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

3

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18

19 **Running title:** Exercise and muscle adaptations

20 **Keywords:** Exercise, insulin sensitivity, muscle, resistance training, voluntary failure

21 **Word count:** 2794

22 **References:** 26

23 **Subject area:** Muscle physiology

24 **New findings**

25 **1. What is the central question of this study?**

26 What is the timecourse of muscular adaptations to short duration resistance exercise training.

27

28 **2. What is the main finding and its importance?**

29 Short duration resistance training results in early and progressive increases in muscle mass
30 and function and an increase in insulin sensitivity.

31 **Abstract**

32 Objectives

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

36 Methods

37 Ten overweight men (age: 36 ± 8 years; height 175 ± 9 cm; weight 89 ± 14 kg; BMI 29 ± 3
38 kg.m^2) were recruited to the study. Resistance exercise training involved three sessions per
39 week for six weeks. Each session involved one set, of nine exercises, performed at 80% of 1
40 repetition maximum (1RM) to volitional failure. Sessions lasted 15-20 minutes. Oral glucose
41 tolerance tests were performed at baseline and post intervention. Vastus lateralis muscle
42 thickness, knee extensor maximal isometric torque and rate of torque development (RTD –
43 measured between 0-50ms, 0-100ms, 0-200ms and 0-300ms) were measured at baseline, each
44 week of the intervention, and after the intervention.

45 Results

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

51 Conclusions

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

54

55

56 **1.1 Introduction**

57 Skeletal muscle has an often underappreciated role in health (Wolfe, 2006) with low muscle
58 strength being linked with increased risk of a range of poor health outcomes, including all-
59 cause, cardiovascular disease (CVD), cancer and respiratory disease mortality (Celis-Morales
60 *et al.*, 2018). Similarly a low muscle strength has been shown to be associated with higher type
61 2 diabetes incidence. Findings are more equivocal for low muscle mass with some studies
62 finding an association with type 2 diabetes incidence whilst others find no such association (Li
63 *et al.*, 2016; Hong *et al.*, 2017). Furthermore, the increased risk of CVD mortality that is seen
64 in people with type 2 diabetes, is attenuated in those with high grip strength (Celis-Morales *et*
65 *al.*, 2017). This suggests that the maintenance of muscle strength/mass is important for
66 metabolic health. Resistance exercise – the most efficacious method to increase muscle
67 strength/mass – has been found to consistently improve insulin sensitivity in people with type
68 2 diabetes (Umpierre *et al.*, 2011) and, although there are fewer studies, the available data
69 indicates a similar effect in healthy adults (Flack *et al.*, 2011; Conn *et al.*, 2014).

70

71 It is, therefore, not surprising that the current physical activity recommendations include advice
72 for adults to perform muscle strengthening activities on two days per week (WHO, 2011).
73 When recommending resistance exercise training there are many variables to be taken into
74 consideration, including the number of sets, repetitions and load. The American College of
75 Sports Medicine (ACSM) recommend that for novice lifters resistance training 2-3 days per
76 week with 1-3 sets of 8-12 repetitions with a training load of 60-85% one-repetition maximum
77 (1RM) promotes muscular hypertrophy and can maximize strength (Ratamess *et al.*, 2009).
78 The strength of the evidence in support of these recommendations has, however, been
79 challenged by several researchers (e.g. Carpinelli, 2009; Fisher *et al.*, 2011a).

80

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

90

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

94

95 **1.2 Materials and methods**

96 *1.2.1 Ethical Approval*

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

101 *1.2.2 Participants*

102 Ten men (age: 36 ± 8 years; height 175 ± 9 cm; weight 89 ± 14 kg; BMI 29 ± 3 kg.m²)
103 volunteered to participate in the current study. All participants had BMI >25 kg.m², participated
104 in less than 2 h per week of moderate/high intensity aerobic exercise, undertook no resistance
105 training, and were normotensive, free from injury, metabolic or cardiovascular disease.

