The effect of short duration resistance training on insulin sensitivity and muscle adaptations in overweight men

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New findings

1. What is the central question of this study?
What is the timecourse of muscular adaptations to short duration resistance exercise training.

2. What is the main finding and its importance?
Short duration resistance training results in early and progressive increases in muscle mass and function and an increase in insulin sensitivity.

Abstract

Objectives
The aim of the current study was to investigate the effects of six weeks of resistance exercise training, compromised of one set of each exercise to voluntary failure, on i) insulin sensitivity and ii) the time-course of adaptations in muscle strength/mass.

Methods
Ten overweight men (age: 36 ± 8 years; height 175 ± 9 cm; weight 89 ± 14 kg; BMI 29 ± 3 kg.m²) were recruited to the study. Resistance exercise training involved three sessions per week for six weeks. Each session involved one set, of nine exercises, performed at 80% of 1 repetition maximum (1RM) to volitional failure. Sessions lasted 15-20 minutes. Oral glucose tolerance tests were performed at baseline and post intervention. Vastus lateralis muscle thickness, knee extensor maximal isometric torque and rate of torque development (RTD – measured between 0-50ms, 0-100ms, 0-200ms and 0-300ms) were measured at baseline, each week of the intervention, and after the intervention.

Results
Resistance training resulted in a 16.3 ± 18.7% (P<0.05) increase in insulin sensitivity (Cederholm index). Muscle thickness, maximal isometric torque and 1RM increased with training ending the intervention 26.9 ± 8.3%, 10.3 ± 2.5%, 18.3 ± 4.5 higher (P<0.05 for both) than baseline, respectively. RTD50ms and 100ms, but not RTD200ms and 300ms, increased (P<0.05) over the intervention period.

Conclusions
Six weeks of single set resistance exercise to failure results in improvements in insulin sensitivity and increases in muscle size and strength in young overweight men.

1.1 Introduction
Skeletal muscle has an often underappreciated role in health (Wolfe, 2006) with low muscle strength being linked with increased risk of a range of poor health outcomes, including all-cause, cardiovascular disease (CVD), cancer and respiratory disease mortality (Celis-Morales et al., 2018). Similarly a low muscle strength has been shown to be associated with higher type 2 diabetes incidence. Findings are more equivocal for low muscle mass with some studies finding an association with type 2 diabetes incidence whilst others find no such association (Li et al., 2016; Hong et al., 2017). Furthermore, the increased risk of CVD mortality that is seen in people with type 2 diabetes, is attenuated in those with high grip strength (Celis-Morales et al., 2017). This suggests that the maintenance of muscle strength/mass is important for metabolic health. Resistance exercise – the most efficacious method to increase muscle strength/mass – has been found to consistently improve insulin sensitivity in people with type 2 diabetes (Umpierre et al., 2011) and, although there are fewer studies, the available data indicates a similar effect in healthy adults (Flack et al., 2011; Conn et al., 2014).
It is, therefore, not surprising that the current physical activity recommendations include advice for adults to perform muscle strengthening activities on two days per week (WHO, 2011). When recommending resistance exercise training there are many variables to be taken into consideration, including the number of sets, repetitions and load. The American College of Sports Medicine (ACSM) recommend that for novice lifters resistance training 2-3 days per week with 1-3 sets of 8-12 repetitions with a training load of 60-85% one-repetition maximum (1RM) promotes muscular hypertrophy and can maximize strength (Ratamess et al., 2009). The strength of the evidence in support of these recommendations has, however, been challenged by several researchers (e.g. Carpinelli, 2009; Fisher et al., 2011a).

Indeed it has been demonstrated recently that if exercise is performed to volitional failure then gains in muscle mass and strength are similar regardless of the load at which exercise is performed (Mitchell et al., 2012; Morton et al., 2016). The early time-course of adaptations to such exercise remains to be established. Interestingly it was also found that there was no difference in changes in muscle mass/strength comparing one and three sets to failure of each exercise (Mitchell et al., 2012). This may have important public health implications as the time commitment of exercise can be reduced, and it is well established that time is a major barrier to exercise participation (Trost et al., 2002), but the exercise remain efficacious. However, it remains to be established if this shorter duration exercise can also improve insulin sensitivity.

