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The effect of an acute exercise-heat stress on subsequent human thermoregulatory and sweat variables

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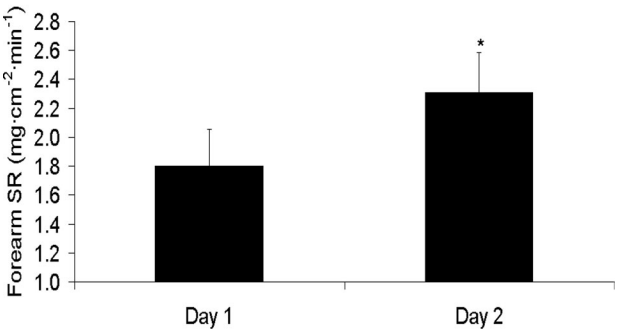
Repeated exposure to exercise in the heat has been associated with a reduction in heart rate (HR), rectal temperature (T_{re}) and skin temperature (T_{sk}), and an increase in sweat rate (SR) following 5-6 days (Shvartz *et.al.* 1973). Sweat composition also adapts, with a reduction in sweat [Na^+] found after 4 days (Allsopp *et.al.* 1998). These adaptations may occur earlier within the acclimation process, hence the present study investigated the effect of a single exercise-heat exposure on these variables.Five male subjects (age 26±7 y, mass 81.727±8.680 kg, peak oxygen uptake (VO_{2peak}) 4.1±0.6 $L.min^{-1}$, means ± S.D.) completed a familiarisation trial involving a 2 h exercise bout (42±4 % VO_{2peak}) in a hot-humid environment (38 ºC, 60 % RH) with no fluid replacement. From this, the volume of fluid required to maintain euhydration during subsequent tests was calculated. Seven days following familiarisation, the experimental trial started, consisting of two exercise heat exposures on consecutive days. The exercise and environmental conditions were those of the familiarisation, except euhydration was maintained. Whole body SR was calculated from changes in body mass and regional sweat was collected at the forearm. Sweat electrolytes were determined with the use of indirect Ion Selective Electrodes and osmolality was determined using freezing-point depression. T_{re}, T_{sk} and HR were measured every minute. Blood samples were collected from an indwelling catheter in the antecubital vein and plasma aldosterone was analysed with a commercially available radioimmunoassay kit. Percentage change in plasma volume was estimated using the method of Dill & Costill (1974).Comparison of the two euhydrated days by Student's paired t-test indicated that whole body SR increased significantly from day 1 (1.07 ±0.05 $L.h^{-1}$) to day 2 (1.16 ±0.04 $L.h^{-1}$) ($P<0.01$) as did the regional SR at the forearm ($P<0.01$) (Figure 1). There was no change in sweat [Na^+] (Figure 1), [K^+], [Cl^-], osmolality or percentage plasma volume change. Repeated measures ANOVA indicated no change in HR, T_{re}, T_{sk}, or plasma aldosterone at rest or after exercise.The present study indicates an increase in SR occurred without a concurrent increase in sweat [Na^+] following an acute exercise-heat stress. Since sweat [Na^+] is known to increase with increasing SR (Allan & Wilson 1971), our results suggest that the adaptation reflects an increased reabsorption of Na^+ in the duct of the sweat gland.

Figure 1. Forearm SR and sweat [Na^+] following 2 consecutive heat exposures.
Mean ± S.E.M. * denotes *P*<0.01.



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Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C66

Effects of altered localised temperature on spinal reflex excitability in young and older women

