C1

The response to resistance training is attenuated in aged individuals after disuse muscle atrophy

C. Suetta[1], L. Justesen[1], L. Hvid[2], U. Christensen[2], S. Magnusson[1], M. Kjaer[1] and P. Aagaard[2]

[1]Institute of Sports Medine, Bispebjerg Hospital & Center of Healthy Aging, University of Copenhagen, Copenhagen NV, Denmark and [2]2Institute of Sport Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark

Sarcopenia has long been recognized as a major cause of muscle strength loss in old age, however, the additional impact of immobilisation and re-training on muscle mass and architecture has not previously been investigated in elderly human individuals.

Nine old men (age 61-74 yrs) and eleven young (age 21-27 yrs) underwent 2 weeks of unilateral whole leg casting followed by 4 weeks of re-training. Maximal voluntary contraction strength, neuromuscular activation, anatomical muscle cross sectional area, quadriceps muscle volume, muscle fibre pennation angle, physiological cross sectional area and specific force were assessed before, after immobilisation and again after re-training.

Both old and young men experienced decreases in anatomical muscle cross sectional area, muscle fiber pennation angle, maximal voluntary contraction strength and specific force after 2 weeks of immobilisation ($p<0.05$). However, muscle fiber pennation angle and anatomical muscle cross sectional area were more reduced in young than old men (OM: - 4.7%, YM: -8.1%, $p<0.05$) and subsequent, re-training led to larger increases in anatomical muscle cross sectional area, quadriceps muscle volume and muscle fibre pennation angle ($p<0.05$) in young compared to old men. In contrast, quadriceps activation was reduced in old men after immobilisation (OM: - 9.9 %, $p<0.05$) while young men were unaffected (YM: -1.0 %, n.s.).

The present study is the first to demonstrate that aging alters the neuromuscular response to short-term disuse and recovery in humans. Notably, immobilisation has a greater impact on the efferent neuronal function in old individuals, while young individuals were more affected at the muscle level. In addition, old individuals showed an attenuated response to re-training after immobilisation compared to young individuals.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C2

Mechanism of immobilisation-induced muscle atrophy and subsequent testosterone-mediated muscle mass gains during exercise rehabilitation in humans

D. Constantin[1], J. Miller[1], M. Block[1], D. Constantin-Teodosiu[1], R. Hill[1], P. Krasney[1,2] and P.L. Greenhaff[1]

[1]School of Biomedical Sciences, University of Nottingham, Nottingham, UK and [2]Pfizer Pharmaceuticals, Groton, CT, USA

The molecular mechanisms regulating muscle mass changes during immobilisation (de Boer et al. 2007), resistance exercise (Wilkinson et al. 2008) and androgen administration in humans are unclear. We aimed to investigate molecular changes associated with: (i) immobilisation-induced muscle atrophy; and (ii) testosterone-mediated augmentation of muscle mass gains during rehabilitation exercise training in humans. Lean tissue mass (DEXA) was determined in the dominant leg of 12 untrained, healthy, male volunteers (age 20.5±0.6 yrs, BMI 23.6±0.7 kg.m^2) before and after 3 wks of limb immobilisation, and at pre-determined time points during 6 wks of isokinetic rehabilitation training (5 x 30 contractions, 3 x wk). Subjects also received weekly intra-muscular injections of vehicle (Control, n=6) or testosterone (600 mg, n=6) commencing immediately following immobilisation. Vastus lateralis biopsies were obtained immediately before and after immobilisation, and after 24 h and 1, 4, and 6 wks of exercise rehabilitation, and were used to determine the expression of proteins involved in the ubiquitin-proteasome pathway and the Akt-mTOR-p70S6k anabolic signalling axis. The study was approved by the University of Nottingham Medical School Ethics Committee. Data are expressed as mean±SEM, and statistical analysis was performed using ANOVA.

Lean tissue mass declined by 7.2+1.5% after 3-wks of immobilisation, but this had no effect on the expression of MAFbx and MURF-1 or phosphorylated Akt^{Ser473}, GSK3β^{Ser9}, p70S6k^{Thr389} and 4EBP-1$^{Thr37/46}$. The increase in lean tissue mass from basal was greater in the testosterone group after 4 (8.7±0.8%) and 6 wks (11.0±0.8%) of rehabilitation compared to Control (2.4±0.7, $P<0.001$; 3.1±0.6%, $P<0.001$). This testosterone mediated augmentation of lean tissue mass was paralleled by down-regulation of MAFbx (70±80%, $P<0.05$) and MuRF1 (24.0±12.0%, $P<0.05$) expression at 6 weeks, and increased phosphorylation of Akt^{Ser473} (36±24%, $P<0.05$; 23±10%, $P<0.05$), GSK3β^{Ser9} (24±11%, $P<0.05$; 22±10%, $P<0.05$), and p70S6k^{Thr389} (44±22%, $P<0.05$; 62±31%, $P<0.05$) at 4 and 6 wks, respectively, compared with Control.

This study shows immobilisation induced muscle atrophy was not associated with the upregulation of MAFbx and MURF-1 protein expression in humans, and confirms that anabolic signalling is not blunted under these conditions. Restoration of lean tissue mass during rehabilitation training was augmented by testosterone, and this was accompanied, but was not preceded by, the suppression of MAFbx and MURF-1 expression and increased anabolic signalling.

de Boer MD, Maganaris CN, Seynnes OR, Rennie MJ & Narici MV. (2007). *J Physiol* **583**, 1079-1091

Wilkinson SB, Phillips SM, Atherton PJ, Patel R, Yarasheski KE, Tarnopolsky MA & Rennie MJ. (2008). *J Physiol* **586**, 3701-3717

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C3

Four and a half LIM domain 1 (FHL1) is associated with activity, strength and MHC IIa expression in quadriceps of patients with chronic obstructive pulmonary disease (COPD)

J. Riddoch Contreras[1], A. Sathyapala[2], G. Marsh[2], M.I. Polkey[2] and P. Kemp[1]

[1]National Heart and Lung Institute, Imperial College, London, UK and [2]National Heart and Lung Institue, Royal Brompton Hospital, London, UK

Muscle atrophy is common systemic feature of advanced COPD. Although primarily a lung disease, muscle atrophy is an important prognostic factor in the mortality caused by COPD but the mechanisms leading to muscle dysfunction remain unknown. FHL proteins are actin binding proteins that can shuttle between the cytoplasm and the nucleus and have been shown to be important in cell differentiation and protein turnover. Recent data has shown that mutations in FHL1 lead to muscle wasting and that over expression of FHL1 causes hypertrophy and increases the proportion of type IIa fibres in some muscles (Cowling *et al*) suggesting that it may be involved in COPD associated muscle atrophy. FHL1, type I MHC, type IIa MHC and RPLPO mRNA levels were measured in 41 patients and 18 healthy age matched controls by quantitative RT-PCR. Strength was measured as maximal voluntary contraction of the quadriceps and activity measured by triaxial accelerometry. Statistical analysis was performed using the Mann-Whitney U test and Spearman's rank correlation. COPD patients had a reduced FEV1 (COPD 35% vs control 108% of predicted), were less active (COPD 56.03± 7.03 mins/day vs cont 100±10.88 mins/day) and were weaker (maximal voluntary contraction COPD 29.6± 1.5kg vs cont 36.2± 2.5kg) than the controls. The expression MHC type I was reduced 3 fold and the expression of MHC type IIa was increased 1.5 fold in the patients compared to the controls. FHL1 expression was not different between patients and controls. Correlation of FHL1 expression with activity and strength showed an inverse correlation of both FHL1 mRNA and protein with strength (R^2=-0.408, p<0.01) and activity (R^2=-0.552 p<0.005) in the patients but not in the controls. FHL1 mRNA was also strongly correlated with the expression of type IIa mRNA in both patients (R^2=0.495 p<0.001) and controls (R^2=0.491 p<0.01) but was not correlated with type I MHC in either group. The inverse correlation between FHL1 mRNA and activity and strength observed in patients is surprising given previous data in human and animal studies showing increased FHL1 expression following exercise. However, FHL1 has been shown to be associated with hypertrophy and we and others have found that Akt phosphorylation is increased in patients with reduced activity or muscle wasting compared to controls (Doucet *et al*). Our data correlating FHL1 with type IIa MHC suggests that FHL1 may also modify the expression of MHC type IIa in humans as well as rodents.

Cowling BS *et al* (2008) J Cell Biol **183**,1033-1048

Doucet *et al* (2007) Am J Respir Crit Care Med **176**, 261-269.

This work was supported by GlaxoSmithKline

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C4

Characterizing a role for the PGC-1α related co-activator (PRC) in C2C12 muscle cells

A. Philp and K. Baar

Division of Molecular Physiology, University of Dundee, Dundee, UK

Transcriptional co-activators have emerged as potent regulators of metabolism. The most characterised co-activator is the peroxisome proliferator activated receptor-γ co-activator 1α (PGC-1α), which has been identified as a master regulator of mitochondrial biogenesis (Spiegelman and Handschin, 2008). Less well characterized is the PGC1-α related co-activator PRC which shares similarities with PGC1-α, including an acidic NH2-terminal region, an LXXLL signature for nuclear co-activators, and a central proline rich region (Scarpulla, 2008). The aim of this study was to elucidate if PRC has a functional role in skeletal muscle. Five days following differentiation, C2C12 myotubes were treated for 72h with Glucose, Lactate, Pyruvate, Sodium Bicarbonate (5-50mM) or Sodium Chloride (50mM) as an osmotic control. For cell contraction experiments, myotubes were subjected to either low (1Hz, 3h), moderate (10Hz 3h) or high (100Hz, 0.5h) frequency contractions using custom-built stimulation units. Over-expression studies were performed using a plasmid containing the full-length cDNA of PRC in the mammalian expression vector pSV-SPORT. Transient transfections were carried out overnight using lipofectamine and 2ug of plasmid DNA. Following treatment, cells were collected in lysis buffer (50mM Tris pH 7.5; 250mM Sucrose; 1mM EDTA; 1mM EGTA; 1% Triton X-100; 1mM NaVO4; 50mM NaF; 0.10% DTT; 0.50% PIC), centrifuged for 5 mins at 8,000 RPM and the supernatant removed. The levels of mitochondrial metabolic proteins were determined by western blotting using commercially available antibodies. Real time quantitative PCR was performed to measure relative mRNA expression using an Eppendorf Light Cycler, SYBR green PCR plus reagents (Sigma Aldrich, Dorset, UK) and custom designed primers. Differences between groups were assessed by students paired t-tests (SPSS version 10); all results are expressed as Mean ± SEM. PRC expression was increased by pyruvate treatment (207%) as was cytochrome-c (206%) and COX-1 (117%), however there was no effect of lactate, glucose or NaHCO3 on PRC expression. Low frequency contraction increased PRC expression by 37% (1h), 147% (3h) and 37% (6h). This response was less pronounced than PGC-1α (457%, 6h), whilst PRC expression did not change at any of the other frequencies examined. Over-expression of PRC increased the protein content of PRC (22%), COX-2 (57%) and COX-5 (55%). This was coupled with an increase in basal cell respiration (48%) and glucose uptake (41%). These data indicate that PRC can increase respiratory chain function in

skeletal muscle cells and is sensitive to alterations in muscle activity and nutrient availability, potentially suggestive of a role for PRC in skeletal muscle adaptation to endurance type exercise.

Scarpulla RC (2008) Physiol Rev 88(2):611-38.

Handschin C and Spiegelman BM (2008) Nature 454:463-9.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

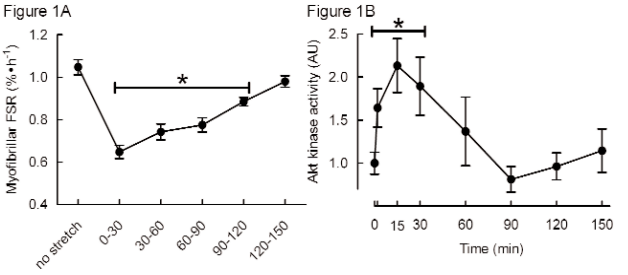
C5

Cyclic stretch reduces myofibrillar protein synthesis despite increases in Focal Adhesion Kinase and anabolic signalling in L6 cells

P.J. Atherton[1], N.J. Szewczyk[1], A. Selby[1], D. Rankin[1], K. Hillier[2], K. Smith[1], M.J. Rennie[1] and P. Loughna[2]

[1]Clinical Physiology, University of Nottingham, Derby, UK and [2]School of Veterinary Medicine and Science, University of Nottingham, Sutton Bonnington, UK

Muscle protein synthesis is modulated by mechanical stimuli: during strenuous muscular activity, protein synthesis is suppressed (Rose et al., 2009) but increases afterwards, resulting in a net increase of protein if sufficient amino acids are available (Rennie and Tipton, 2000). In life, muscles are subjected to shortening forces due to contraction, but are also subject to stretching forces during lengthening. It would be inefficient if contraction and stretch had different effects on muscle protein turnover, but little is known about the topic. To investigate this, we measured myofibrillar and sarcoplasmic protein synthesis (MPS, SPS, respectively) by incorporation of ^{13}C proline using gas chromatography-mass spectrometry and anabolic signalling by phospho-immunoblotting and kinase assays in cultured L6 skeletal muscle cells. Aside for unstretched controls, all cells were cyclically stretched using a 1Hz sine wave for 30 min and sampled at 2, 15 and 30 min and over 30 min intervals up to 120 min after stopping stretch (n=6 technical replicates/condition). One-way ANOVA with Tukey's post-hoc testing was used to assess differences in protein synthesis and signalling between stretched and unstretched cells; data are presented as mean±SEM where significance was set at P<0.05. During stretch, SPS was unaffected, whereas MPS was suppressed by 40±0.03% (P<0.01; see Figure 1A) before returning to basal rates 90-120 min after stopping stretch. Paradoxically, anabolic signalling was stimulated with peak values after 2-30 min: e.g. focal adhesion kinase (FAK Tyr576/577; +28±6%), protein kinase B activity (Akt; +113±31%; see Figure 1B), p70S6K1 (ribosomal S6 kinase Thr389; 25±5%), 4E binding protein 1 (4EBP1 Thr37/46; +14±3%), eukaryotic elongation factor 2 (eEF2 Thr56; -47±4%), and extracellular regulated protein kinase 1/2 (ERK1/2 Tyr202/204; +65%±9%); all P<0.05. After stopping stretch, except for Akt activity, stimulatory phosphorylations were sustained: e.g. FAK (+26±11%) for □30 min, eEF2 for □60 min (peak -45±4%), 4EBP1 for □90 min (peak +33±5%), and p70S6K1 which remained elevated throughout (peak +64±7%); all P<0.05. Neither AMPK (Adenosine monophosphate-activated protein kinase) Thr172 or ACCβ (acetyl-CoA carboxylase) Ser79 phosphorylation were affected by stretch. Thus acute cyclic stretch specifically suppresses MPS despite paradoxical increases in activity/phosphorylation of elements thought to increase anabolism (i.e. Akt-mTORC1 signalling). Given the absence of inhibitory $Ca2^{+}$-eEF2K-eEF2 (Rose et al., 2009) and AMPK signalling, we propose the existence of other mechanisms regulating the inhibition of muscle protein synthesis induced by mechanical activity.