The aims of the current study, therefore, were to investigate the effects of 6 weeks of resistance exercise training, compromised of 1 set of each exercise to voluntary failure, on i) insulin sensitivity and ii) the time-course of adaptations in muscle strength/mass, in overweight men.
1.2 Materials and methods

1.2.1 Ethical Approval

Participants provided written informed consent and the study was approved by the Ethics Committee of the College of Medical Veterinary and Life Sciences at the University of Glasgow (Project Number 200160094), and adhered to the declaration of Helsinki except for registration in a database.

1.2.2 Participants

Ten men (age: 36 ± 8 years; height 175 ± 9 cm; weight 89 ± 14 kg; BMI 29 ± 3 kg.m$^2$) volunteered to participate in the current study. All participants had BMI >25 kg.m$^2$, participated in less than 2 h per week of moderate/high intensity aerobic exercise, undertook no resistance training, and were normotensive, free from injury, metabolic or cardiovascular disease.

1.2.3 Study protocol

During a baseline visit, after an overnight fast, participants’ body composition (air displacement plethysmography), vastus lateralis muscle thickness (ultrasound) and knee extensor maximal isometric torque (during a maximal voluntary contraction (MVC)) were measured and an oral glucose tolerance test (OGTT) undertaken (see below for details). A 7-day food diary was then used to measure habitual dietary intake. Participants 1RM was then determined for the following exercises: leg press, bench press, leg extension, shoulder press, leg flexion, seated row, calf raise, latissimus pulldown and biceps curl (M2 machine, Inspire Fitness ®, Corona, CA, USA). Following this, participants began the 6-week resistance training programme. The resistance training intervention comprised three sessions per week, with each session consisting of one set of each of the aforementioned nine exercises at 80%1RM to volitional failure. Participants 1RM for each exercise was re-measured at week 3.
and the load adjusted accordingly. Sessions were carried out on a Monday, Wednesday and Friday at a time suitable for the participant, with each session lasting approximately 15-20 minutes. Prior to each Friday session, vastus lateralis muscle thickness and knee extensor maximal isometric torque were measured.

Three days after the final training session, after an overnight fast, a second OGTT was performed and body composition, vastus lateralis muscle thickness, knee extensor maximal isometric torque measured. Measurements were taken at the same time of the day by the same investigator. The participants were asked to refrain from any other resistance exercise training for the duration of the study and to maintain their usual physical activity and dietary habits.

1.2.4 Procedures

Vastus Lateralis Muscle thickness: Muscle thickness was assessed non-invasively via ultrasound at baseline and post-training. Ultrasound is a valid and reliable method used to assess changes in muscular thickness and cross-sectional area (Franchi et al., 2018). Transverse images of the right vastus lateralis muscles for all participants were made with a portable brightness mode (B-mode) ultrasound-imaging device (Echoblastor 128 Ext, Telemed Ltd®, Lithuania) using an 7.5Hz linear array transducer. Prior to image collection, anatomical locations were identified and marked with a pen. Measurements were taken 70% of the distance between the lateral condyle of the femur and greater trochanter. Great care was taken to ensure the same limb positioning and consistent, minimal pressure, limiting compression of the muscle. In addition, to increase acoustic coupling and minimize near field artefacts, a water-soluble transmission gel was applied to the skin. All ultrasound images were digitized and analyzed with ImageJ software ver. 1.37 (NIH, Bethesda, Maryland).
Muscle thickness was measured from the subcutaneous adipose tissue-muscle interface to the muscle-bone interface. All measurements were made by the same investigator (IAD) pre- and post-intervention.

*Knee extensor maximal isometric torque and rate of torque development (RTD):* Maximal isometric torque of the right knee extensor muscles was measured during an MVC with the participants seated securely with the use of seatbelts and a knee angle of 90°. Participants were asked to contract maximally for approximately 5s with contractions repeated ≥3 times with the highest values used for subsequent analysis. Force was recorded throughout the contraction with a load cell (Biometrics, Newport, UK). The rate of torque development (RTD) was calculated from the MVC data. The torque at time instants 0, 50, 100, 200 and 300ms was determined and the RTD for each time interval calculated by subtracting from the torque at each time point the torque at 0 and dividing by the time interval (Aagaard et al., 2002).