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The ability of the CNS to respond to pertubations through modulation of spinal reflex excitability (SRE) has been shown to be affected by ageing (Mynark & Koceja, 2002). Increased excitability levels have been demonstrated with reduced local temperature in young subjects (Oksa *et al.* 2000). This modulation could be critical for older individuals who already have impairment in postural control mechanisms (Horak *et al.* 1989). The purpose of this study is to investigate the sensitivity of the SRE to altered local temperature in both young and older women.Ten young (age 22.3 ± 3.3 years, stature 1.63 ± 0.07 m, body mass 58.4 ± 6.6 kg) and 10 older (age 72.5 ± 3.2 years, stature 1.61 ± 0.07 m, body mass 68.3 ± 9.5 kg) healthy females completed three counterbalanced trials on the same day: a control followed by a cooling and a warming trial. Legs were cooled ≅3°C from control muscle temperature (T_m) or warmed ≅3°C from control T_m. Local temperature was monitored from the measurement of T_m of the vastus lateralis of the dominant leg using a flexible thermistor. SRE was assessed by measuring the soleus H reflex response with the subjects in a seated position. Progressively increasing stimuli intensity were applied until maximum H and M waves were achieved. Data (mean ± S.D.) were analysed using a two-way (age x condition) repeated measures ANOVA with multiple paired t tests (Bonferroni correction) as a post hoc where appropriate. Alpha level was set at $P<0.05$.A significant increase in SRE was found with cooling in the young subjects only (H/M, +27.0%, Table 1). Both groups exhibited a similar lengthening of the reflex latency with cooling (Hlat, +6.0% in young and +3.8% in older,

Table 1) and shortening with warming (-4.6% in young and -4.9% in older, Table 1). The increase in SRE, with cooling, could imply a compensatory modulation in response to the potentially detrimental delay of the reflex in younger subjects which was not observed in older subjects.

Table 1. Maximum M and H wave characteristics for the young (Y) and older (O) groups with control, cooling and warming conditions

		Cooling	Control	Warming
M (mV)	Y	10.6± 2.3	10.2 ± 2.9	8.1 ± 2.1 [a,b]
	O	8.5 ± 3.1	6.8 ± 1.7	6.5 ± 2.4 [a,b]
H (mV)	Y	5.1 ± 2.5	3.7 ± 2.6	2.8 ± 2.0 [a,b]
	O†	2.0 ± 1.2	1.9 ± 1.8	1.2 ± 1.1 [b]
H/M (%)	Y	50.4 ± 23.2 [a]	36.8 ± 23.8	36.4 ±26.4
	O†	21.2 ± 9.2	25.4 ± 19.7	16.4 ±10.4 [b]
Hlat (ms)	Y	32.1 ± 2.5 [a]	30.1 ± 2.7	28.7 ± 2.3 [a,b]
	O†	35.4 ± 4.8 [a]	34.1 ± 4.1	32.4 ± 3.5 [a,b]

n=8 for both groups, †significant difference between groups, [a] significantly different to control, [b] significantly different to cooling.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C67

Effect of temperature on skeletal muscle energy turnover during dynamic knee extensor exercise in humans

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Temperature is a potent modulator of skeletal muscle contractile and metabolic properties. An increase in muscle temperature, as a result of the ambient conditions or as a consequence of metabolic heat production, may influence energy turnover during exercise. The aim of this study was to investigate the effect of muscle temperature on human skeletal muscle energy turnover during single leg knee-extensor exercise.Nine male subjects performed dynamic knee extensor exercise for 10 min at a moderate intensity (~ 85% peak workrate, 43 ± 4 W; mean ± S.E.M.) and frequency of 60 contractions per minute. Exercise was performed under conditions of normal (N) and elevated muscle temperature (ET) through passive heating. Aerobic energy turnover (muscle oxygen uptake; VO_2) was determined from measurements of thigh blood flow (constant infusion thermodilution technique) and femoral arterial-venous differences for oxygen content (a-v O_2diff). Anaerobic energy turnover was estimated from measurements of lactate release as well as muscle lactate accumulation and PCr utilisation based on analysis of muscle biopsies obtained before and after each exercise bout.Quadriceps muscle temperature at the start of exercise was 34.5 ± 0.6°C in N compared to 37.2 ± 0.2°C during ET ($P < 0.05$). Thigh VO_2 was the same between the two temperature conditions throughout exercise. However, analysis of the mono-exponential rise in VO_2 during the initial 3 min of exercise revealed a greater amplitude ($P < 0.05$) in ET compared to N (0.64 ± 0.07 vs. 0.48 ± 0.04 l min^{-1} respectively). The total release of lactate was the same between conditions. There were no differences in lactate accumulation or PCr utilisation between temperature conditions. The mean rate of energy turnover (aerobic + anaerobic) was the same between each temperature condition (198.9 ± 9.4 vs. 209.0 ± 13.3 J s^{-1} ; N and ET, respectively). These results demonstrate that passively elevating muscle temperature prior to moderate intensity single-leg knee-extensor exercise had no effect on skeletal muscle energy turnover. However, it was observed that the kinetics of the oxygen uptake response in the initial phase of exercise was influenced by muscle temperature.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