*Asterisks over bars indicate significantly different (P<0.05) from no stretch conditions.

Rennie MJ & Tipton KD (2000). Protein and amino acid metabolism during and after exercise and the effects of nutrition. Annu Rev Nutr 20, 457-483.

Rose AJ, Alstead TJ, Jensen TE, KobberØ JB, Maarbjerg SJ, Jensen J, & Richter EA (2009). A Ca2+-CaM-eEF2K-eEF2 signalling cascade, but not AMPK, contributes to the suppression of skeletal muscle protein synthesis during contractions. J Physiol, In press.

We thank BBSRC (BB/X510697/1 and BB/C516779/1), the EC EXEGENESIS and University of Nottingham. PA is an RCUK Fellow.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C6

The effects of hydrogen peroxide on contractile properties of skinned muscle fibres of the rat: a model for ageing?

S.F. Gilliver, J. Rittweger, D.A. Jones and H. Degens

IRM, Manchester Metropolitan University, Manchester, UK

Oxidative damage to tissues is thought to play a role in the age-related changes in muscle function. Several groups have found that incubating single skinned muscle fibres with hydrogen peroxide (H_2O_2) leads to reduced calcium sensitivity and loss of force (1) and a decrease in maximum shortening velocity (2). As yet, no study has determined how the capacity to generate power. Maximum instantaneous power is determined by the maximum velocity of unloaded shortening (*Vmax*), isometric force (*Po*), and the curvature (*a*/*Po*) of the force-velocity relationship. The purpose of this study was therefore to examine the effects of oxidative damage the determinants of power. Rats were killed humanely at 8 weeks, the soleus muscle excised and skinned single fibres prepared using established procedures (3,4). Fibres were activated in pCa 4.5 solutions at 15□C

and underwent a series of isotonic shortening steps (5). Fifteen fibres were subjected to an initial series of contractions and then again after 4-min incubation in 50 mM H_2O_2. Control fibres (n = 6) were subjected to the same testing procedure except that they were incubated in normal relaxing solution between tests. Incubation in H_2O_2 caused a 20% and 25% drop in *Po* and *Vmax*, respectively, while peak power fell approximately 34% (Fig 1). In contrast,,*a/Po* rose 18% (decreased curvature), tending to maintain power. The control fibres showed only small and non-significant changes. The novel feature of these results is that *a/Po* increased with oxidative damage. Old muscle fibres are reported to have low shortening velocity (4) but it is not known whether they have high values of *a/Po*. If this proves to be the case it would suggest that H_2O_2 treatment is a useful model for examining the reported age-related changes in contractile characteristics.

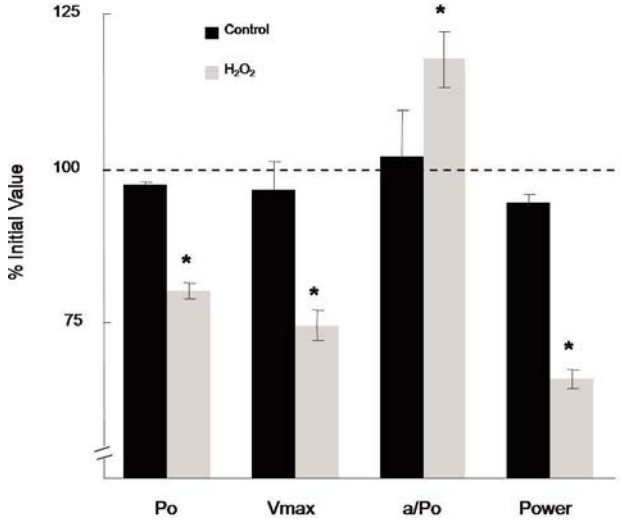


Figure 1. Effect of H_2O_2 on contractile properties of skinned single fibres. Measures expressed as a percentage of initial values (Mean ± SEM). *indicates values that differed significantly from initial fibres ($p<0.05$; paired Student's T test).

Murphy RM *et al.* (2008). J Physiol **586**, 2203-2216.

Prochniewicz E *et al.* (2008). Am J Physiol Cell Physiol **294**, C613-26.

Larsson L & Moss RL (1993). J Physiol **472**, 595-614.

Degens H *et al.* (1998). Acta Physiol Scand **163**, 33-40.

Bottinelli R *et al.* (1996). J Physiol **495**, 573-586.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

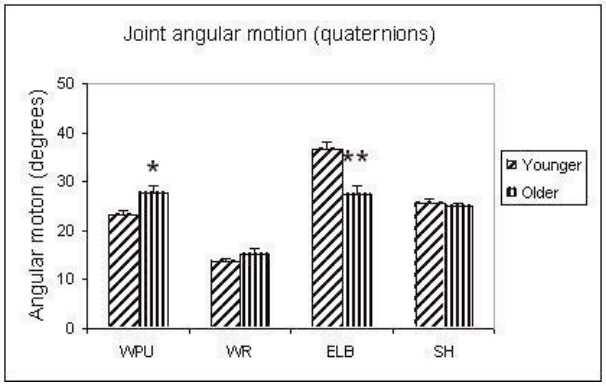
C7

Changes in upper limb reaching synergies with human ageing

M. Mayston[1], S.F. Farmer[3] and C. Hopkins[2]

[1]Neuroscience, Physiology, Pharmacology, University College London, London, UK, [2]Physiotherapy, Royal Hospital for Neurodisability, London, UK and [3]Neurology, University College London, London, UK

Not much is known about the effects of ageing on the important upper limb functions of manipulation and movement of objects. Furthermore, it is important to understand the effects of normal ageing on upper limb movement synergies in order to improve the understanding of the pathophysiology and management of neurological conditions e.g. stroke. The aim of this study was to investigate the effects of hand-dominance and age on upper limb reaching functions. With ethical approval we studied 16 participants (age range 22-82 years, 55.1 ± 20.4: mean + SD: 4 male, 2 left-handed). Participants were excluded if they had previous neurological and/or musculoskeletal problems. Participants performed a reaching task involving movement of the shoulder, elbow and wrist in 3-D space. These movements were measured using the Cartesian Optoelectronic Dynamic Anthropometer (CODA;Charnwood Dynamics, UK) motion analysis system. Participants picked up and moved a cup across a table, released it, and then brought their arm back to the starting position. The task was carried out five times and data from all the trials were used in the analyses. Both left and right upper limbs were tested. Quaternion angles (angular motion) were calculated from the kinematic data using Matlab (Mathworks Inc, USA) routines developed for this study. Hand dominance did not significantly affect this task (Paired t-test: $P>0.05$), therefore data from left and right sides were pooled prior to age comparison. For the purposes of comparison subjects were divided into younger and older age groups (age 22-54 years, n=9 vs 64-82 years, n=7). Significant changes in angular motion were found with increasing age. There were increases in angular motion of the wrist at object pick up (Unpaired t-test: $P < 0.05$) and a significant decrease in total elbow movement (Unpaired t-test: $P < 0.05$). These data are displayed in Figure 1. Linear regression between angular motion at shoulder, elbow and wrist and age showed that wrist angular motion at object pick up, but not object release increased ($F(1,158)=5.2$) whilst shoulder and elbow angular motion decreased ($F(1,158)=7.7$; $F(1,158)=17.8$; ANOVA; $P < 0.05$ for shoulder, elbow and wrist pick-up).These results suggest that there are changes in movement synergies with ageing. The total angular movement at the shoulder and elbow decreases whilst total angular movement at the wrist increases. We do know yet whether the increase in wrist movement is compensatory for the decreases in shoulder and elbow movement.



Mean+/-SEM angular motion at wrist pick up (WPU) and release (WR), elbow (ELB) and shoulder (SH), pooled for left and right sides. Diagonal lines=subjects aged < 60 years (n=9 subjects; 90 trials); vertical lines = subjects aged >60 years (n=7 subjects; 70 trials). * = p<0.01; * * = p< 0.001

Professor Roger Woledge, Imperial College London, for writing the Matlab programmes.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C8

Skeletal bone properties in smokers and non-smokers with similar physical activity levels; a peripheral quantitative computed tomography study

R.C. Wüst[1,2], K. Winwood[3], H. Degens[2] and J. Rittweger[2]

[1]Institute of Membrane and Systems Biology, University of Leeds, Leeds, UK, [2]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK and [3]Department of Exercise and Sport Science, Manchester Metropolitan University, Manchester, UK

Smoking is a known risk factor for fractures. However, the role of confounding factors, in particular physical activity and muscle forces, has not been systemically assessed. Moreover, virtually all studies in the past have relied upon dual x-ray absorptiometry, a method that does not yield anatomically accurate information. Therefore, we have organized a cohort study to compare bone strength indicators (BSI) in non-smokers and smokers that were matched for physical activity, leg muscle size and maximal muscle force. We hypothesised that BSI values in smokers are reduced and that this is aggravated with increasing age and smoking history. In 41 smokers (mean age: 41.0; SD: 16.1 years) and 53 non-smokers (47.5±18.2 years), the tibia and radius were scanned by peripheral quantitative computed tomography (pQCT). In line with our initial hypothesis, BSI values for trabecular bone mineral density and epiphyseal bone mineral content were lower in young smokers (229 (95% C.I.: 212-245) mg/cm^3 and 362 (334-389) mg/mm, respectively) than in young control participants (278 (257-300) mg/cm^3 and 422 (387-457) mg/mm, respectively; p-values 0.002 and 0.008 respectively, ANOVA). Surprisingly, however, such an age-related decline in these parameters was not observed in smokers. As a result the difference in BSI values disappeared in people of 60 years between smokers (260 (239-282) mg/cm^3 and 397 (362-432) mg/mm) and non-smokers (246 (230-263) mg/cm^3 and 370 (344-398) mg/mm) and independent of their smoking history (R^2 ranging from 0.000 – 0.021).

These results suggest that smoking interferes with osteo-regulatory signals at young age, possibly via factors as oxidative stress and/or other substances in cigarette smoke. This interference of smoking with bone homeostasis wanes with age, suggesting that regulation of bone homeostasis is altered during ageing in smokers.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C9

Structural and functional adaptations to eccentric *versus* conventional resistance training in older adults

N.D. Reeves[1], C.N. Maganaris[1], S. Longo[2] and M.V. Narici[1]

[1]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK and [2]Laboratory of Sports Analysis and Human Performance, University of Milan, Milan, Italy

Resistance training is effective for attenuating age-related muscle weakness and inducing positive morphological adaptations in skeletal muscle (e.g. 1). Conventional resistance training involves lifting and lowering the same load, but because skeletal muscle can develop higher forces when it contracts eccentrically (2), it is likely under-loaded during the eccentric (lowering) contraction phase. We hypothesised that eccentric-only training (using higher loads) would yield greater muscle structural and strength gains than conventional resistance training. Nine older adults (mean±SD age: 74±3 years) were assigned to a conventional (CONV) resistance training group performing both concentric and eccentric contractions and ten (age: 67±2 years) to an eccentric-only (ECC) training group. Both groups trained the knee extensors 3 times per week for 14 weeks at 80% of the 5-repetition maximum, specific to each training mode. Knee extensor torque was assessed with an isokinetic dynamometer during isometric, concentric and eccentric contractions over a range of angular velocities (0–200 deg s^{-1}). Vastus lateralis muscle architecture (fascicle length, pennation angle and muscle thickness) was measured *in vivo* at rest using ultrasonography. Training loads in the ECC group were 40-110% higher, but the training volumes were equivalent because the CONV group performed more repetitions (P>0.05; independent t-test). Resistance training increased fascicle length in both groups, but this was significantly greater in the ECC (20±14% increase) than the CONV (8±8% increase) group. Conversely, pennation angle significantly increased in the CONV (35±15%), but not the ECC (5±6%) group. Muscle thickness increased to a similar extent in both groups (~12±11%; P<0.05). An increase in fascicular length following resistance training suggests the addition of sarcomeres in-series, consistent with animal models after chronic and intermittent stretch (3,4). An increase in pennation angle is consistent with the addition of sarcomeres in-parallel. These results raise the possibility that the stimulus for adding sarcomeres in-series and in-parallel may be different. In the ECC group, eccentric knee extensor torque increased by 9-17% across velocities (P<0.05; dependent t-test), but concentric torque was unchanged (P>0.05). Conversely, in

the CONV group, concentric torque increased by 22-37% across velocities ($P<0.05$), but eccentric torque was unchanged ($P>0.05$). Despite much higher loads being used by the ECC group, isometric strength increased similarly between groups (~8%), suggesting that mechanical stress may not be the only stimulus influencing strength gains. Considering the present findings, to match the force-velocity properties of skeletal muscle, an optimal training stimulus should involve using higher loads for the eccentric contraction phase than the concentric phase.

Reeves ND, Narici MV & Maganaris CN (2006). Myotendinous plasticity to ageing and resistance exercise in humans. Exp Physiol 91, 483-498.

Katz B (1939). The relation between force and speed in muscular contraction. J Physiol 96, 45-64.

Williams PE, Catanese T, Lucey EG & Goldspink G (1988). The importance of stretch and contractile activity in the prevention of connective tissue accumulation in muscle. J Anat 158, 109-114.

Holly RG, Barnett JG, Ashmore CR, Taylor RG & Mole PA (1980). Stretch-induced growth in chicken wing muscles: a new model of stretch hypertrophy. Am J Physiol 238, C62-71.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C10

The effect of age on exercising calf blood flow and vascular conductance in men

L.M. Lane[1], H. Reilly[1], S. Green[2] and M. Egaña[1]

[1]Physiology, Trinity College Dublin, Dublin, Ireland and [2]Physiology, University of Otago, Dunedin, New Zealand

Ageing in men is associated with a number of physiological adaptations that result in lower resting muscle blood flow (BF) and vascular conductance (VC)[1]. However, it has recently been reported that the vasodilatory capacity in ageing men appears to be well preserved during leg graded exercise of the knee extensor muscles[1]. We examined leg VC responses during a graded incremental exercise in ageing men, using a calf plantar flexion exercise model. Inactive aged (68 ± 4 yr; n=8) and young (22 ± 1 yr; n=9) male volunteers participated in this ethically approved study performing a graded intermittent calf plantar flexion exercise (6s duty cycle: 2 s contraction, 4 s relaxation) to failure on a custom-built calf ergometer at a tilt of 67□. Calf BF was measured contraction by contraction using venous occlusion plethysmography. Volunteers also performed a forearm reactive hyperaemic test to assess forearm VC. Data was analysed using ANOVA and presented as mean ± S.D. Aged demonstrated a significant decline ($P<0.05$) in resting mean calf VC (0.14 ± 0.07 ml.100ml^{-1}.mmHg^{-1}.10) compared with young (0.20 ± 0.05 ml.100ml^{-1}.mmHg^{-1}.10). During calf plantar flexion incremental exercise this difference was abolished while the aged demonstrated significantly higher ($P<0.05$) mean calf BF at high absolute forces (400N, 700N, 850N) compared to young. No age differences were observed in calf VC responses during all the workloads of the graded test or in forearm BF and VC following the reactive hyperaemic test. Peak calf muscle force during the graded test was significantly reduced ($P<0.001$) in the aged (644±195N) in comparison to the young (967±224N). In conclusion, dspite a reduced muscle performance and resting vascular conductance in the aged group there was no impairment of calf vasodilatory responses to plantar flexion exercises. The mechanisms behind this could be in part attributed to a lower peripheral oxygen extraction capacity with ageing[2].