*Oral glucose tolerance test:* A cannula was inserted into an antecubital vein and a baseline blood sample was collected. Participants then consumed 75g of glucose made up to 300mL with water and further blood samples were collected after 30, 60, 90 and 120 min. Blood samples were analysed for glucose and insulin using a clinically validated analysers.

*Body composition:* Body fat mass and lean mass were measured via an air-displacement plethysmograph (BOD-POD, Cosmed, Shepperton, UK) according to the manufacturer’s guidelines.
Statistical analyses: Time-averaged area-under the curve (AUC) was calculated, using the trapezium rule, for glucose and insulin responses during the OGTT. Glucose and insulin data were also used to estimate insulin sensitivity via the Cederholm index (Cederholm & Wibell, 1990).

\[
\text{Cederholm index} = \frac{75000 + (G_0 - G_{120}) \times 180 \times 0.19 \times \text{BM}}{120 \times \text{G}_{\text{mean}} \times \log(\text{I}_{\text{mean}})}
\]

Where BM is body mass (kg), \(G_0\) and \(G_{120}\) are plasma glucose concentrations at 0 and 120 min (mmol.L\(^{-1}\)), and \(\text{I}_{\text{mean}}\) and \(\text{G}_{\text{mean}}\) are the mean insulin (mU.L\(^{-1}\)) and glucose (mmol.L\(^{-1}\)) concentrations during the OGTT.

Glucose AUC, insulin AUC, Cederholm Index, body composition and 1RM were compared (baseline vs post-training) via paired t-tests. Time-course data (weekly vastus lateralis muscle thickness and knee extensor maximal isometric torque) were compared over time via a repeated measures analysis of variance (ANOVA). Where a main effect was observed in the ANOVA weekly values were compared to baseline values via post-hoc Tukey tests. Data are reported as mean ± standard deviation (SD) unless otherwise stated and statistical significance was set \textit{a priori} at \(p \leq 0.05\). GraphPad Prism software (Version 5) was used for all statistical analyses.
1.3 Results

The habitual energy intake of participants was 2130 ± 410 kcal/day, comprising 82 ± 11 g/day protein, 260 ± 69 g/day carbohydrate and 86 ± 19 g/day fat. Body fat mass was lower (Baseline: 26 ± 13 kg, post-intervention: 24 ± 13 kg, P<0.05) and lean mass higher (63 ± 8 vs 65 ± 7 kg, P<0.05) post-intervention compared to baseline. The 1RM for all nine exercises was higher (P<0.05) post-intervention compared to baseline measures (Table 1). Overall the sum of individual 1RM was 18.3 ± 4.5% higher after the intervention, when compared with baseline.

The time-course analysis revealed main effects (P<0.05) of time for knee extensor maximal isometric torque and vastus lateralis muscle thickness (Figure 1). Knee extensor maximal isometric torque was 26.9 ± 8.3% higher and vastus lateralis muscle thickness 10.3 ± 2.5 % higher after the intervention compared with baseline. Post-hoc analysis revealed that knee extensor maximal isometric torque and vastus lateralis muscle thickness were higher, compared to baseline at weeks 2, 3, 4, 5, 6 and post-intervention. Main effects of time (P<0.05) were seen for RTD50 and 100, but not RTD200 and 300, with post-hoc analysis finding no significant differences between the time points (Figure 2).

After the intervention the time-averaged glucose and insulin AUC were lower (7.4 ± 12.8% and 12.0 ± 17.0% respectively, both P<0.05) relative to at baseline (Figure 3). At baseline the Cederholm index was 61.6 ± 18.0 mg.l².mmol⁻¹.mU⁻¹.min⁻¹ and this increased to 71.3 ± 22.9 mg.l².mmol⁻¹.mU⁻¹.min⁻¹ after the intervention (P<0.05), an increase of 16.3 ± 18.7%.
1.4 Discussion

The current study has demonstrated that six weeks of resistance exercise, comprising one set to volitional failure of nine exercises – taking 15-20 min per session – undertaken three times per week resulted in a 16% improvement in insulin sensitivity in healthy overweight men. On top of this, increases in muscle strength, size and RTD50 and 100 were also observed. Whilst previous work has shown that single set resistance exercise to failure can increase muscle strength (Mitchell et al., 2012) the current study is the first study to demonstrate that such simple exercise, with a weekly time commitment of less than one hour, can increase insulin sensitivity in overweight men and to also demonstrate the time-course of adaptations in muscle strength and size.