106

107 *1.2.3 Study protocol*

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

120 suitable for the participant, with each session lasting approximately 15-20 minutes. Prior to
121 each Friday session, vastus lateralis muscle thickness and knee extensor maximal isometric
122 torque were measured.

123

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

129

130 ***1.2.4 Procedures***

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

145

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

155

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

160

161 *Body composition:* Body fat mass and lean mass were measured via an air-displacement
162 plethysmograph (BOD-POD, Cosmed, Shepperton, UK) according to the manufacturer's
163 guidelines.

164

165 *Statistical analyses:* Time-averaged area-under the curve (AUC) was calculated, using the
166 trapezium rule, for glucose and insulin responses during the OGTT. Glucose and insulin data
167 were also used to estimate insulin sensitivity via the Cederholm index (Cederholm & Wibell,
168 1990).

$$\text{Cederholm index} = \frac{75000 + (G_0 - G_{120}) \times 180 \times 0.19 \times \text{BM}}{120 \times G_{\text{mean}} \times \log(I_{\text{mean}})}$$

169

170 Where BM is body mass (kg), G_0 and G_{120} are plasma glucose concentrations at 0 and 120 min
171 (mmol.L^{-1}), and I_{mean} and G_{mean} are the mean insulin (mU.L^{-1}) and glucose (mmol.L^{-1})
172 concentrations during the OGTT.

173

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

181

182 **1.3 Results**

183 The habitual energy intake of participants was 2130 ± 410 kcal/day, comprising 82 ± 11 g/day
184 protein, 260 ± 69 g/day carbohydrate and 86 ± 19 g/day fat. Body fat mass was lower (Baseline:
185 26 ± 13 kg, post-intervention: 24 ± 13 kg, $P < 0.05$) and lean mass higher (63 ± 8 vs 65 ± 7 kg,
186 $P < 0.05$) post-intervention compared to baseline. The 1RM for all nine exercises was higher
187 ($P < 0.05$) post-intervention compared to baseline measures (Table 1). Overall the sum of
188 individual 1RMs was $18.3 \pm 4.5\%$ higher after the intervention, when compared with baseline.

189

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

198

199 After the intervention the time-averaged glucose and insulin AUC were lower ($7.4 \pm 12.8\%$
200 and $12.0 \pm 17.0\%$ respectively, both $P < 0.05$) relative to at baseline (Figure 3). At baseline the
201 Cederholm index was 61.6 ± 18.0 $\text{mg.l}^2.\text{mmol}^{-1}.\text{mU}^{-1}.\text{min}^{-1}$ and this increased to 71.3 ± 22.9
202 $\text{mg.l}^2.\text{mmol}^{-1}.\text{mU}^{-1}.\text{min}^{-1}$ after the intervention ($P < 0.05$), an increase of $16.3 \pm 18.7\%$.

203

204 **1.4 Discussion**

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

214

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

229

230 The present data adds to the evidence base for the health benefits of resistance exercise, which
231 includes a reduction in blood pressure, improvements in blood lipids and an association with
232 lower mortality (Cornelissen *et al.*, 2011; Stamatakis *et al.*, 2018). Thus, it is clear why the
233 physical activity recommendations include muscle strengthening activities (WHO, 2011). It is
234 surprising, however, that participation in muscle strengthening activities is so low. Indeed
235 analysis in Scotland has shown that only 31% of men and 24% of women met the muscle
236 strengthening guideline, which is around half the numbers of those that meet the guidelines for
237 aerobic physical activity (Strain *et al.*, 2016). Although the reasons for this are not clear the
238 reported barriers to participation in resistance exercise training are broadly similar to those
239 reported for general physical activity ^{e.g.} (Troost *et al.*, 2002; Burton *et al.*, 2017), although there
240 are some specific barriers to resistance exercise (e.g. fear of looking too muscular and perceived
241 risk of a heart attack, stroke or death). Time, as with for general physical activity, is cited as a
242 major barrier to resistance exercise training participation and the current study, by employing
243 a single set of exercise, has shown that a relatively time-efficient form of resistance exercise
244 training remains effective at improving insulin sensitivity and increasing muscle size and
245 function. Together with previous work (Burd *et al.*, 2010; Fisher *et al.*, 2011; Mitchell *et al.*,
246 2012; Morton *et al.*, 2016) this data indicates that the current, and somewhat complex,
247 recommendations (Ratamess *et al.*, 2009) for resistance exercise could be changed to provide
248 clear and simple advice that people should perform a single set to failure at a load acceptable
249 to them.