Parker BA *et al.* (2008). *J App Physiol* **104(3)**, 655-664.

Dinenno FA *et al.* (1999). *Circulation* **100**, 164-170.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C11

Resistance training with blood flow restriction enhances the gains in calf blood flow in older people

R. Ferguson and S. Patterson

School of Sport and Exercise Sciences, Loughborough University, Loughborough, Leicestershire, UK

The effect of low load resistance training with blood flow restriction on muscle strength is well established in young (Takarada et al, 2000) and now older people (Patterson and Ferguson, 2009). We have also recently shown that low load resistance training with blood flow restriction enhances reactive hyperaemic blood flow (RHbf) to a greater extent compared to resistance training alone in young people (Patterson and Ferguson, 2008). However, the effect of this type of training on blood flow capacity in older individuals is currently unknown. The purpose of this study therefore was to determine the effect of low load resistance training combined with blood flow restriction on calf vascular capacity of older people. 11 healthy untrained participants (68 ± 2 yr, 170 ± 7 cm, 78 ± 8 kg) volunteered for the study which had local ethics committee approval. Participants trained 3 days per week for 4 weeks consisting of 3 sets of dynamic calf plantar-flexion to failure separated by 1 min rest. Participants trained both limbs at 25% of 1RM, one without and the other with blood flow restriction (110 mmHg) above the knee. Calf blood flow at rest (Rbf) and following reactive hyperaemia (RHbf) was assessed pre- and post-training using venous occlusion strain gauge plethysmography. Statistical analysis were performed using a repeated measures two-way (time x limb) ANOVA. Results are expressed as means ± standard deviation (SD). Rbf was similar between limbs at baseline and increased by 14% following resistance training with restricted blood flow and 18% in resistance training with normal blood flow (main effect for time, $P<0.05$), with no differences between limbs. The increase ($P<0.05$) in RHbf was greater (19.1 ± 5.1 to 26.8 ± 5.6 ml.min-1.100ml-1) following resistance training with blood flow restriction compared to the increase (21.7 ± 8.2 to 25.4 ± 6.5 ml.min-1.100ml-1) when resistance training was performed with normal blood flow. We have demonstrated that 4 weeks resistance training at 25% 1RM with blood flow restriction increased RHbf in older people by a greater extent compared to low load resistance training alone. Therefore as well as enhancing strength this type of training may also result

in muscles that have a better endurance and ability to resist fatigue.

Patterson & Ferguson. (2008). Annual Congress of the European College of Sports Sciences

Patterson & Ferguson. (2009). Proceedings of The Physiological Society

Takarada Y et al. (2000). J. Appl. Physiol. 88: 2097-2106.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C12

Short-term insulin administration in sport adversely affects lipid profile and packed cell volume despite increasing body mass index

M.R. Graham[1,3], P.J. Evans[2], P. Ryan[1], B. Davies[3] and J.S. Baker[4,3]

[1]The Newman Centre for Sport and Exercise Research, Newman University College, Birmingham, UK, [2]Diabetes and Endocrinology, Royal Gwent Hospital, Newport, UK, [3]Health and Exercise Science Research Unit, University of Glamorgan, Cardiff, UK and [4]Division of Sport, University of West of Scotland, Glasgow, UK

Insulin administration in uncontrolled keto-acidosis reverses lipolysis, proteolysis, ketogenesis, and gluconeogenesis. It is protein anabolic in the insulin-resistance of renal failure when administered with amino-acids (Lim et al., 2003). The "intelligent" athlete wants to inhibit proteolysis hoping to enhance performance and because it is undetectable by urinalysis (Holt and Sonksen, 2008). Administration establishes an in-vivo hyper-insulinaemic clamp, increasing muscle glycogen, before and in the recovery stages of strenuous exercise, believed to increase power, strength and stamina and assist recovery (Sonksen, 2001). This study investigated the effects of 30 days of insulin administration (0.12 IU.kg-1.day-1) combined with weight training on anthropometry, psychological profile, cardiovascular and respiratory variables and exercise performance on 12 weight lifters (I), aged between 23 and 46 years, compared to 12 non-drug using age matched exercise controls (EC) and 12 non-drug using age matched sedentary controls (SC), who were examined twice, one month apart. Anthropometry, respiratory muscle-function, endurance exercise and arterial pulse wave velocity were investigated. Biochemical analysis included; haemoglobin, packed cell volume (PCV), glucose and lipid profile. All data was analysed using parametric analysis of variance (ANOVA) and because of small sample sizes, re-analysed by the non-parametric analogue of the ANOVA (Kruskal-Wallis test).
Body mass index (BMI) significantly increased within the I-group (30.8 ± 3.2 vs. 31.2 ± 3.2, kg.m-2, P<0.05). PCV significantly increased within the I-group (0.45 ± 0.01 vs. 0.47 ± 0.02, ratio; P<0.05) and was significantly increased compared with EC on-insulin administration (month 2; 0.47 ± 0.02 vs. 0.44 ± 0.01, ratio; P<0.05). Triglycerides significantly increased within the I-group (1.78 ± 0.5 vs. 1.94 ± 0.5, mmol/L; P<0.05). Maximum inspiratory pressure (MIP) significantly increased within the I-group (MIP: 117 ± 32 vs. 122 ± 28, cm.H2O; P<0.05).
Exogenous insulin increases glucose metabolism in athletes determined by euglycaemic insulin-clamp technique (Sato et al., (1986). Physiological hyper-insulinaemia stimulates the activity of amino acid transport and synthesis in human skeletal muscle (Bonadonna et al., 1993).
Insulin administration is still prevalent in sport and may be catastrophic. It's short term use may increase performance, but may also predispose individuals to increased cardiovascular risk, similar to sedentary controls. Further research in this area is required to educate sportspersons that bigger is not necessarily better. However, there may be an application for its medical use in cachectic disease states, or even in the ageing musculoskeletal system.

Bonadonna RC et al. (1993). Effect of Insulin on System A Amino Acid Transport in Human Skeletal Muscle. J Clin Invest 91, 514-521.

Holt RI and Sonksen PH. (2008). Growth hormone, IGF-I and insulin and their abuse in sport. Br J Pharmacol 154, 42-556.

Lim VS et al. (2003).Insulin Is Protein-Anabolic in Chronic Renal Failure Patients. J. Am. Soc. Nephrol. 14, 2297-2304.

Sato Y et al. (1986). Improved insulin sensitivity in carbohydrate and lipid metabolism after physical training. Int J Sports Med 7, 307-310.

Sonksen PH (2001). Insulin, growth hormone and sport. J Endocrinol 170, 13-25.

To Dr A T Kicman and Mr Christiaan Bartlett, Kings College, London, for analytical work.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C13

Combination of a low-carbohydrate diet with high intensity interval training - Influence on insulin sensitivity, blood lipids and whole body metabolism in obese sedentary individuals

F. Sartor, H. de Morree, V. Matschke, S. Marcora, J. Thom and H. Kubis

School of Sport, Health and Exercise Sciences, Bangor, UK

High sugar and fat intake as well as low physical activity are known risk factors for the development of insulin resistance and type 2 diabetes. We hypothesize that particular chronic high glucose availability without high metabolic demand might generate metabolic alterations which increase the risk for type 2 diabetes. Therefore a combined diet and exercise intervention should counteract and revert any accumulated health risks related to malnutrition and exercise deficiency. We adopted a low-carbohydrate diet combined with high-intensity interval training (HIT) to improve insulin sensitivity, whole body metabolism and blood lipid profile in overweight sedentary individuals. Overweight sedentary subjects (n=19; BMI=32±3) were randomly assigned to an exercise – diet (DE) or diet only (D) group. Subjects (DE) trained three times a week on a cycle-ergometer (4 min 90% VO2peak, 3 min rest, 10 bouts) for two weeks and followed a low carbohydrate diet (35% carbohydrates, 15% proteins, 50% fats, 33% unsaturated) while the D group followed the diet protocol only. Post intervention Oral Glucose Insulin Sensitivity (OGIS) was significantly improved in both groups (OGIS(ml x min-1 x m-2): DE 377±70 to 396±68; D 365±91 to 404±87), and blood lipids (plasma triglycerides: DE 1.44±1.1 to 1.05±0.74, D 1.33±0.37 to 0.97±0.25; LDL: DE

2.97±0.74 to 2.76±0.66, D 3.43±0.63 to 3.17±0.69 and total cholesterol: DE 4.60±0.94 to 4.24±0.83, D 5.00±0.76 to 4.49±0.88 (mmol/l)) were significantly reduced. Moreover, RER was reduced in both groups (DE 0.91±0.06 to 0.88±0.06, D 0.92±0.07 to 0.86±0.07) while VO2max was increased by 16% in the DE group only. Additionally glycogen levels in muscle biopsies have been reduced in both groups revealing a reduction of glucose availability. It is evident that a low-carbohydrate diet alone can improve important parameters related to insulin resistance and type 2 diabetes while a combination of HIT and diet additionally mediate beneficial cardiovascular adaptations which are known to lower health risks in obese individuals.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C14

Age-related alterations in the ventilatory and cerebrovascular responsiveness to CO_2: rest and exercise

S.J. Lucas[1,2], C.J. Murrell[1], K.N. Thomas[1], J.D. Cotter[2] and P.N. Ainslie[1]

[1]Department of Physiology, University of Otago, Dunedin, New Zealand and [2]School of Physical Education, University of Otago, Dunedin, New Zealand

Cerebrovascular CO_2 reactivity is a vital homeostatic function that helps regulate central pH, and therefore affects the respiratory central chemoreceptor stimulus. With healthy human ageing, both cerebral blood flow (CBF) and ventilatory (VE) responsiveness to hypercapnia are reduced; thus, alterations in CBF and cerebrovascular CO_2 reactivity may affect VE responsiveness to CO_2 with ageing. Although cerebrovascular reactivity to CO_2 is enhanced during exercise, potentially as a means to maintain central CO_2 homeostasis, the extent to which this relationship might be influenced by exercise intensity or ageing is not known. We examined the hypothesis that, both at rest and with progressive exercise, there would be a differential age-related alteration in cerebrovascular and VE responsiveness to CO_2. Ventilation and blood flow velocity in the middle cerebral arterial (MCAv) were monitored continuously in 13 young (mean±SD, 24±5 y) and 11 older (64±5 y) participants at rest and during exercise at 30 and 70% of measured heart rate range (HRR) with and without hypercapnia (5% CO_2; 3 min). Cerebrovascular and VE reactivities to CO_2 were characterised by the slope of their relation to increasing end-tidal PCO_2. During normocapnia, MCAv was lower (all $P<0.01$) in the older compared to the younger aged group at rest (48.5 v 63.3 $cm.s^{-1}$) and during exercise (51.8 v 74.3 $cm.s^{-1}$ and 51.0 v 75.9 $cm.s^{-1}$, at 30% and 70% HRR respectively). At rest, cerebrovascular reactivity and VE sensitivity were lower in the older compared to younger aged group (2.02 v 2.48 $\%\Delta MCAv.mmHg^{-1}$ and 0.70 v 1.04 $L.min^{-1}.mmHg^{-1}$, respectively), although not significantly ($P>0.05$). During exercise, however, increases in cerebrovascular reactivity were greater in the older group compared to the responses of the younger group for both the 30% and 70% HRR workloads (4.84 v 3.78 and 5.72 v 3.54 $\%\Delta MCAv.mmHg^{-1}$). In the older group, when compared to the young, VE sensitivity remained lower during exercise ($P<0.01$) and unchanged ($P>0.05$) compared to rest. At 70% HRR only, age was directly related to elevations in MCAv-CO_2 reactivity (r=0.64, $P<0.01$) and inversely related to VE sensitivity (r=-0.54, $P=0.01$). Collectively, these data indicate that the age-related elevations in CBF-CO_2 reactivity during exercise, especially at higher exercise intensities, may act to attenuate VE sensitivity to CO_2.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C15

High intensity exercise tolerance in humans: the physiological significance of O_2 uptake kinetics

S.R. Murgatroyd, C. Ferguson, S.A. Ward, B.J. Whipp and H.B. Rossiter

Institute of Membrane and Systems Biology, University of Leeds, Leeds, UK

The tolerable duration (t_{lim}) of very-heavy intensity (VH) exercise demonstrates a hyperbolic relationship with the external power output (P); the curvature constant (W') being equivalent to a fixed amount of work above the power asymptote (critical power; CP) which is the upper limit for steady state exercise [1]. The physiological determinants of CP and W' are unclear, however. As the ability to sustain exercise (i.e. prolong t_{lim}) is associated with the capacity to transport and utilise O_2, we were interested in the relationship between pulmonary O_2 uptake (VO_2) kinetics and the P-t_{lim} parameters. We hypothesised that: 1) a high CP would be associated with a fast fundamental VO_2 time constant (τ), by minimising the O_2 deficit accumulation at a given P; and 2) W′ (suggested to reflect the rate of muscular fatigue-induction [2]) would relate to the slow component magnitude (ΔVO_2sc), via hastening the attainment of the upper limit of VO_2 (VO_2max). Fourteen healthy men, aged 20–34 yr gave informed consent to undertake cycle ergometry (Excalibur Sport, Lode, NL) with breath-by-breath VO_2 measurement by mass-spectrometry and turbinometry (MSX, Morgan Medical, UK). On different days they performed: 1) an incremental-ramp to estimate lactate threshold (LT); 2) a series of constant-work rate (CWR) tests to t_{lim} to determine VO_2max, CP and W′; and 3) repeated CWR tests, normalised to induce t_{lim} in 6 min (WR_6), for estimation of τ_{VH} and ΔVO_2sc. Seven men also repeated CWR at 80% LT (MOD) for estimation of τ_{MOD}. LT averaged 2.11±0.37 l/min (26±5 ml/kg/min) and VO_2max 4.18±0.49 l/min (51±7 ml/kg/min). WR_6 (296±29 W) was tolerated for 365±17 s. CP ranged 171 to 294 W and τ_{VH} 18.3 to 37.6 s in these relatively "fit" young subjects. In addition, τ_{MOD}

and τ_{VH} did not differ (t-test p>0.05; mean difference -0.1±1.8 s; range -1.4 to +2.5 s; c.f. [3]), each strongly and inversely correlated to CP: R^2=0.91 and 0.90, respectively. W′ (range 12.8–29.9 kJ) was directly correlated (R^2=0.71) with ΔVO_2sc (425–957 ml/min). Our findings support the notion that rapid VO_2 kinetics reduce the stress to homeostasis, allowing high power outputs to be sustained. Although the design of this study did not allow resolution of the mechanisms determining the correlation between CP and τ_{VH} (and τ_{MOD}), the projected relationship is consistent with reported values of CP and τVO_2 in subjects ranging from elite endurance athletes to the healthy elderly [4,5]. The VO_2sc likely reflects supplementary muscle O_2 consumption due to additional fibre recruitment; this presaging muscular fatigue. W', a notional energy store [1], may therefore better reflect the accumulation of fatigue-related metabolites to a 'critical' level [2]: a notion supported by the correlation of ΔVO_2sc and W'. Collectively, these data support VO_2 kinetics as a major determinant of very-heavy intensity exercise tolerance.