Previous work has demonstrated that resistance exercise can improve insulin sensitivity in people with type 2 diabetes (Umpierre et al., 2011) and, although there are fewer studies, the available data indicates a similar effect in healthy adults (Flack et al., 2011; Conn et al., 2014). The current study agrees with these findings and has added to the body of evidence in healthy adults by showing that insulin sensitivity increases by ~16%. Importantly, the exercise protocol in present study where participants performed a single set to volitional failure for each exercise, with the sessions lasting 15-20 minutes, involved a much smaller time-commitment than the majority of previous resistance training interventions which generally involved multiple (2-4) sets of exercise for each muscle group (Flack et al., 2011; Umpierre et al., 2011; Conn et al., 2014) Thus, the present resistance training intervention may be pragmatically more appealing to many. Further study is needed investigate the effects a similar time-efficient resistance exercise training protocol in higher risk groups or those already with type 2 diabetes. A key limitation of the present study is that we have only
included men and whilst we have no reason to think responses would differ in women, this remains to be established.

The present data adds to the evidence base for the health benefits of resistance exercise, which includes a reduction in blood pressure, improvements in blood lipids and an association with lower mortality (Cornelissen et al., 2011; Stamatakis et al., 2018). Thus, it is clear why the physical activity recommendations include muscle strengthening activities (WHO, 2011). It is surprising, however, that participation in muscle strengthening activities is so low. Indeed analysis in Scotland has shown that only 31% of men and 24% of women met the muscle strengthening guideline, which is around half the numbers of those that meet the guidelines for aerobic physical activity (Strain et al., 2016). Although the reasons for this are not clear the reported barriers to participation in resistance exercise training are broadly similar to those reported for general physical activity e.g. (Trost et al., 2002; Burton et al., 2017), although there are some specific barriers to resistance exercise (e.g. fear of looking too muscular and perceived risk of a heart attack, stroke or death). Time, as with for general physical activity, is cited as a major barrier to resistance exercise training participation and the current study, by employing a single set of exercise, has shown that a relatively time-efficient form of resistance exercise training remains effective at improving insulin sensitivity and increasing muscle size and function. Together with previous work (Burd et al., 2010; Fisher et al., 2011; Mitchell et al., 2012; Morton et al., 2016) this data indicates that the current, and somewhat complex, recommendations (Ratamess et al., 2009) for resistance exercise could be changed to provide clear and simple advice that people should perform a single set to failure at a load acceptable to them.
Another novel aspect of the current study is that we have investigated the early time-course of adaptations in muscle size and strength, with measures made on a weekly basis, during resistance exercise training. Similar work in young healthy men and using a different resistance exercise protocol (6 weeks of training (6 * 8 repetitions at 75%1RM) 3 times per week) measured muscle strength every 10-11 days, and vastus lateralis muscle thickness and muscle protein synthesis every 3 weeks (Brook et al., 2015). Whilst Brook et al found that strength increases progressively over the 6 weeks, muscle thickness and muscle protein synthesis were only increased during the first, but not the second, half of the intervention. The authors, therefore, concluded that hypertrophy predominates in the early part of resistance exercise training and then after ~3 weeks this response wanes. The current study, however, disagrees with this assertion with muscle size and strength increasing progressively during the 6-week training period. This is more in line with the findings of Damas and colleagues who found hypertrophy from 3-10 weeks of resistance exercise training (3 sets, 9-12 repetitions per set with load adjusted to maintain this repetition range and each set to failure) in young healthy men, although no hypertrophy was evident in the first 3 weeks of training. The differences between these studies may relate to the participants studied, methods and/or the resistance exercise training intervention employed but we are currently unable to uncover the precise reasons. This is also the first study to measured RTD after such exercise and we found that RTD50 and 100, but not RTD200 and 300, increased over the exercise intervention. Previous work has found that longer term more (14 weeks) traditional resistance exercise can increase RTD 50, 100, 200 and 300 (Aagaard et al., 2002). It may be that a longer duration of resistance training to failure would be required to see such increases.

