T2D patients [10] suggests caution when interpreting previous findings. Resistance exercise has recently been reported to provide a similar 24-h continuous glucose response to aerobic exercise [11], although the resistance exercise bout in this study only focused on the legs and was not whole-body exercise as recommended [5].

Resistance exercise has been theorized to lead to transient insulin resistance through increased inflammatory profiles caused by exercise-related muscle damage [12]. Although we did not measure muscle damage directly, our findings of no change to IL-6, TNF-α or leptin, suggest that a lack of insulin sensitivity response is not due to increased inflammatory profiles. Additionally, adiponectin is thought to provide an early indication of changes to insulin sensitivity, and while we found no statistically significant response, a 23% reduction in adiponectin may indicate some short-term impairment of insulin sensitivity following a single resistance exercise session.

Despite previous reports of improved insulin sensitivity [3,4] and glycaemic control [11] within 24 h of a resistance exercise session in T2D patients, we found that insulin sensitivity was not modulated over subsequent days following a similar exercise protocol. In conclusion, these findings suggest that a single session of resistance exercise as measured in this study does not improve nor impair insulin sensitivity in inactive middle-aged individuals with T2D. Therefore, it may be that resistance exercise should be completed on a daily basis, at least initially, until ongoing improvements to insulin sensitivity can be observed. Whether continuous glucose profiles change over subsequent days is currently unclear.

**Table 1.** Response of markers of inflammation to a single resistance exercise session (mean ± standard deviation).  

<table>
<thead>
<tr>
<th>Marker</th>
<th>Pre-exercise</th>
<th>24 h postexercise</th>
<th>p value</th>
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<tbody>
<tr>
<td>Adiponectin (ng ml⁻¹)</td>
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<tr>
<td>N = 8</td>
<td>6.1 ± 6.6</td>
<td>4.7 ± 2.9</td>
<td>0.50</td>
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<tr>
<td>Leptin (ng ml⁻¹)</td>
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<tr>
<td>N = 9</td>
<td>23.1 ± 16.8</td>
<td>25.2 ± 14.3</td>
<td>0.37</td>
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<td>IL-6 (pg ml⁻¹)</td>
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<td></td>
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<tr>
<td>N = 7</td>
<td>5.8 ± 1.8</td>
<td>5.9 ± 2.3</td>
<td>0.75</td>
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<tr>
<td>TNF-α (pg ml⁻¹)</td>
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<tr>
<td>N = 3</td>
<td>2.6 ± 0.7</td>
<td>2.8 ± 0.7</td>
<td>0.80</td>
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IL-6, interleukin-6; TNF-α, tumour necrosis factor-alpha.

**References**