250

251 Another novel aspect of the current study is that we have investigated the early time-course of
252 adaptations in muscle size and strength, with measures made on a weekly basis, during
253 resistance exercise training. Similar work in young healthy men and using a different resistance

254 exercise protocol (6 weeks of training (6 * 8 repetitions at 75% 1RM) 3 times per week)
255 measured muscle strength every 10-11 days, and vastus lateralis muscle thickness and muscle
256 protein synthesis every 3 weeks (Brook *et al.*, 2015). Whilst Brook et al found that strength
257 increases progressively over the 6 weeks, muscle thickness and muscle protein synthesis were
258 only increased during the first, but not the second, half of the intervention. The authors,
259 therefore, concluded that hypertrophy predominates in the early part of resistance exercise
260 training and then after ~3 weeks this response wanes. The current study, however, disagrees
261 with this assertion with muscle size and strength increasing progressively during the 6-week
262 training period. This is more in line with the findings of Damas and colleagues²⁵ who found
263 hypertrophy from 3-10 weeks of resistance exercise training (3 sets, 9-12 repetitions per set
264 with load adjusted to maintain this repetition range and each set to failure) in young healthy
265 men, although no hypertrophy was evident in the first 3 weeks of training. The differences
266 between these studies may relate to the participants studied, methods and/or the resistance
267 exercise training intervention employed but we are currently unable to uncover the precise
268 reasons. This is also the first study to measure RTD after such exercise and we found that
269 RTD50 and 100, but not RTD200 and 300, increased over the exercise intervention. Previous
270 work has found that longer term more (14 weeks) traditional resistance exercise can increase
271 RTD 50, 100, 200 and 300 (Aagaard *et al.*, 2002). It may be that a longer duration of resistance
272 training to failure would be required to see such increases.

273

274 The current study is not without limitations. Whilst we selected overweight individuals for this
275 study as they were more likely to be a population who would benefit from such exercise. The
276 participants recruited to the current study, were however, all relatively insulin sensitive and so
277 whether these results hold true in a more “at risk” population remains to be determined. We
278 hypothesise this would be the case as more traditional resistance exercise regimens have been

279 shown to improve insulin sensitivity in people with insulin resistance/type 2 diabetes
280 (Umpierre *et al.*, 2011). On top of this the current study did not include a control arm and so
281 the true magnitude of the effect of resistance exercise may differ from that currently reported
282 here. A further large scale randomised controlled trial is, therefore, needed to confirm these
283 findings.

284

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

290

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293 Competing Interests

294 The authors have no conflicts of interest to declare.

295 Author Contributions

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

303

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384

385

386

387 **Figure captions**

388 **Figure 1. Knee extensor maximal isometric torque (A) and vastus lateralis (B) thickness**
389 **time-course of adaptations in response to six weeks of resistance exercise training.** Data
390 are presented as mean (SD) * denotes a significant ($P<0.05$) difference from baseline values.

391 **Figure 2. Knee extensor RTD time-course of adaptations in response to six weeks of**
392 **resistance exercise training.** Data are presented as mean (SD).

393 **Figure 3. Plasma insulin (A) and glucose (B) concentrations and time-averaged insulin**
394 **(C) and glucose (D) responses during an oral glucose tolerance test, before and after six**
395 **weeks of resistance exercise training.**

396 Data are presented as mean (SD) * denotes a significant ($P<0.05$) difference from baseline
397 values

398

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

402

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

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