The current study is not without limitations. Whilst we selected overweight individuals for this study as they were more likely to be a population who would benefit from such exercise.
The participants recruited to the current study, were however, all relatively insulin sensitive and so whether these result hold true in a more “at risk” population remains to be determined. We hypothesise this would be the case as more traditional resistance exercise regimens have been shown to improve insulin sensitivity in people with insulin resistance/type 2 diabetes (Umpierre et al., 2011). On top of this the current study did not include a control arm and so the true magnitude of the effect of resistance exercise may differ from that currently reported here. A further large scale randomised controlled trial is, therefore, needed to confirm these findings.

In conclusion, the current study has shown that 6 weeks of single set resistance exercise to failure results in improvements in insulin sensitivity and progressive increases in muscle size and strength in young overweight men. Such exercise, which is of shorter duration to the more traditional and recommended multiple set resistance exercise training, may be a useful tool to improve muscle and metabolic health.
Funding

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Competing Interests

The authors have no conflicts of interest to declare.

Author Contributions

Conception or design of the work - ADI, SRG. Acquisition, analysis, or interpretation of data for the work - ADI, FFAA, JW, LJ, JMRG, SRG. Drafting of the work or revising it critically for important intellectual content - All Authors. Approved the final version of the manuscript - All Authors. Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - All Authors. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.


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’ S CORNER Physical Activity Advice Only or Structured With HbA 1c Levels in Type 2 Diabetes. *JAMA* 306, 607–610.


Figure captions

Figure 1. Knee extensor maximal isometric torque (A) and vastus lateralis (B) thickness time-course of adaptations in response to six weeks of resistance exercise training. Data are presented as mean (SD) * denotes a significant (P<0.05) difference from baseline values.
Figure 2. Knee extensor RTD time-course of adaptations in response to six weeks of resistance exercise training. Data are presented as mean (SD).
Figure 3. Plasma insulin (A) and glucose (B) concentrations and time-averaged insulin (C) and glucose (D) responses during an oral glucose tolerance test, before and after six weeks of resistance exercise training.

Data are presented as mean (SD) * denotes a significant (P<0.05) difference from baseline values.
Table 1. One-repetition maximum for training exercises before and after 6 weeks of resistance exercise training. Data are mean (SD)* denotes a significant difference from baseline values.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Baseline (kg)</th>
<th>Post-intervention (kg)</th>
<th>Percentage increase (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg press 1RM (lbs)</td>
<td>89 ± 18</td>
<td>104 ± 23*</td>
<td>16 ± 5</td>
</tr>
<tr>
<td>Leg extension 1RM (lbs)</td>
<td>72 ± 14</td>
<td>85 ± 13*</td>
<td>19 ± 9</td>
</tr>
<tr>
<td>Calf press 1RM (lbs)</td>
<td>89 ± 24</td>
<td>101 ± 25*</td>
<td>16 ± 8</td>
</tr>
<tr>
<td>Leg flexion 1RM (lbs)</td>
<td>50 ± 14</td>
<td>63 ± 12*</td>
<td>26 ± 13</td>
</tr>
<tr>
<td>Chest press 1RM (lbs)</td>
<td>57 ± 209</td>
<td>69 ± 10*</td>
<td>22 ± 8</td>
</tr>
<tr>
<td>Seated row 1RM (lbs)</td>
<td>65 ± 8</td>
<td>76 ± 7*</td>
<td>17 ± 5</td>
</tr>
<tr>
<td>Lat pulldown 1RM (lbs)</td>
<td>51 ± 6</td>
<td>61 ± 8*</td>
<td>19 ± 9</td>
</tr>
<tr>
<td>Biceps curl 1RM (lbs)</td>
<td>51 ± 5</td>
<td>60 ± 5*</td>
<td>17 ± 8</td>
</tr>
<tr>
<td>Triceps curl 1RM (lbs)</td>
<td>26 ± 6</td>
<td>33 ± 6*</td>
<td>28 ± 17</td>
</tr>
<tr>
<td>Sum of individual 1RMs (lbs)</td>
<td>551 ± 76</td>
<td>651 ± 91*</td>
<td>18 ± 4</td>
</tr>
</tbody>
</table>