[1] Poole DC *et al*. (1988). *Ergonomics* **31**, 1265-1279.

[2] Coats EM *et al*. (2003). *J Appl Physiol* **95**, 483-490.

[3] Özyener F *et al*. (2001). *J Physiol* **533**, 891-902.

[4] Heubert RAP *et al*. (2005). *Int J Sports Med* **26**, 583-592.

[5] Overend TJ *et al*. (1992). *Eur J Appl Physiol* **64**, 187-193.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C16

ACTN3 R577X genotype and falls in elderly females: Is there a relationship?

R. Judson[1,3], H. Wackerhage[2,3], A. Mavroeidi[2], R. Barr[1], H.M. Macdonald[1], A. Ratkevicius[2,3], D.M. Reid[1] and L.J. Hocking[1]

[1]Bone and Musculoskeletal Research Programme, Division of Applied Medicine, University of Aberdeen, Aberdeen, UK, [2]Bone and Musculoskeletal Research Programme, School of Medical Sciences, University of Aberdeen, Aberdeen, UK and [3]Molecular Exercise Physiology, School of Medical Sciences, University of Aberdeen, Aberdeen, UK

Alpha-actinin-3 (ACTN3) is a sarcomeric protein localised to the Z-line of type II muscle fibres. A nonsense polymorphism in the ACTN3 gene (p.R577X) has been identified; the X/X genotype is present in ~16% Caucasians and results in ACTN3 deficiency. R577X genotype has been associated with altered muscle performance and function in elite athletes and among the general population. Reduced muscle function is an established risk factor for falling in the elderly, which is a significant public health problem. We therefore tested the hypothesis that ACTN3 genotype variation is associated with the incidence of falling in elderly women.

We studied 1313 Caucasian postmenopausal women aged 60-80 years from the North of Scotland Osteoporosis Study for whom DNA samples were available (mean age 69.7 ± 5.5 years). Self-reported data on falls was collected at recruitment and at 4- and 6-year follow-ups. ACTN3 genotyping was performed by DdeI restriction digest. Case-control association analyses were performed using PLINK statistical genetics software. Cross-sectional analysis of fallers versus non-fallers at baseline was performed. Further, individuals who reported having fallen at more than one time point (recurrent fallers) were compared with those who did not report falling at any time point (never fell). Correction for potential confounders (age, height, weight) was performed by logistic regression. Power was calculated using the Quanto program.

Genotype frequencies for baseline fallers (n=349) and non-fallers (n=871) were R/R=28%, R/X=53%, X/X=19% and R/R=30%, R/X=51%, X/X=19%, respectively. For recurrent fallers (n=113) versus never fell (n=271), frequencies were R/R=27%, R/X=56%, X/X=17% and R/R=29%, R/X=49%, X/X=22%, respectively. There was no significant association between ACTN3 genotype and falls (baseline or recurrent) under any model, even with correction.

These findings indicate that ACTN3 R577X does not play a major role in influencing falls risk in elderly women. The sample size examined here has >80% power to detect additive effects with odds ratio of 1.3 for each copy of allele X. However, muscle function is one of many complex interacting risk factors for falls, and individual genetic effects on falls risk - as for other common, complex disorders - will likely be smaller. We are in the process of genotyping a further 3300 samples from another cohort of elderly women to enable us to examine this further.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C17

Characteristics of walking in young and elderly humans and in elderly fallers

K.M. Cook and C. Smith

Applied Biomedical Research, King's College London, London, UK

Older people tend to walk more slowly than younger people (Dingwell & Marin 2006), but it is not clear if this is different for elderly fallers - nor whether there is a change in the quality of their walk. Our study compared 34 young subjects (mean 28 sd 10 years) 43 elderly subjects (72 sd 5) and 20 elderly fallers (75 sd 4, who self-reported an average of 1.8 trips in the previous year). Walking in a laboratory setting was measured by both CODA mpx30 (Charnwood Dynamics, UK) 3D motion analysis and with bi-axial accelerometers (ADXL202, Analogue Devices, UK). Longer walks (22m) could be measured only by the accelerometers with data acquisition via an iPAQ Pocket PC. Subjects were asked to walk either at their normal speed or to walk slowly. The young walked faster than both older groups and the older non-fallers walked faster than the older fallers (Bonferroni p<0.02). Somewhat surprisingly the older fallers walked much slower during the slow walk trials (34% of normal c.f. 61% for non-fallers), despite same instructions to all participants. Activity, estimated as the SD of acceleration, was measured in the mediolateral and vertical directions at the spine (L5) and ankle. This was directly proportional to walking speed (R^2 = 0.91) for mediolateral motions but show a quadratic term

at higher speeds for vertical movements. An index was thus used of (sd acceleration) / (walking speed) which essentially measures the untidiness of walking. No significant differences were found in this index for movements in the vertical direction. However there was a significant increase only for elderly fallers in mediolateral movements at both spine and ankle positions but only for the self-selected slow walk (Spine L5: young 0.11 se 0.01, elderly 0.11 se 0.01, fallers 0.20 se 0.02 g / m/s). The mediolateral movements at the ankle were further analysed by chopping the record into mid-swing and terminal-swing phases, each 15% of the stride time. This showed that the larger part of the increase in variability of movements in the fallers occurred during the terminal-swing phase. Although the records from accelerometers are a compound of changes in linear acceleration and angular changes in gravitational acceleration, our comparison with CODA measurements show they give an effective way of quantifying variability of movements. After correcting for changes in walking speed both elderly and young subjects had the same variability. However fallers were characterised by having a considerably larger variability index for mediolateral movements at slow walking speeds. This was due in part to them choosing to walk at a much lower speed and part from the increased sd of acceleration. The latter appears to be substantially associated with the terminal-swing phase, i.e. uncertainty of foot placement.

Dingwell, JB & Marin LC (2006) Journal of

Biomechanics 39, 444-452.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C18

Quantitative component analysis of the Timed Up and Go (TUG) test performed by young and older adults

J. Bergmann, C. Alexiou and C. Smith

Applied biomedical research, King's College London, London, UK

Falls are common in old age and frequently cause severe injury. Although not all falls result in major injury, 20% of them still require medical attention (1). It is crucial to determine which older people are at high risk of falling in order to prevent injury and initiate appropriate interventions. One of the most widely used clinical test to determine fall risk is the Timed Up and Go (TUG) test. The TUG is a quick, simple and effective test of basic mobility skills, and consists of a person standing up from a seated position, walking 3 meters, turning 180□and walking back to sit down in the chair under timed conditions (2). The different components i.e. standing up, walking, turning and sitting down, that occur during the TUG have recently been quantified using gyroscopes and accelerometers (3). We used a similar method to objectively time each functional component independently and determine how much every component contributed to the total outcome in a group of healthy young (n=11; mean age=20 years; range=19-21 years), and old (n=11; mean age=68 years; range=60-76 years) people. Data was normally distributed as found by the Kolmogorov-Smirnov test and Q-Q plots. An Independent Samples T-Test was used to determine differences between the two groups. Pearson correlation coefficients (r) were calculated for each component to establish how well they related to the total TUG time. Total TUG time and the component times of standing up, turning and walking back, differed significantly ($p<0.05$) between age groups. No difference was found between young and old subjects during walking of the first 3 meters ($p=0.81$) and sitting down ($p=0.18$). The greatest differences between groups were found for the total TUG time ($p=0.001$) and turning time ($p=0.007$). All components correlated well to the total TUG time (range; r= 0.344-0.727) in the young people, except for the standing up component that showed no correlation ($p=0.50$) with the total TUG time. In the group of older people all components correlated (range; r=0.266-0.719) with the total TUG time. However, the standing up component still had the lowest correlation. These results show that although the total TUG time differs between young and old people, not all components allow for a clear distinction between the two age groups. This suggests that certain tasks (e.g. turning) are better in distinguishing between age groups then others (e.g. walking of the first three meters). Furthermore, although some components correlated well with the total TUG time, other components, especially the standing up component, related poorly or not at all to the total TUG time. Thus, proving that additional information about basic mobility skills can be obtained by performing a quantitative component analysis of the TUG test.

American Geriatrics Society, British Geriatrics Society, and American Academy of

Orthopaedic Surgeons Panel on Falls Prevention, 2001. Guideline for the Prevention of Falls in Older Persons. Journal of the American Geriatrics Society 49, 664-672

Podsiadlo, D. and S. Richardson, The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc, 1991. 39(2): p. 142-8.

Higashi, Y., K. Yamakoshi, T. Fujimoto, M. Sekine, and T. Tamura, Quantitative evaluation of movement using the timed up-and-go test. Engineering in Medicine and Biology Magazine, IEEE, 2008. 27(4): p. 38-46.

This work was funded by a joint Medical Research Council and Graduate School Studentship of KCL.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

C19

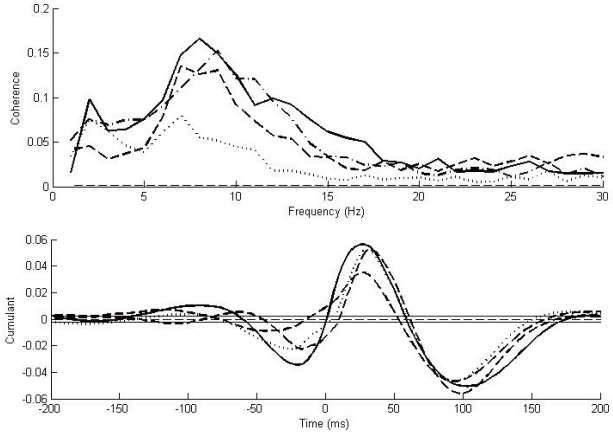
Developmental changes and functional role of 6-12 Hz oscillatory modulation of human slow hand movements

S.F. Farmer[1,2], J.A. Stephens[3] and K.M. Deutsch[3]

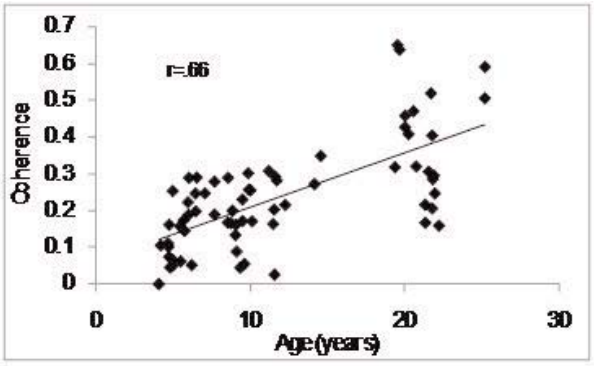
[1]Institute of Neurology, University College London, London, UK, [2]Clinical Neuroscience, Imperial College Healthcare NHS Trust, London, UK and [3]Department of Physiology, University College London, London, UK

In humans slow hand and finger movements are characterized by 6-12 Hz discontinuities visible in raw records and spectra of motion signals such as acceleration (Valbo & Wessberg, 1993; Kakuda et al., 1999). This pulsatile behavior is correlated with motor unit synchronization at 6-12 Hz as shown by significant coherence at these frequencies between pairs of motor units and between the motor units/surface EMG and the acceleration recorded from the limb part controlled by the muscle. We

have studied the developmental profile of 6-12 Hz oscillations during static contraction and slow wrist extension and flexion movements though spectral analysis of EMG and acceleration signals. We recorded simultaneous extensor carpi radialis (ECR) EMG and wrist acceleration from 67 subjects aged between 4 and 25 years during either a steady wrist extension task or slow externally paced wrist flexion and extension movements. Subjects were divided into 4 age ranges: 4-6 years (n=21), 7-9 years (n=15), 10-14 years (n=11) and adults (20-25 years, n= 20). In all subjects we compared the EMG-acceleration coherence recorded during slow wrist movements to that recorded during steady wrist extension against gravity. We also measured the speed of repetitive fine finger movements. During steady wrist extension and slow movement, EMG-acceleration coherence increases with age. In adults and older children, compared to steady muscle contraction, wrist movement produced greater additional 6-12 Hz oscillatory drive. In adults, there was significant coherence between ECR EMG and wrist acceleration in the range 6-12 Hz, maximal at 8-9 Hz (see Figure 1). In the age ranges 7-9 years and 10-14 years coherence magnitude values were less than those of the adult subjects. EMG-acceleration data from children aged 4-6 years showed little movement related coherence in the frequency range 6-12 Hz. Statistical comparison using ANOVA and the Chi2 difference of coherence test revealed statistically significant ($P<0.05$) increases in movement induced coherence with increasing age. The strength of 6-12 Hz EMG-acceleration slow movement-induced coherence was positively correlated with age (see Figure 2) and speed of fine finger movements. We have shown that 6-12 Hz coherence and the pulsatile control of human movement increase with maturity. This study provides further evidence that oscillations in the human motor system increase with development. We suggest that with age peripheral oscillations are incorporated into a developing oscillatory neural network, which may have implications for normal human motor development and age-related increases in movement velocity.



Pooled coherence and cumulant between EMG and acceleration during movement: Bold=adult; Dash-dot=10-14 yrs; Dash=7-9 yrs; Dot=4-6 yrs



Change in movement induced 6-12 Hz EMG-acceleration coherence with age.

Valbo AB & Wessberg J (1993). J. Physiol. 469, 673-691.

Kakuda N et al. (1999). J. Physiol. 520, 929-940.