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Muscle adaptations to computer-guided strength training with eccentric overload

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This study investigated adaptations to a novel form of strength training in comparison with adaptations to conventional leg curler training. It was carried out under the standards of the Helsinki Declaration and approved by the ethics committee of the University of Heidelberg. 18 untrained male subjects performed 4 weeks of low resistance - high repetition knee extension exercise. Nine of them trained on a conventional weight resistance device (leg curler, CON/ECC group, 6x 25 repetitions/session), with loads equivalent to 70 % of the concentric one-repetition maximum (1RM) in both the concentric and eccentric phase of movement. The other 9 trained on a newly developed computer-driven device (CON/ECC-OVERLOAD group, 3x 25 repetitions/session), with the concentric load equivalent to 70 % of the concentric 1RM and the eccentric load equivalent to 70 % of the eccentric 1RM (on average 2.32 x the concentric 1 RM). Biopsies were taken from the right m. vastus lateralis and analysed for the contents of marker mRNAs (myosin heavy chain isoforms, glycolytic enzymes, myoglobin, VEGF), using real time RT-PCR quantitation. Statistical analyses were performed using 2x2 repeated measures ANOVA. The post hoc Tukey test was used for between-test differences and a Student's paired t-test for comparing pre- and post-training from each group.The training resulted in significantly increased peak torque (+5%; $p \leq 0.05$) and a tendency to increased muscle cross sectional area (+4%; $p = 0.092$) for the CON/ECC OVERLOAD group but not for the CON/ECC group. Strength endurance capacity was only significantly increased (+8%; $p < 0.05$) in the CON/ECC group. The RT-PCR analysis

yielded no significant training induced differences in any of the marker mRNAs in the biopsies of the CON/ECC group. In the CON/ECC-OVERLOAD group, significantly increased myosin heavy chain (MHC) IIa (+30%) and lactate dehydrogenase (LDH) A (+70%) mRNAs were found, together with a tendency for increased MHC IIx mRNA (average 3-fold, but large variation; $p = 0.056$) and high correlations between the changes in MHC IIx and LDH A mRNAs ($r = 0.97$, $p = 0.001$). These results indicate a shift towards a faster, more glycolytic type of gene expression pattern in the m. vasti laterales of the CON/ECC-OVERLOAD group in response to training. We suggest that the increased eccentric load in the CON/ECC-OVERLOAD training leads to distinct adaptations towards a stronger, faster muscle.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.

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Is the rate of human muscle protein synthesis fibre-type specific?