UCL Comprehensive Biomedical Research Center

Imperial College London Academic Health Sciences Center

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC2

Arterial blood oxygen saturation and heart rate and their relationship to acute mountain sickness at altitude. A field study

T. Parks[1], G. Brierley[2], C. Wilson[1] and C. Wolff[3]

[1]University of Cambridge School of Clinical Medicine, Cambridge, UK, [2]The Royal Berkshire NHS Foundation Trust, Reading, UK and [3]Clinical Pharmacology and Anaesthetics, William Harvey Research Institute, Barts and The London, London, UK

Compensation for hypobaric hypoxia at altitude through increased blood flow and delivery of oxygen is a recognised phenomenon[(1-2)]; however, its relationship to acute mountain sickness is not yet understood. We measured arterial blood saturation ($S_{a,O2}$) and heart rate (HR), at rest and separately during two minutes exercise, by pulse-oximetry in eight subjects, normally resident at sea level, during a 28-day expedition in the Peruvian Andes at altitudes ranging from 3324–5176m (55–68 kPa). We assessed acute mountain sickness using the Lake Louise Consensus scoring system[(3)]. Data were collected twice daily on most days of the expedition. In all but one subject, a significant inverse relationship ($p=\leq 0.01$) was observed between all the resting HR (HRrest) and resting $S_{a,O2}$ ($S_{a,O2}$rest) values for each individual subject. Despite that, daily estimates of a surrogate for resting oxygen delivery (HRrest x $S_{a,O2}$rest) remained within a narrow, near constant, range. Mean values were calculated for $S_{a,O2}$rest, HRrest and acute mountain sickness score for the whole trip for each subject. The mean $S_{a,O2}$rest values varied from 81.3% to 93.2%. The mean HRrest also varied considerably, from 70 bpm to 106 bpm, with the coefficients of variation inversely related to $S_{a,O2}$rest values ($r=0.795$, $p=0.032$). Mean acute mountain sickness scores were significantly related to $S_{a,O2}$rest values in all but one subject ($r=0.926$, $p=0.002$). The outlier attended the expedition only for 20 days and did not undertake the exercise study. Mean individual $S_{a,O2}$ values for exercise ($S_{a,O2}$Ex) correlated with, but were significantly lower than $S_{a,O2}$rest ($S_{a,O2}Ex = 1.3363 \times S_{a,O2}rest - 33.734$, $r=0.975$, $p<0.001$). The mean acute mountain sickness scores correlated with $S_{a,O2}$Ex ($r=0.917$, $p=0.003$). Acute mountain sickness appears to be related to $S_{a,O2}$, which, in turn, indicates (inversely) the degree of respiratory compensation for ambient hypoxia. HR variation, here, suggests cardiac output compensation; such compensation appeared more pronounced in those subjects with lower $S_{a,O2}$.

Wolff CB (2007) Adv Exp Med Biol **599**, 169-182.

Wolff CB (2003) Adv Exp Med Biol **510**, 279-284.

Hackett PH & Oeltz O (1992) In: Hypoxia and Mountain Medicine, edited by Sutton JR et al. Burlington: Queen City Printers, 327-330.

The authors wish to acknowledge the advice of David Collier and thank Doug Thake for lending the team the pulse-oximeters. The expedition was made possible by generous grants from a number of organisations including the Cambridge University Expeditions Fund, the Wellington College Bevir Memorial Trust and the Selwyn College Cott Fund.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC3

The effect of l-menthol on thermoregulation and sensation during exercise in a hot and humid environment

J. Gillis, M. Barwood and M.J. Tipton

Department of Sport and Exercise Science, University of Portsmouth, Portsmouth, UK

L-menthol elicits a cool sensation when applied to the skin (McKemy *et al.,* 2002). This raises the possibility of using l-menthol to increase thermal comfort when working in the heat. Before this is recommended, the effect of l-menthol on body temperature regulation should be determined. The aim of the present study was to determine the effect of 0.2% l-menthol on body temperature regulation. It was hypothesized that there would be no difference in the measured responses between a l-menthol and Control condition during moderate and high intensity exercise. Eight volunteers visited the laboratory on three occasions separated by at least 24h. On the first day they completed a peak power test; on the second and third days they completed a 115min cycle in the heat (31□C, 70% relative humidity) comprised of a 10min warm-up cycling at 35% of peak power output (PPO), 45min of seated rest on the cycle ergometer, exercise at 45% of PPO for 40min followed by exercise at 70%PPO. Participants undertook two counterbalanced conditions: (1) upper body spraying with 0.20% l-menthol at 35, 50 and 95min (2) upper body spraying with a Control solution containing no l-menthol at corresponding times. Measures: Heart rate (HR), rectal (Tre), skin (Tskin), mean skin (MST) and mean body (Tbody) temperatures, sweat rate (SR), thermal comfort (TC), thermal sensation (TS), and irritation (IRR). Analyses were undertaken up to the 97 minute, after which time subject withdrawal reduced participant numbers. No significant differences (repeated-measures analysis of variance, $P<0.05$) were observed in HR, Tskin, MST, SR or TC, between conditions. Tre and Tbody were significantly higher ($P<0.032$) at some time points (5, 15, 25, 35, 85, 95min [pairwise comparison]), but the absolute difference between conditions was less than 0.1□C. Perceptually, participants felt significantly cooler ($P<0.023$) when l-menthol was applied, but all participants noted some form of irritation following the application of l-menthol, no irritation was reported in the Control condition. The hypothesis is supported and it is concluded that, under the conditions of the present experiment, the application of a solution containing 0.2% l-menthol does not have a detrimental impact on body temperature regulation when compared to a Control solution without l-menthol. Although l-menthol made participants feel cooler, they were no more comfortable, probably due to the irritation caused by l-menthol.

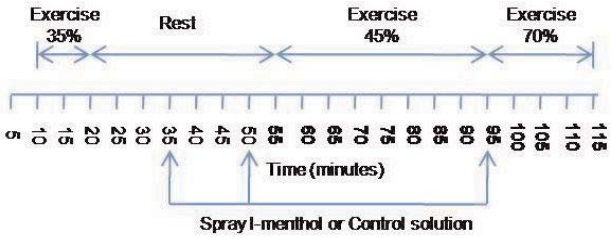


Figure 1. The experimental timeline.

McKemy, D.D., Neuhausser, W.M., Julius, D. (2002). Identification of a cold receptor reveals a general role for TRP channels in thermosensation, *Nature, 416,* 52-58.

This work was funded by UKSport.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC4

Calcium entry through TRPC1 channels induces calpain activation and controls myoblasts migration

N. Zanou, M. Louis, M. Van Schoor and P. Gailly

Physiologie cellulaire, Université catholique de Louvain, Bruxelles, Belgium

Myoblasts migration is a key step in myogenesis and regeneration. It allows myoblasts alignment and fusion into myotubes. This process has been shown to involve m- or μ-calpains, two calcium-dependent cysteine proteases. In the present paper, we measured calpain activity in situ (fluorometric measurements) and show, for the first time, a peak of activity at the beginning of the differentiation process. We also observed a concomitant and transient increase of the influx of Ca2+ and of the expression of TRPC1 protein. Besides, we recently reported that, in adult skeletal muscle fibres, calpains were specifically activated by a store-operated entry of calcium. In the present study, we therefore repressed the expression of TRPC1 in myoblasts and studied its influence on Ca2+ fluxes and on differentiation. TRPC1 knocked down myoblasts presented a largely reduced store-operated entry of calcium and a significantly diminished transient influx of calcium at the beginning of differentiation. The concomitant peak of calpain activity was abolished. TRPC1 knocked down myoblasts also presented an accumulation of myristoylated alanine-rich C-kinase substrate (MARCKS), an actin-binding protein, substrate of calpain. Finally, their fusion into myotubes was significantly slowed down, due to a reduced speed of cell migration. Accordingly, migration of control myoblasts was inhibited by 2 to 5 μM GsMTx4 toxin, an inhibitor of TRPC1 or by 50 μM Z-Leu-Leu, an inhibitor of calpain. In contrast, stimulation of control myoblasts with IGF-1 increased the basal influx of Ca2+, activated calpain and accelerated migration. These effects were not observed in TRPC1 knocked down cells. We therefore suggest that an entry of calcium through TRPC1 channels induces a transient activation of calpain, a subsequent proteolysis of MARCKS, allowing in its turn, myoblasts migration and fusion.

Leloup, L., Mazeres, G., Daury, L., Cottin, P. and Brustis, J. J. (2006). Involvement of calpains in growth factor-mediated migration. Int J Biochem Cell Biol 38, 2049-63.

Dedieu, S., Poussard, S., Mazeres, G., Grise, F., Dargelos, E., Cottin, P. and Brustis, J. J. (2004). Myoblast migration is regulated by calpain through its involvement in cell attachment and cytoskeletal organization. Exp Cell Res 292, 187-200

Ducret, T., Vandebrouck, C., Cao, M. L., Lebacq, J. and Gailly, P. (2006). Functional role of store-operated and stretch-activated channels in murine adult skeletal muscle fibres. J Physiol 575, 913-24.

Vandebrouck, A., Ducret, T., Basset, O., Sebille, S., Raymond, G., Ruegg, U., Gailly, P., Cognard, C. and Constantin, B. (2006). Regulation of store-operated calcium entries and mitochondrial uptake by minidystrophin expression in cultured myotubes. Faseb J 20, 136-8.

We thank Dr J. Lebacq and Dr N. Morel for helpful discussions. This work was supported by the

Association française contre les myopathies (AFM), the Association belge contre les maladies neuromusculaires

(ABMM), and by a grant ARC 05/10-328 from the General Direction of Scientific

Research of the French Community of Belgium.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC5

The effect of whole body vibration on muscle activity and motoneuron excitability

D. Newham[1], R. Pollock[1] and F.C. Martin[2]

[1]Division of Applied Biomedical Research, King's College London, London, UK and [2]Elderly Care Unit, Guys and St Thomas' NHS Foundation Trust, London, UK

There are contradictory reports about the effects of whole body vibration (WBV) on human performance, muscle strength, power, balance and bone mineral density (Bosco et al. 1999; de Ruiter et al. 2003). This may partly be due to differences in vibration protocols as the optimal settings are unclear, as are the mechanisms responsible for any vibration related neuromuscular improvements. We investigated the effect of high (5.5mm) and low (2.5mm) amplitude vibration at a range of frequencies (5-30 Hz) on muscle activity and also the effects of WBV on motoneuron excitability. Surface EMG (soleus, gastrocnemius lateralis, anterior tibialis, rectus femoris, biceps femoris and gluteus maximus) was recorded from 12 participants (aged 31 ± 12 years; height 1.76 ± 0.1 m; mass 72.7 ± 17.6 kg, mean + SD) during WBV and compared it with that recorded while performing a maximal voluntary contraction (MVC). The EMG signal was filtered to remove motion artefact at the vibration frequency and associated harmonics (Abercromby et al. 2007). Motoneuron excitability was determined in 12 participants (32 ± 9 years; 1.71 ± 0.1 m; 66.6 ± 15.2 kg) by the H :M ratio in the soleus muscle with percutaneous electrical stimulation before, immediately after and then 5, 10, 20 and 30 mins after a 5 min bout of WBV (30 Hz, 4 mm). Statistical analysis was performed using repeated measures ANOVA with post hoc analysis where appropriate. WBV increased activation levels of all muscles, most markedly in the lower leg (Fig.). Activity of soleus peaked at 43.4 ± 4.6% MVC (30 Hz, high amplitude, mean ± SE) compared with 23.1 ± 6.1 % in gluteus maximus (10 Hz high amplitude). The relationship between frequency and EMG activity appeared to be linear for all muscles other than rectus femoris and gluteus maximus which showed no effect of frequency. High amplitude WBV resulted in greater activation, with increases ranging from 1.2 – 20.6 % of MVC, however this was not always significant ($p<0.05$). The resting H : M (0.51 ± 0.13) was unaffected by WBV. These results indicate that WBV at high amplitudes and frequencies provides the greatest stimulus for muscle activation. The greater activity in lower leg muscles will damp vibration (Wakeling et al. 2002) and reduce that at higher segments, therefore aiding balance and stability. Whether the muscles were performing voluntary or involuntary contractions is unclear. The levels of activity would be insufficient for hypertrophy in young healthy individuals, suggesting neural mechanisms may mediate any improvements in strength and power after WBV, although they do not appear to involve changes in motoneuron excitability.

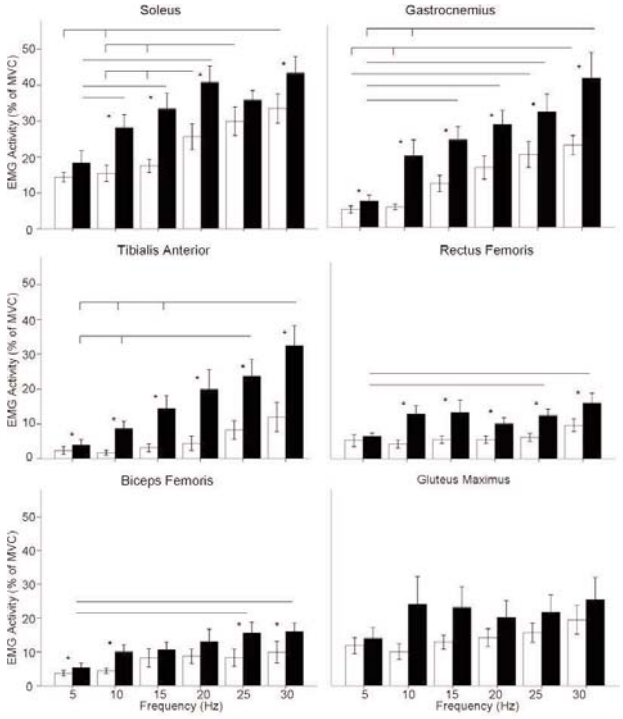


Figure. Mean ± SE of filtered EMG signal recorded in all muscles during WBV represented as a percentage of MVC activity. Black bars show activity during high amplitude vibration. White bars show activity during low amplitude vibration. Horizontal bars indicate significant difference in activity levels between frequencies during either high or low amplitude vibration ($P<0.05$). * high amplitude activity is significantly greater than low ($P<0.05$).

Abercromby AFJ et al. (2007). Medicine & Science in Sports & Exercise 39: 1642-1650.

Bosco C et al. (1999). Clinical Physiology 19: 183-187.

de Ruiter CJ et al. (2003). European Journal of Applied Physiology 88: 472-475.

Wakeling JM et al. (2002). Journal of Applied Physiology 93: 1093-1103.

We are grateful for support from Research into Ageing

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC6

Frequency domain analysis of abnormal cortical drive in individuals with congential mirror movements

S.F. Farmer[1,2], L.M. James[2,3], J.A. Stephens[3] and D.M. Halliday[4]

[1]Institute of Neurology, University College London, London, UK, [2]Neurology, Imperial College Healthcare NHS Trust, London, UK, [3]Department of Physiology, University College London, London, UK and [4]Department of Electronics, University of York, York, UK

The mechanisms of congenital mirror movements (MM) are not fully understood. We examined two contrasting hypotheses of MM production using EEG-EMG coherence and partial coherence analysis. Hypothesis 1: MM are produced by the same area of the motor cortex providing via aberrant corticospinal pathways synchronizing drive to the motoneuron pools on left and right sides of the spinal cord during attempted unilateral voluntary muscle activation. Hypothesis 2: during attempted unilateral voluntary activation there is bilateral co-activation of left and right motor cortices and it is this co-activation that produces mirrored EMG activity. We postulated that if a single cortical area is responsible for mirrored EMG activity then use of partial coherence analysis will differentiate this from a scenario in which both motor cortices activate to produce the common descending drive. We studied 6 subjects with congenital MM and 8 normal control subjects. We recorded simultaneously the EEG and right and left 1DI EMGs. During unilateral voluntary contraction in 6 MM subjects coherence was calculated between EEG contralateral to the activated hand and EMGs from the voluntarily activated and the mirroring hand. In MM subjects ~20 Hz coherence and triphasic cumulant was present between the motor cortex EEG and both EMGs. Using the mirroring EMG as predictor the partial coherence between the EEG and the activated hand EMG was calculated. In 5/6 MM subjects the partial coherence at ~20 Hz was less than the coherence-indicating that the mirroring EMG receives coherent drive from the ipsilateral motor cortex and that this drive is shared with the voluntary EMG. In 8 controls we calculated EEG-EMG coherence during bilateral activation. In controls the ~20 Hz coherence was detected between the EEG and the contralateral EMG. Calculation of the partial coherence with the ipsilateral EMG as predictor did not show a reduction. No components of the ipsilateral EMG in normals were coherent with the EEG-contralateral EMG correlation. In 4/6 MM subjects during bilateral activation task there was reduction of the EEG-EMG coherence when using the other EMG as predictor. Finally in the MM subjects we calculated EEG-EMG coherence between the EEG contralateral to the voluntarily activated hand with the ipsilateral motor cortex EEG as predictor. In no cases was the coherence reduced. Thus in the MM subjects there was no evidence for abnormal left-right EEG synchronization as a cause of MM. We conclude that the dominant mechanism underlying congenital MM is the delivery of abnormal synchronizing drive from a single area of the motor cortex that projects to the left and right motoneurone pools via contralateral and ipsilateral corticospinal pathways.