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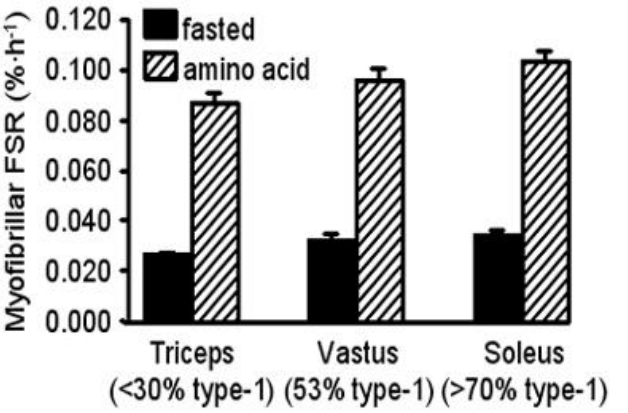
In animals the rate of muscle protein synthesis (MPS) is higher in red, oxidative muscles than white, glycolytic muscles. It is commonly assumed that the same is true in human beings. There are no data, however, from studies in human beings to support this assumption; in fact, there are indications to the opposite. First, the population variance of the rate of MPS in human vastus is small (~13%) although the fibre-type composition of the vastus ranges from ~30 - 70% type-1 in the general population. Secondly, the reported basal rates of MPS are similar among different muscles (e.g., rectus abdominus, vastus, deltoid, tibialis, multifidus) that are known to vary markedly in fibre-type composition. To investigate whether or not fibre-type composition affects human MPS we measured the rate of incorporation of [1,2-^{13}C]leucine into vastus, triceps, and soleus after an overnight fast and subsequently during infusion of a mixed amino acid solution (75 mg·kg^{-1}·h^{-1}) in six young, healthy men (27±1y; 76±4 kg; all data are means±SEM); fibre-type composition was determined in aliquots of the biopsies. Vastus was 55±4% type-1 fibres, triceps <25% and soleus >65%. The basal myofibrillar fractional synthetic rates (FSR, %·h-1) were 0.031±0.002 (vastus), 0.027±0.001 (triceps) and 0.035±0.002 (soleus); amino acids increased myofibrillar FSR ~2-fold above basal to 0.93±0.004 (vastus), 0.086±0.005 (triceps) and 0.097±0.005 (soleus). There was a significant main effect (two-way repeated measures ANOVA) for amino acid infusion ($P<0.001$) and the muscle studied (triceps FSR being ~15% smaller than those of soleus and vastus; $P<0.05$). These data suggest that in human, unlike animal muscle, fibre-type composition is not a very important determinant of the rate of muscle protein synthesis.



This study was approved by the Copenhagen and Fredriksberg communities ethics committee, Denmark and was supported by grants from the Danish Medical Research Council, the US National Institutes of Health, The Wellcome Trust and UK Medical Research Council.

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Tumour necrosis factor alpha mRNA is constitutively expressed in human skeletal muscle, and may be inducible by acute endotoxaemia

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Sepsis-induced skeletal muscle protein catabolism may be mediated by systemic TNF-α. Immune cell TNF-α production is well recognised, but recent studies suggest that TNF-α may also be present in muscle (Saghizadeh *et al*, 1996). We tested the hypothesis that *in-vivo* endotoxaemia would induce TNF-α gene expression in human skeletal muscle. In this Local Research Ethics Committee-approved study 8 healthy male volunteers, mean (SD) age 32.0 (4.4) yr were examined twice, in random order and 2 weeks apart. On one occasion they received 4ng/kg *i.v* E.coli lipopolysaccharide (LPS), and on the other the same volume of *i.v* sterile normal saline. Automated pulse rate, rectal temperature and oxygen consumption (VO_2), and arterialised venous plasma concentrations of cortisol, IL-6 and TNF-α were measured hourly, for one hour before and 6 hours following *i.v* LPS/saline. Percutaneous quadriceps femoris biopsies were obtained (conchotome technique) immediately prior to LPS, and 6 hours after *i.v* LPS/saline. Tissue samples were immediately fixed in neutral formalin, later processed into paraffin wax and 7 micron sections cut and mounted onto silicon-based glue-coated slides, for *in-situ* hybridisation. This employed an S^{35}-labelled cDNA probe to TNF-α, with autoradiographic product disclosure. TNF-α label was manually semi-quantitated thrice by one blinded examiner (score 0-3 for grain count per cell, and 0-3 for % of cells positive for grain). Statistical comparisons of the systemic effects of LPS used repeated measures ANOVA and, where

treatment/time interactions were apparent, with post-hoc Student's t-test using Bonferroni corrections for multiple comparisons. LPS caused fever, tachycardia and marked increases in plasma cortisol, IL-6 and TNF-α concentrations (saline/LPS comparisons made at peak LPS-induced change): pulse rate 64.4 (8.8) *vs* 90.6 (10.3) bpm, core temperature 36.4 (0.2) *vs* 37.8 (0.3) °C, VO_2 120.2 (8.3) *vs* 145.9 (18.7) ml/min/m^2, cortisol 159.8 (46.6) *vs* 721.6 (105.6) nmol/L, IL-6 11.0 (8.7) *vs* 1074.0 (754.9) pg/mL and TNF-α 13.9 (7.7) *vs* 960.7 (589.6) pg/mL, $p<0.01$ for each comparison. Tissue TNF-α label was present at similar levels before LPS and after saline, mean scores 1.44 (0.81) and 1.39 (0.63) respectively, but increased to mean score 2.03 (1.13) following LPS. TNF appears to be constitutively expressed in human skeletal muscle, and may be inducible by systemic LPS. This suggests that local induction of TNF-α may be important in skeletal muscle metabolic responses to endotoxaemia.

Saghizadeh M *et al.* (1996). *J Clin Invest* **97**: 1111-1116.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.

C72

Intervertebral disc nutrition via the endplate may not be affected by degeneration

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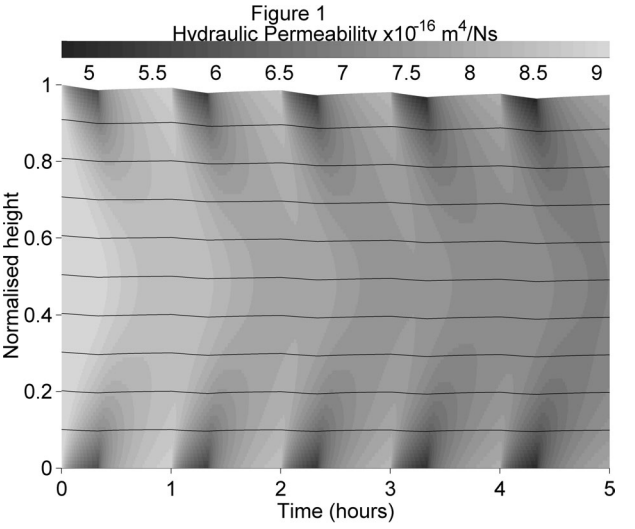
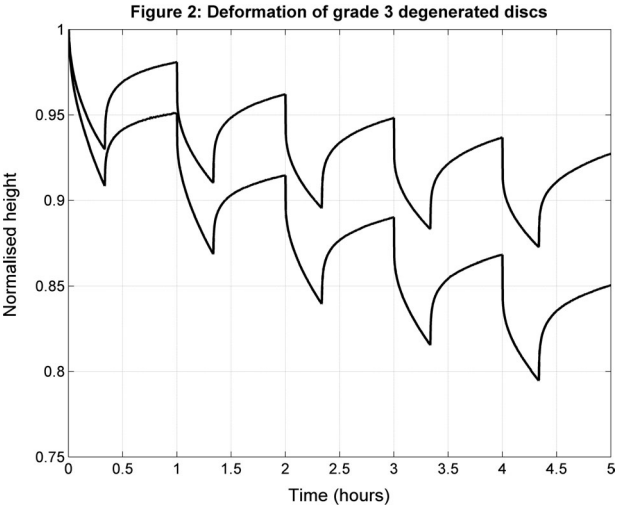
Intervertebral disc (IVD) degeneration can be associated with cartilage endplate (CEP) calcification (Roberts *et al.* 1996) and a corresponding reduction in permeability, but any causal mechanism is yet to be established. The permeability of the CEP may play an important role in IVD degeneration by controlling the convective and diffusive transport of metabolites into the nucleus pulposus (NP) (Urban *et al.* 1982).A poroelastic model of the IVD, which includes osmotic pressure and strain-dependent permeability, has been shown to accurately describe the behaviour of non-degenerate IVDs (Riches *et al.* 2002). This model was modified to incorporate the CEP by utilising a boundary condition that equated the fluid flux through the top of the disc with the fluid flux through a rigid porous layer representing the CEP. Other model parameters remained unchanged. The effect of a loss of CEP permeability on the mechanics of the NP was predicted by using three different CEP permeabilities: ($1x10^{-15}$ m^4/Ns, $5x10^{-16}$ m^4/Ns and $1x10^{-16}$ m^4/Ns). Two fresh IVDs with Thompson grade 3 degeneration were subjected to 5 cycles of 1MPa loading consisting of 20 minutes compression followed by 40 minutes expansion (Dhillon *et al.* 2001). Experimental results were compared to the model.Figure 1 shows the model height and internal IVD permeability distribution for a CEP permeability of $1x10^{-16}$ m^4/Ns. The change in height with time is effectively linear for both compression and expansion. Conversely, the deformation behaviour for degenerated IVDs was not linear (Figure 2).Whilst IVD degeneration reduces the osmotic pressure and the water content of the IVD, IVD degeneration does not affect tissue permeability (Iatridis *et al.* 1998). Therefore, the time-dependent deformation behaviour for degenerate and non-degenerate IVDs should be similar, unless the permeability of the CEP is reduced to less than that of the NP, as shown in this study. Since our preliminary data do not exhibit a linear height change, we can conclude, at least for these two IVDs, that even after significant IVD degeneration, the permeability of the CEP is greater than that of the NP, and as a consequence there may be limited or no hinderance to NP nutrition. The large height variation seen experimentally suggests a reduced aggregate modulus and a reduced osmotic pressure compared to non-degenerate IVDs