UCL Comprehensive Biomedical Research Centre

Imperial College London Academic Health Sciences Centre

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC7

Voluntary activation and force variation during maximal voluntary contraction depend on muscle temperature

M. Brazaitis[1], A. Skurvydas[1], A. Ratkevicius[2] and L. Daniuseviciute[1,3]

[1]Department of Applied Physiology and Physiotherapy, Lithuanian academy of physical education, Kaunas, Lithuania, [2]School of Medical Sciences, College of Life Sciences and Medicine, Institute of Medical Sciences, University of Aberdeen, Aberdeen, Scotland, UK and [3]Department of Physical Education, Kaunas Technological University, Kaunas, Lithuania

It is well known that high environmental temperatures are associated with impaired exercise performance and accelerated muscle fatigue (Nybo & Nielsen 2001). However, the mechanism of this phenomenon is not entirely clear. In general, exercise-induced fatigue can be due to limitations in the skeletal muscles or in the nervous system (Bigland-Ritchie et al 1986; Ratkevicius et al 1998; Streckis et al 2007). It is possible that muscular temperature plays a special role in voluntary activation of skeletal muscles. Muscle relaxation accelerates at high temperatures and could impair force generation as higher motor unit (MU) firing rates will be required to produce the same force compared to exercise at lower muscle temperatures (Todd et al 2005). However, there is little evidence to support this hypothesis and we decided to examine it in greater detail. However, force variation has not been studied during MVC at different muscle temperatures. Impairment in voluntary activation is observed during a continuous MVC (Streckis et al 2007). It can be hypothesized that force variation will be elevated during MVC at high muscle temperatures as ability to maintain voluntary activation of skeletal muscles becomes compromised. On the other hand, force variation should decrease in pre-cooled muscles as their relaxation rate would decrease facilitating force maintenance during continuous contractions. The aim was to investigate if voluntary activation (VA) and force variation during maximal voluntary contraction (MVC) depend on muscle temperature. Ten volunteers performed a 2-min MVC of the knee extensors under the control conditions as well as after the muscle heating and cooling in CON, HT and CL experiments, respectively. Peak torque, torque variation as well as muscle voluntary activation and half-relaxation time (HRT) were assessed during the exercise. Lower body heating increased muscle and core temperatures while cooling lowered muscle temperature, but did not affect core temperature. At 30-s MVC, peak torque was lower in HT compared to CON and CL experiments (52.6±2.3 vs 69.0±2.3 and 65.6±1.9% of initial MVC, respectively, $P<0.001$)(Figure 1A). From 30-s to 2-min MVC, torque remained lower, torque variation (Figure 1C) larger and VA more depressed ($P < 0.01$) (Figure 1B) in HT compared to CON and CL experiments. In CL experiment, VA was higher compared to CON experiment when assessed from 60-s to 2-min MVC which corresponded to a significant slowing in HRT (Figure 1D) of the cooled muscles. It is concluded that muscle heating impairs VA of the exercising muscles while cooling has an opposite effect. This was at least partially mediated by changes in muscle relaxation rate.

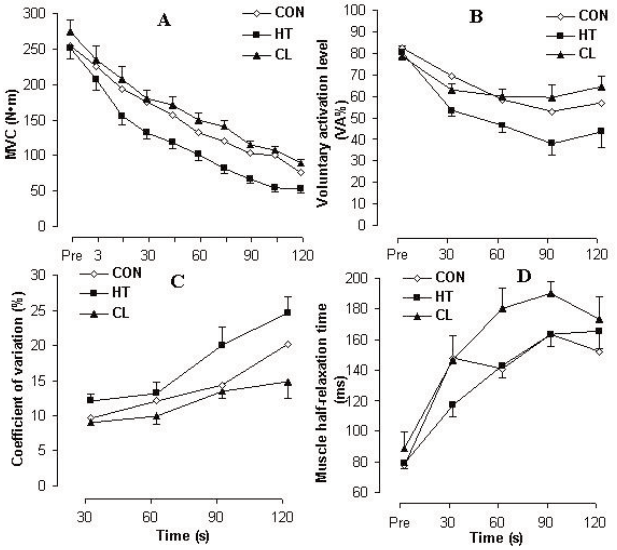


Fig 1. Peak torque (A), voluntary activation index (VA) (B), coefficient of variation (CV) (C) for torque and half-relaxation time (D) during the 2-min maximal voluntary contraction (MVC) in control (CON) experiment and experiments with body heating (HT) and cooling (CL), respectively. Values for time point 0 are taken from initial measurements using 5-s MVC efforts in these experiments. Data are means ± SEM.

NYBO, L. and B. NIELSEN. Hyperthermia and central fatigue during prolonged exercise in humans. J. Appl. Physiol. 91:1055-1060, 2001.

TODD, G., J.E. BUTLER, J.L. TAYLOR and S.C. GANDEVIA. Hyperthermia: a failure of the motor cortex and the muscle. J. Physiol. 563:621-31, 2005.

STRECKIS, V., A. SKURVYDAS and A. RATKEVICIUS. Children are more susceptible to central fatigue than adults. Muscle Nerve 36:357-363, 2007.

BIGLAND-RITCHIE, B., F. FURBUSH and J.J. WOODS. Fatigue of intermittent submaximal voluntary contractions: central and peripheral factors. J. Appl. Physiol. 61:421-429, 1986.

RATKEVICIUS, A., A. SKURVYDAS, B. QUISTORFF, E. POVILONIS and J. LEXELL. Effects of contraction duration on low-frequency fatigue in repetitive voluntary and exercise-induced exercise of human quadriceps muscle. Eur. J. Appl. Physiol. 77:462-468, 1998.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC8

The kinetics of pulmonary oxygen uptake during the transition to moderate intensity exercise from a raised metabolic rate in humans

T.S. Bowen[1], S.R. Murgatroyd[1], D.T. Cannon[1], T.J. Cuff[2], A.F. Lainey[2], A.D. Marjerrison[2], J.M. Kowalchuk[2,3] and H.B. Rossiter[1]

[1]Institute of Membrane and Systems Biology, University of Leeds, Leeds, UK, [2]School of Kinesiology, The University of Western Ontario, London, ON, Canada and [3]Department of Physiology and Pharmacology, The University of Western Ontario, London, ON, Canada

On transition to moderate intensity exercise (i.e. below the lactate threshold; LT) the rate of adaptation (τ) of pulmonary O_2 uptake (VO_2) is slower when initiated from a higher compared to a lower work rate [1-3]. This has been ascribed to a slowed adaptation in skeletal muscle blood flow [2,3] or the intrinsic properties of the recruited muscles [1]. However, the role of the pre-transition metabolic rate remains unclear. That is, are the slower VO_2 kinetics a consequence of the raised pre-transition VO_2, or due to the *de-novo* recruitment of motor units with inherently slower activation of oxidative metabolism? To elucidate this, we determined VO_2 kinetics at the onset of a step change in work rate with and without a raised metabolic rate. We hypothesised that VO_2 kinetics would be slower in the upper compared to the lower reaches of the moderate-intensity domain [1,3] due to the intrinsically slower kinetics of the newly recruited motor units, such that the τ of the fundamental VO_2 response (τVO_2) would be insensitive to an alteration of pre-transition metabolic rate. Following informed consent, 6 healthy men completed ramp-incremental cycle ergometry to the limit of tolerance to estimate LT. Subjects then completed repeats of: 1) two equal step transitions, 20W-45%LT (S1) immediately followed by 45%-90%LT (S2); 2) two exercise bouts (R1, R2), each 20W-90%LT separated by 30s at 20W to allow VO_2 to recover to ~45%LT i.e. a pre-transition level similar to S2; and 3) two bouts of 20W-90%LT exercise separated by 12 min at 20W (F1, F2). τVO_2 was estimated from breath-by-breath measurements (mass-spectrometry and turbinometry) using non-linear least squares analysis [4], and compared by repeated-measures ANOVA. The τVO_2 was 27 ± 4 s on transition from 20W-90%LT with a raised metabolic rate (R2), which was not different ($p>0.05$) from τVO_2 measured during S2 (25 ± 5 s); the pre-transition VO_2 being well matched (R2: 1.31 ± 0.11 $L.min^{-1}$; S2 1.24 ± 0.06 $L.min^{-1}$; $p>0.05$). These were both greater ($p<0.05$) than τVO_2 manifest during S1 (18 ± 5 s). As expected, τVO_2 following 'full' recovery (F2: 24 ± 4 s) was not different from control (F1: 23 ± 7 s; R1: 23 ± 3 s). These data are consistent with previous findings [1-3] that VO_2 kinetics are slower in the upper reaches of the moderate-intensity domain, but suggest that this is consequent to the high pre-transition metabolic rate. This may be due to: 1) an increased ATP production requirement when exercise is initiated from a less favourable ΔG_{ATP}; or 2) a reduction in the sensitivity of ADP-stimulated VO_2 above the Km. It is assumed that the same motor units are recruited in R1 and R2 suggesting that these mechanisms operate within the active musculature. We therefore conclude that VO_2 kinetics are sensitive to the pre-transition metabolic rate from which they are estimated.

Brittain CJ, Rossiter HB, Kowalchuk JM & Whipp BJ. (2001). Effect of prior metabolic rate on the kinetics of oxygen uptake during moderate-intensity exercise. Eur J Appl Physiol 86, 125-134.

Hughson RL & Morrissey M. (1982). Delayed kinetics of respiratory gas exchange in the transition from prior exercise. J Appl Physiol 52, 921-929.

MacPhee SL, Shoemaker JK, Paterson DH & Kowalchuk JM. (2005). Kinetics of O2 uptake, leg blood flow, and muscle deoxygenation are slowed in the upper compared with lower region of the moderate-intensity exercise domain. J Appl Physiol 99, 1822-1834.

Whipp BJ & Rossiter HB. (2005) The kinetics of oxygen uptake: physiological inferences from the parameters. In Jones AM & Poole DC (Eds). Oxygen Uptake Kinetics in Sport, Exercise and Medicine. Routledge, London, pp. 62-94.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC9

Relationship between hand grip and quadriceps strength in young and older people

D. Samuel[1], K. Wilson[1], H. Martin[2], R. Allen[3], A. Aihie Sayer[2] and M. Stokes[1]

[1]School of Health Sciences, University of Southampton, Southampton, UK, [2]MRC Epidemiology Resource Centre, University of Southampton, Southampton, UK and [3]Institute of Sound & Vibration Research, University of Southampton, Southampton, UK

Quadriceps strength is a predictor of falls in older people (1). However grip strength is easier to measure and considered a good indicator of general strength (2), and has been adopted widely in epidemiological studies. It is unclear how closely grip and quadriceps strength correlate, particularly in older people. This study aimed to determine the relationship between grip and quadriceps strength in older people. Thirty-eight adults were studied: 20 young (10 male; aged 20-32 years, mean 24) and 18 older people (9 male; 62-82 years, mean 72). Maximal voluntary contractions (MVC) of the quadriceps muscle were measured with the subject seated in a test rig with a custom-built strain gauge. Grip strength was measured using an electronic Jamar dynamometer (Biometrics Ltd, UK). The best of three isometric contractions for both muscles were used in the analysis. Grip and quadriceps strength (Newtons) were greater in young than older adults of the same gender, and greater in males than females of similar age (Table 1). When grip strength was divided by quadriceps strength to produce a ratio, the values for young adults were similar in males and females (mean ratio 0.75, indicating quadriceps was approx. 25% stronger; Table 1). The ratios were increased in older adults (p=0.5), in whom the strength of the two muscle groups was approximately equal. Pearson's correlation indicated a strong relationship between grip and quadriceps strength ($p<0.05$), with correlation coefficients (r) of 0.83 and 0.70 for the young and older groups respectively. Grip and quadriceps strength were significantly correlated in younger and older people. The reduced muscle strength in the older groups was expected but their higher grip/quadriceps strength ratios demonstrated a greater loss of quadriceps than grip strength. The older people in this study were healthy and it remains to be investigated whether the relatively greater rate of decline in quadriceps strength is more exaggerated in those who are frail.

Table 1. Grip and quadriceps strength: MVCs and ratios

Subject Group	Quadriceps MVC (N Mean (SD)	Grip Strength (N) Mean (SD)	Grip/Quads Ratio (N) Mean (SD)
Older Males	399 (99)	410 (57)	1.1 (0.3)
Older Females	225 (88)	229 (37)	1.1 (0.4)
Young Males	585 (123)	444 (92)	0.8 (0.2)
Young Females	431 (139)	298 (60)	0.7 (0.1)

Aniansson A, Zetterberg C, Hedberg M et al. (1984) Clin Orthop Rel Res 191:193-201

Lauretani F, Russo CR, Baninelli S, et al. (2003) J Appl physiol. 95: 1851-1860.