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Riches PE *et al.* (2002) *J. Biomech.*, **35** 1263-1271.
Roberts S, *et al.* (1996) *Spine*, **21** 415-420.
Urban JPG *et al.* (1982) *Clin. Orthop. Relat. Res.*, **170** 296-302.

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The effects of 24 weeks of moderate- or high-intensity exercise on low-density lipoprotein cholesterol: a randomised controlled trial

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Low-density lipoprotein cholesterol (LDL-C) is the primary target of cholesterol lowering therapy and exercise training is regarded as a therapeutic intervention (NCEP, 2002). However, there is insufficient evidence to characterise the dose-response relationship. In particular, it is unclear whether moderate- or high-intensity exercise confers greater reductions in LDL-C. Thus, the present study was undertaken to investigate the effects of exercise intensity on LDL-C.Sixty-six inactive, non-smoking men aged 30-45 years volunteered to take part in this study and agreed not to change their dietary habits during the intervention. Fasting measures of total cholesterol, triglycerides and high-density lipoprotein cholesterol were obtained in order to estimate LDL-C (Friedewald *et al.*, 1972). Physical fitness (maximum oxygen consumption, VO_2 max) and body fat (estimated from skinfolds) were measured in 62 normolipidaemic men before random allocation to a control group ($n = 19$), a moderate-intensity exercise group (three 400 kcal sessions per week at 60% of VO_2 max, $n = 22$) or a high-intensity exercise group (three 400 kcal sessions per week at 80% of VO_2 max, $n = 21$). Baseline measurements and 24-week changes were compared using a one-way ANOVA and, where appropriate, a Bonferroni *post hoc* test. This study was approved by the Local Research Ethics Committee. Results are reported for men who finished the study (Table). There were no inter-group differences in physical fitness, body fat or LDL-C at baseline. Twenty-four-week changes in physical fitness and body fat were significantly different in the exercise groups compared to the control group. Significant changes in LDL-C were only observed in the high-intensity exercise group compared to the control group. The exercise-induced reduction in LDL-C was greater than that attributable to biological variation (Ricos *et al.*, 1999) and was not correlated with the change in body fat ($r = -0.07$). These results suggest that high-intensity exercise is required to reduce LDL-C.

		Control (n = 15)	Moderate (n = 14)	High (n = 13)
Baseline	VO_2 max ($l;min^{-1}$)	29.4±6.5	31±5.7	31.8±6
	Body fat (%)	25±6	23±4	23±4
	LDL-C ($mmol;l^{-1}$)	3.44±0.63	3.61±0.89	4.04±0.75
24-week changes (P vs. control)	VO_2 max ($l;min^{-1}$)	-0.05±0.16	0.38±0.14 (P<.001)	0.55±0.27 (P<.001)
	Body fat (%)	0.95±1.48	-0.31±1.13 (P<.05)	-1.49±1.31 (P<.001)
	LDL-C ($mmol;l^{-1}$)	0.12±0.52	-0.17±0.51	-0.52±0.8 (P<.05)

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This work was supported by the British Heart Foundation.

Where applicable, the experiments described here conform with Physiological Society ethical requirements.