The authors wish to thank the Annual Adventure in Research Grants Scheme, University of Southampton, for financial support, and the participants who took part in the study.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC10

Changes in recumbent cycling cadence influence heart rate variability

H. Lunt, J. Corbett, M. Barwood and M. Tipton

Department of Sports and Exercise Sciences, Portsmouth University, Portsmouth, Hampshire, UK

Total power and high frequency power heart rate variability (HRV) have been reported to decline at moderate exercise intensities when cycling (Arai *et al*., 1989). This may be indicative of the withdrawal of vagal input to the sino-atrial node (Arai *et al*., 1989). Similarly, heart rate (HR) has been shown to increase with cycling cadence, at a constant power output (Gotshall *et al*., 1996). However, the effect of different cycling cadences on measures of HRV has not previously been examined; this may have important implications for studies measuring autonomic responses during cycling. The aim of the present study was to examine the effect of cadence on HRV during cycling at a constant power output. It was hypothesised that HRV would be similar when cycling at different cadences. Following receipt of ethical approval, sixteen males performed three, ten-minute periods of unloaded cycling, on an electronically braked recumbent cycle ergometer, consisting of: 1) a freely chosen cadence (FCC) whilst blinded to the pedalling rate; 2) cadence of 40 revs.min^{-1}; 3) cadence of 80 revs.min^{-1}. All conditions were performed on the same day with FCC first and the other conditions counterbalanced; each test was separated by a recovery period. A three-lead ECG trace was recorded for the calculation of total power and high frequency power using Fast Fourier Transformations. A one-way repeated measures ANOVA, was used to investigate between conditions differences in total power and high frequency power. Significant differences were examined *post-hoc* by pairwise comparisons. Statistical significance was accepted at $P<0.05$ with data presented as means (SD). The mean(SD) FCC was 57(9) revs.min^{-1}.Heart rate was higher at FCC and 80 revs.min^{-1} than 40 revs.min^{-1} (69[9]; 75[4]; 63[6], beats.min^{-1}, respectively).Total power declined with each increment in cadence (1769[1311]; 1367[997] and 925[761] ms^2, for 40 revs.min^{-1}, FCC and 80 rev.min^{-1} respectively). Differences in high frequency power were observed between the FCC and 80 revs.min^{-1} conditions (832[111] and 337[432] ms^2 respectively. It is concluded that total power and high frequency power are reduced as a consequence of increasing cycling cadence, therefore the hypothesis is rejected. This may be indicative of vagal withdrawal resulting in an elevated HR whilst cycling at a FCC and 80 revs.min^{-1}. Studies examining autonomic function during cycling should consider the confounding effects of alterations in cycling cadence.

Arai Y, Saul J, Albrecht P, Hartley L, Lilly L, Cohen R & Colucci W (1989). Modulation of cardiac autonomic activity during and immediately after exercise. *Am J Physiol* **256**, H132-141.

Gotshall R, Bauer T & Fahrner S (1996). Cycling cadence alters exercise haemodynamics. *Int J Sports Med* **17**, 17-21.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC11

Patellar tendon properties and lower limb function in patients with inflammatory arthropathies

V. Matschke[1,2], A.B. Lemmey[1], J.G. Jones[2,1], P.J. Maddison[1,2] and J.M. Thom[1]

[1]School of Sport, Health and Exercise Sciences, University of Bangor, Wales, Bangor, UK and [2]Department Of Rheumatology, Gwynedd Hospital, Bangor, Wales, UK

The structural and mechanical properties of tendons influence postural balance and physical function. Changes in patellar tendon (PT) stiffness have been shown to occur in aging, with training and following stretching exercises, and there are differences of PT stiffness between genders (Reeves *et al.* 2003, Onambélé *et al.* 2007). However, PT stiffness has not been assessed in inflammatory arthropathies. This study therefore investigated the PT properties in stable rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients.

We compared 18 RA patients (13 women, 59.0 ± 2.8 yrs, mean ± SEM) with 18 age- and sex-matched healthy controls (58.2 ± 3.2 yrs), and 7 male AS patients (54.9 ± 2.4 yrs) with 7 healthy men (56.0 ± 5.4 yrs) with paired t-tests. Force production was measured during ramped isometric voluntary knee extension contractions (MVCs) on an isokinetic dynamometer, with concurrent electromyographic recording of vastus lateralis and of biceps femoris activity to account for antagonist co-contraction torque. Resting PT length and cross-sectional area (CSA), and force-related PT elongation were assessed by ultrasonography to determine PT stiffness and Young's modulus (YM = PT stiffness x PT length / PT CSA) (Reeves *et al.* 2003). Lower body physical function was assessed using one-leg standing balance, 8-foot up and go, 50-foot walk and 30-second sit to stand tests. The study had local NHS ethics committee approval.

PT stiffness was significantly lower in RA patients compared to healthy controls by 26.6% ($p = 0.04$). There was no difference in PT CSA. YM tended to be lower in RA by 19.6%, and force production by 10.1%, but these did not reach statistical significance ($p = 0.26$ and 0.13, respectively). Physical function was reduced by 16-25% in the RA group. In the comparison of AS patients with healthy controls PT stiffness tended to be lower by 21.1%, albeit not significantly ($p = 0.16$). However, PT CSA was significantly larger in AS by 25.9% ($p = 0.01$), leading to a significant reduction in YM in AS by 38.3% ($p = 0.02$). Force production and physical function were similar in AS patients and their healthy controls.

In conclusion, although the PT size and force are not reduced in RA, there is an impairment of PT stiffness which could possibly contribute to the reduced physical function observed in RA patients. In AS, however, a thickening of the PT was observed and, with a tendency of reduced PT stiffness, a significantly reduced YM was found, although this was not accompanied by lower body functional impairment. Thus, stable RA and AS patients display differing alterations of tendon characteristics and lower body function, perhaps due to their dissimilar pathogeneses.

Reeves ND *et al.* (2003). *J Physiol.* **548**(Pt 3):971-81

Onambélé GN *et al.* (2007). *J Orthop Res* **25**(12):1635-42

Supported by a grant from the North West Wales NHS Trust.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC12

Post-exercise cooling techniques in hot, humid conditions

M.J. Barwood, S. Davey, J.R. House and M.J. Tipton

Sport and Exercise Science, University of Portsmouth, Portsmouth, Hampshire, UK

Major sporting events, some industrial processes and military operations are often held in hot or humid environmental conditions. Cooling techniques have been used to reduce the risk of heat illness following and between work bouts in the heat, this study compared the efficacy of some of these techniques. Following ethical approval a repeated measures counter-balanced experimental design was used to compare six cooling techniques: hand immersion (HI); whole body fanning (WBF); air cooled garment (ACG); liquid cooled garment (LCG); phase change garment (PCG); a natural cooling control condition (CON). The effectiveness of the cooling conditions were examined over two periods, one between and the other following, two self-paced exercise bouts in 31□C, 70%RH air. It was hypothesised that all cooling techniques would lower body temperature post-exercise in comparison with CON, with HI being the most effective. Nine males (age 22 [3] years; height 1.77 [0.04]m; mass 69.77 [7.14]kg) exercised on a treadmill at a maximal sustainable intensity until rectal temperature (Tre) reached 38.5□C following which they underwent a 15 minute cooling period. They then recommenced exercise until Tre again reached 38.5□C and subsequently undertook a further 30 minute post exercise cooling period with (0-15 min), and without face fanning (15-30 minutes); face fanning was used to assess any benefit to thermal comfort. Heart rate (HR), thermal comfort, body mass, Tre, skin and mean skin temperature (bicep, chest, thigh and calf; Ramanathan, 1964) were measured. Mean body temperature was calculated (Tb; Colin et al., 1971). Based on ∆Tb relative to CON, WBF was most effective in extracting (-) heat from the body ($P = 0.003$; WBF: -137Watts (W); PCG: -129W; HI: -64W; ACG: -46W; LCG: +38W) as a consequence of evaporating more sweat ($P = 0.008$; WBF (90.40 [0.30]%); LCG (84.00 [0.40]%); HI (83.00 [0.20]%); PCG (82.80 [0.20]%), CON (73.90 [0.40]%), ACG (69.80 [0.20]%). There were no consistent significant perceptual differences as a consequence of utilising face fanning ($P>0.05$). The hypothesis was not supported. It is concluded that those techniques (WBF, HI) that utilise physiological responses (sweating, vasodilatation) to augment cooling are likely to be more effective during short periods of cooling than techniques that attempt to override these response (LCG, PCG) and establish a conductive cooling pathway; this takes time.

Colin J, Timbal J, Houdas Y, Boutelier C and Guieu JD. Computation of mean body temperature from rectal and skin temperatures. J Appl Physiol. 1971; 31: 484-489.

Ramanathan NL. A new weighting system for mean surface temperature of the human body. J Appl Physiol. 1964; 19: 531-533.

UKSport

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC13

Twelve months exercise training alters gastrocnemius tendon properties in older women

J.M. Thom[1,2], C.I. Morse[2], O.S. Mian[3] and M.V. Narici[2]

[1]School of Sport, Health and Exercise Sciences, Bangor University, Bangor, UK, [2]Institute for Biophysical and Clinical Research into Human Movement (IRM), Manchester Metropolitan University, Manchester, UK and [3]Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, London, UK

The purpose of this study was to determine the effects of a 12 month holistic exercise training programme on gastrocnemius tendon properties of elderly females and to compare their tendon properties with that of young females.

We investigated the in-vivo mechanical tendon properties of 15 older women (OLD: age range 69-82 years) and 8 younger women (YOUNG: age range 23-30 years). From the OLD group, 14 volunteered to participate in a training programme and were randomly allocated into either a training (TRAIN; n=7) or control (CONT; n=7) group. The TRAIN group undertook a 12 month exercise programme (2 supervised 1 hour sessions and 1 home-based session per week) that consisted of resistance exercises (2-3 sets of 80-100% of 8 repetition maximum) as well as aerobics, walking, stretching and tai chi, whilst the CONT group maintained their normal daily activities. Graded maximal isometric contractions of the plantar flexors were carried out on an isokinetic dynamometer with tendon elongation recorded in real time using ultrasonography at the myotendinous junction of the gastrocnemius lateralis (GL) muscle. Tendon stiffness and Young's Modulus (YM = stiffness x resting tendon length / tendon CSA) were calculated from elongation and force; with MRI used to determine tendon CSA and ankle joint moment arm. The study had local ethics committee approval. Differences between age groups were assessed using independent T-tests and repeated measures ANOVA were used to assess timexgroup interactions.

The GL tendon stiffness at baseline in the OLD group was 60.1% (15.1 ± 1.7 v 25.1 ± 5.3 N.mm^{-1}; mean ± SEM; $P<0.05$) and the YM was 53.0% of that of the YOUNG group ($P<0.01$). Tendon stiffness increased 84% in the TRAIN group following the 12 month exercise programme from 16.1 ± 2.4 N.mm^{-1} to 29.6 ± 4.3 N.mm^{-1} ($P=0.01$). The observed increased stiffness in TRAIN resulted to a greater extent from less tendon elongation (44.6%) than greater force production (4.6%) post training. YM increased 86% in the TRAIN group following the training programme ($P<0.01$). The stiffness and YM of the GL tendon in the CONT group did not significantly change during this period. Carroll *et al.* (2008) recently observed no differences in patellar tendon stiffness with ageing. Site-specific differences and a greater loading due to increased body mass in their older group may explain the discrepancies. In conclusion, although the OLD had significantly lower tendon stiffness and YM prior to training than that of the YOUNG, the values between the TRAIN group and the YOUNG after the 12 month training programme were comparable. Thus showing that the age related decrease in tendon stiffness can be improved by an exercise programme that has shown holistic beneficial effects in elderly populations.

Carroll CC *et al.* (2008). J Appl Physiol **105**, 1907-1915.

Supported by European Commission Framework V funding (Better-Ageing project, No. QLRT-2001-00323)

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC14

Differential effects of endotoxaemia on protein metabolism in fast-twitch skeletal muscle and myocardium of the rat

A.J. Murton, N. Alamdari, S.M. Gardiner, D. Constantin-Teodosiu, R. Layfield, T. Bennett and P.L. Greenhaff

Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, The University of Nottingham, Nottingham, UK

It is unclear whether during endotoxaemia, the myocardium is protected from the same rapid reduction in protein content that is classically observed in fast-twitch skeletal muscle (Crossland *et al.*, 2008) and if so, whether this is reflected by differential responses in the molecular mechanisms thought to regulate tissue protein content. To investigate this further, conscious male Sprague Dawley rats, previously implanted with jugular venous catheters under general anaesthesia (fentanyl and medetomidine, 300 μg kg^{-1} each i.p.), were administered lipopolysaccharide intravenously for 24 h (LPS; 150 μg kg^{-1} h^{-1}; n=6) or, as means of a control, saline (0.4 ml h^{-1}; n=8), after which the extensor digitorum longus (EDL) and myocardium were removed under terminal anaesthesia (sodium pentobarbital, i.v.). The protein-to-DNA ratio, a marker of protein content, was significantly reduced in the EDL following LPS infusion (23% ± 17% (SE); $P<0.05$), but was no different from controls in the myocardium. Furthermore, a significant increase in components associated with ubiquitin-proteasome mediated protein degradation, namely MAFbx, MuRF1 and 20S proteasome subunit α1 mRNA levels, was observed in the EDL compared to control, but not in the myocardium (Table 1). In contrast, an elevation in phosphorylation of p70 S6K Thr^{421}/Ser^{424} residues ($P<0.05$), and 4E-BP1 Thr^{37}/Thr^{46} residues ($P<0.05$), was seen exclusively in the myocardium of LPS-treated animals (Fig. 1), consistent with an elevation in protein translation initiation. In summary, these findings suggest that the myocardium does not undergo the same atrophy response as skeletal muscle dur-

ing endotoxaemia, at least partly due to the absence of genomic and signalling events in the myocardium typically associated with increased muscle proteolysis and the suppression of protein synthesis.

TABLE 1: Fold changes in MuRF1, MAFbx and proteasome subunit α1 mRNA levels from corresponding control value in EDL and myocardium in response to LPS.

	MuRF1	MAFbx	Proteasome subunit α1
EDL	19.5 ± 1.9 †	3.7 ± 0.7 †	4.2 ± 0.6 †
Myocardium	0.8 ± 0.2	0.6 ± 0.2	1.5 ± 0.1 †

Values are mean ± SE. Indicates different from control (P<0.05 ANOVA)

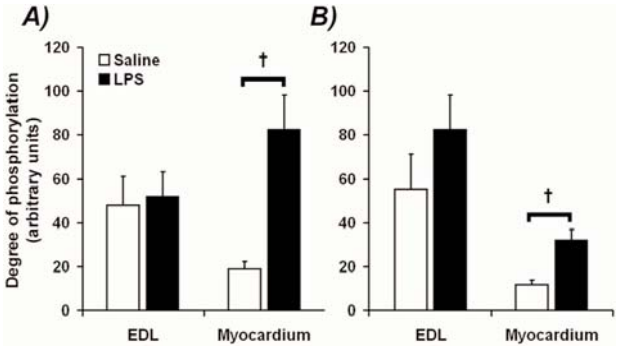


FIGURE 1: A) p70 S6K Thr^{421}/Ser^{424} and B) 4E-BP1 Thr^{37}/Thr^{46} phosphorylation in EDL and myocardium in response to LPS infusion. Values are mean ± SE (arbitrary units). significantly different from control (P<0.05 ANOVA).

Crossland H. *et al.*, (2008) J Physiol **586**, 5589-5600.

This work was funded by the Medical Research Council.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC15

Skeletal muscle fibre size and function of the myostatin null mouse in response to exercise

A. Matsakas[1], A. Otto[1], R. Macharia[2] and K. Patel[1]

[1]School of Biological Sciences, University of Reading, Reading, UK and [2]Royal Veterinary College, London, UK

Myostatin is a potent inhibitor of skeletal muscle development. Absence of myostatin results in an hypermuscular phenotype through a combination of fibre hypertrophy and hyperplasia. However, the myostatin null mouse has been shown to be weaker than wild-type animals with a compromised capacity to generate force (Amthor et al. 2007). The aim of this study was to determine the response of myostatin null muscle to chronic exercise, assessed through physiological, histological and morphological analysis of the extensor digitorum longus muscle (EDL). Two different exercise regimes were used; compulsory swim activity or spontaneous running activity for 5 weeks. Both exercise regimes undertaken by the animals in this study resulted in an increase in specific force in the null group but no differences were induced in the wild type. The two groups responded independently to exercise in terms of fibre composition. In the trained wild type mice a bidirectional shift was detected, from either type I or IIX/B towards IIA (Table 1).

In contrast the myostatin nulls displayed a slight general glycolytic to oxidative transition. Trained animals responded in changes to fibre size dependent on genotype and exercise regime (Figure). Morphometric analysis showed that the IIB fibres of the wild type EDL displayed a remarkable decrease in area of 43% in response to spontaneous running activity, while the myostatin nulls showed only a reduction of 22%. Swim training resulted in 34% and 26% smaller cross sectional areas in the null and wild type groups respectively. In addition, elevated nuclear to cytoplasmic ratio was obeserved in both genotypes following exercise training, with more pronounced changes in the wild type animals. These data provide novel evidence that the myostatin null muscle is generally less plastic that the wild type muscle with regard to long term muscle activity and less prone to changes in myofibre phenotype.

	EDL					
Groups	**I**	**I/IIa**	**IIa**	**IIa/IIx**	**IIx**	**IIb**
MSTN +/+ sedentary	3.1±0.8[d]	5.0±1.6	0.8±0.4	0.5±0.2	21.3±1.9[b]	69.3±0.8[a]
MSTN -/- sedentary	-	0.4±0.4	2.2±1.1[c]	0.2±0.2	11.2±2.4	86.0±4.1
MSTN +/+ wheel running	0.3±0.3[d]	4.3±1.7	5.4±1.0	0.3±0.4	22.6±2.1[b]	67.1±2.8[a]
MSTN -/- wheel running	-	1.3±0.9	2.4±2.0	0.1±0.1	14.5±2.8	81.8±3.5
MSTN +/+ swimming	1.7±0.5[d]	6.6±0.7	1.4±1.1	0.7±0.3	28.5±0.5[b]	61.1±1.5[a]
MSTN -/- swimming	0.7±0.5	1.1±0.9	0.3±0.3[c]	0.2±0.2	14.2±6.1	83.6±8.3

Table 1. Myosin heavy chain isoform profile of the EDL muscle given in percentage

Cells with the same symbol (a,b,c,d) differ at the p≤0.05 level, n=4-6 animals per group, mean±SD

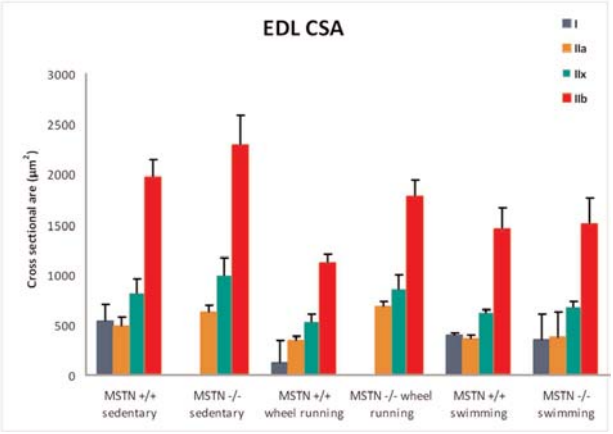


Figure. Myofibre cross sectional area of the extensor digitorum longus muscle

Amthor H, Macharia R, Navarrete R, Schuelke M, Brown SC, Otto A, Voit T, Muntoni F, Vrbóva G, Partridge T, Zammit P, Bunger L, Patel K. Lack of myostatin results in excessive muscle growth but impaired force generation. Proc Natl Acad Sci. 2007, 104:1835-1840

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC16

Can brain activity be used as an objective measure of thermal perception?

S.L. Davey[1], M. Tipton[1] and J. Holman[2]

[1]Sport & Exercise, University of Portsmouth, Portsmouth, UK and [2]Dept. of Electroencephalography, St. Mary's Hospital, Portsmouth, UK

Subjective measurements of thermal comfort (TC) and temperature sensation (TS) are used to assess thermal environments, but tend to have large inter-individual variability, making them unsuitable for group descriptions of subjective feelings. As a consequence a more objective measure of thermal perception would be useful.

Nielsen et al (2001), found a strong relationship between oesophageal temperature (T_{oes}) and the α/β index of electroencephalographic (EEG) activity during cycling in the heat. When a similar protocol was followed, a relationship between the subjective measurement of rating of perceived exertion (RPE) and T_{oes} was established (Nybo & Nielsen, 2001). As TC and TS are correlated with both T_{oes} and RPE (via body temperature), the possibility exists that α/β index reflects TC and TS rather than T_{oes}. This hypothesis was tested in the present experiment.

Following ethical approval and informed consent, the EEG activity of fifteen cortical regions (F_4,F_3,F_7,F_8,C_4,C_3,C_z,P_4,P_3,O_2,O_1,T_4,T_3) were recorded (Trackit T24, Lifelines, UK) in five physically active males during three, 20 minute periods of cycling at work intensities that elicited 50, 75, and 85% of maximum heart rate, followed by 40 minutes of rest. Each trial was conducted in 35ºC air, 50% RH. Fast Fourier transformation was used to obtain power spectrum areas in α (8-13 Hz) and β (13-13 Hz). Percentage change of α and α/β activity from rest were used as indicators of arousal level (Nielsen et al, 2001). TC, TS, RPE and rectal temperature (T_{RE}) were also measured alongside the EEG recordings. Pearson correlation coefficients were used to describe any relationships. Paired-sample t-tests were used to analyse comparisons.

During exercise T_{RE} increased by 1.02 ± 0.3□C to 38.51± 0.52□C. Increases in TRE and RPE were significantly correlated ($r = 0.91$; $P<0.001$). Increases in T_{RE} were associated with an elevated α activity in the frontal regions F_3 ($r = 0.567$; $P<0.05$) and F_7 ($r = 0.66$; $P<0.05$). Elevations in α activity and RPE were also correlated in these regions (F_3: $r = 0.66$; $P < 0.05$; F_7: $r = 0.56$; $P<0.05$). No relationships were established between α and α/β activity and TS or TC. With the omission of RPE, by comparing α and α/β activity during and post-exercise rest, at the same T_{RE}, α/β activity was only significantly elevated at the cortical region F_4 (9.00 ± 22.37% vs. 33.24 ± 10.66%; $P<0.05$). However, a 1□C increase in T_{RE} caused an increase ($P<0.05$) in α/β activity in all the frontal regions (F_3: 4.31 ± 32.52% vs. 58.99 ± 50.00; F_4: 11.50 ± 12.68% vs. 48.74 ± 17.12; F_7: -7.59 ± 10.87% vs. 55.04 ± 30.16%; F_8: 1.78 ± 17.22% vs. 45.77 ± 24.12%).

It is concluded that changes in brain activity are not a valid objective measurement of TC and TS. Therefore, the experimental hypothesis is rejected. Brain activity also appears to be associated with alterations in T_{RE} rather than RPE.

Neilsen, B. et al (2001) Brain activity and fatigue during prolonged exercise in the heat. Eur J Physiol 442: 41-8.

Nybo, L. & Nielsen, B. (2001) Perceived exertion is associated with an altered brain activity during exercise with progressive hyperthermia. J Appl Physiol 91: 2017–23.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC17

Schizotypal personality traits and olfactory acuity in a normal population

N. Flaum and T. Jacob

School of Biosciences, Cardiff University, Cardiff, UK

Smell, emotions, memory and cognitive functions are strongly related and olfactory deficits are present in many neurodegenerative diseases, e.g. Parkinson's disease, Alzheimer's disease, Huntington's disease, multiple sclerosis and significantly schizophrenia, as well as some other disorders, e.g. epilepsy, migraine, depression and obsessive compulsive disorder. The close connections between brain structures involved in olfactory processing and those in personality and emotions, principally limbic and orbitofrontal cortical structures, are thought to be responsible. Smaller hippocampus and amygdala volumes have been found to correlate with olfactory ability in young schizophrenics (Rupp et al, 2005). We set out to investigate the relationship between schizotypal personality traits and olfactory ability in a healthy population of 100 university students (50 male, 50 female) aged 18-30 years. Subjects completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) of 74 questions (the higher the score the greater the schizotypal personality) and their olfactory function was measured using the University of Pennsylvania Smell Identification Test (UPSIT; max. score 40). They also answered a questionnaire concerning their age, gender, stage of menstrual cycle and oral contraceptive use in women, drug, cannabis and cigarette use, and family and personal history of any relevant neurological or psychiatric condition. Normally distributed SPQ scores between 0-45 were found, with a mean (± standard deviation) of 18.44 (±10.48). For the UPSIT the scores ranged from 21-38 with a mean of 31.06 (±3.67). A significant negative correlation between SPQ and UPSIT values was found ($p = 0.031$). This was stronger in women, and for the negative SPQ subscore. Women showed greater olfactory acuity ($p = 0.009$). The effects of menstrual cycle and oral contraceptives were not significant. Drug and cannabis use, despite previous findings that various drugs damage olfactory acuity and that cannabis use is correlated with increased schizotypal scores (Dumas et al., 2002), had no significant effect. Family history of depression was linked to lower UPSIT and higher negative SPQ subscores ($p=0.025$) indicating a possible genetic component. Smokers had significantly higher SPQ scores ($p = 0.017$), especially in positive ($p = 0.019$) and disorganised subscores ($p = 0.013$). The results suggest that olfactory deficits are proportionally related to degree of schizotypy. This negative correlation between olfactory function and schitzotypal personality has not been recorded before in a healthy population. If olfactory deficits in schizophrenia are related to the pathology of personality disorders in a graded manner, this pro-

vides further insight into the pathology of these conditions. This relationship is influenced by a number of other factors, principally gender, smoking and family history.

Dumas, P. et al. (2002) Psychiatry Res 109, 27-35.

Raine, A. (1991) Schizophrenia Bull. 17, 555-564.

Rupp, C.I. et al. (2005) Schizophrenia Res 1374, 149-161.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC18

The time course of myonuclear accretion during hypertrophy in young adult and old rat plantaris muscle

S.F. Van der Meer[1], R.T. Jaspers[2], D.A. Jones[1] and H. Degens[1]

[1]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK and [2]Research Institute MOVE; Faculty of Human Movement Sciences, VU University Amsterdam, Amsterdam, Netherlands

Muscle hypertrophy involves the activation and incorporation of satellite cell nuclei into existing muscle fibres, to keep the myonuclear domain relatively constant (1). However, it is not known whether accretion of myonuclei precedes or follows the increase in fibre cross-sectional area and whether this time-course is affected by age. The left plantaris muscle of 5- and 25-month-old male Wistar rats was overloaded by denervation of its synergists for 1, 2 or 4 weeks (n=3-5) with the contra-lateral plantaris muscle serving as control. All surgeries were carried out under isoflurane anaesthesia and aseptic conditions. During the terminal experiment the animals were killed by an intraperitoneal injection of an overdose of pentobarbital sodium. Myonuclei were counted in haematoxylin-stained cross-sections. Data were analysed with ANOVA. Myonuclear domain of type I was smaller than that of type II fibres ($p = 0.001$). Moreover, the myonuclear domain of type II fibres was larger in the glyocolytic than in the oxidative regions of the muscle ($p = 0.007$). This indicates that the number of myonuclei per muscle fibre is not only determined by size, but also by fibre type and location of the fibre in the muscle. The proportion of central nuclei was approximately ten times higher in old than in young adult muscles irrespective of overload ($p < 0.001$). While muscle hypertrophy became significant two weeks after overload (33% in young adult; $p = 0.008$), the increase in myonuclear number was significant only at four weeks of overload ($p < 0.0001$). The time course and magnitude of hypertrophy was similar in young adult and old rats. In conclusion, our data indicate that acquisition of new myonuclei is not necessary for the initial hypertrophy. In addition, despite indications in the literature that muscle regeneration is impaired in 25-month-old rats our study shows that the ability to develop hypertrophy was not attenuated or delayed at this age.

Allen, D.L., R.R. Roy, V.R. Edgerton, 1999. Myonuclear domains in muscle adaptation and disease. Muscle Nerve 22:1350-1360.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC19

Posture dependent changes in motor responses of ankle dorsi- and plantar flexors to transcranial magnetic stimulation

K.N. Mileva[1], J.L. Bowtell[1] and A.R. Kossev[2]

[1]Academy of Sport, FESBE, London South Bank University, London, UK and [2]Institute of Biophysics, Bulgarian Academy of Sciences, Sofia, Bulgaria

The aim of this study was to investigate the corticospinal and intracortical excitability associated with ankle extensor and flexor muscle activation during postural tasks. Motor evoked potentials (MEPs) evoked by transcranial magnetic stimulation (TMS) of the leg area of the motor cortex were recorded in tibialis anterior (TA) and soleus (SOL) muscles of 7 healthy male adults (mean±SEM, 36±4y, 181±3cm, 82±5kg) whilst in upright standing (110s) and static squat (330s). Five single suprathreshold (120% resting TA motor threshold) and five paired TMS pulses were delivered during each condition (short-interval intracortical inhibition, SICI, interstimulus interval, ISI=3ms; or intracortical facilitation, ICF, ISI=13ms). Data were analysed using 2-way repeated measures ANOVA, and post hoc tests with Holm-Sidak corrections where appropriate. During standing TA MEP responses to single TMS were not significantly different from SOL although background SOL EMG activation was more than 5 times higher than TA (523±127%, $p=0.018$, Fig 1). TA MEP amplitudes were significantly higher at ISI=13ms (80±24%, $p=0.009$) and lower at ISI=3ms (-33±15%, $p=0.050$) compared to SOL MEPs indicative of increased ICF and SICI to TA motoneurons during standing. Single TMS during squat evoked significantly higher MEP amplitudes in TA than in SOL (194±69%, $p=0.008$) although background SOL EMG activity was almost 4 times higher than in TA (402±152%, $p=0.014$). During squat, TA MEP amplitudes at both ISI=13ms and ISI=3ms were not significantly different from SOL. TA EMG background activity (42±9%, $p=0.037$), TA MEP amplitude (253±112%, $p=0.002$) and total area (254±106%, $p=0.017$) in response to single TMS were significantly higher during squat than standing. During squat compared to standing, MEPs in both muscles at ISI=3ms tended to be only slightly higher, whereas TA but not SOL MEPs at ISI=13ms were significantly smaller (-35±7%, $p=0.007$). Neither SOL background activity nor SOL MEP parameters were different between standing and squat. Excitability of the cortical representations of lower leg muscles appears to be muscle and task-specific and may be differentially modulated according to the postural role of the muscle. SICI and ICF networks can be modulated independently and as for arm and hand muscles, disinhibition appears to be a more important mechanism for plastic intracortical changes than increased facilitation.

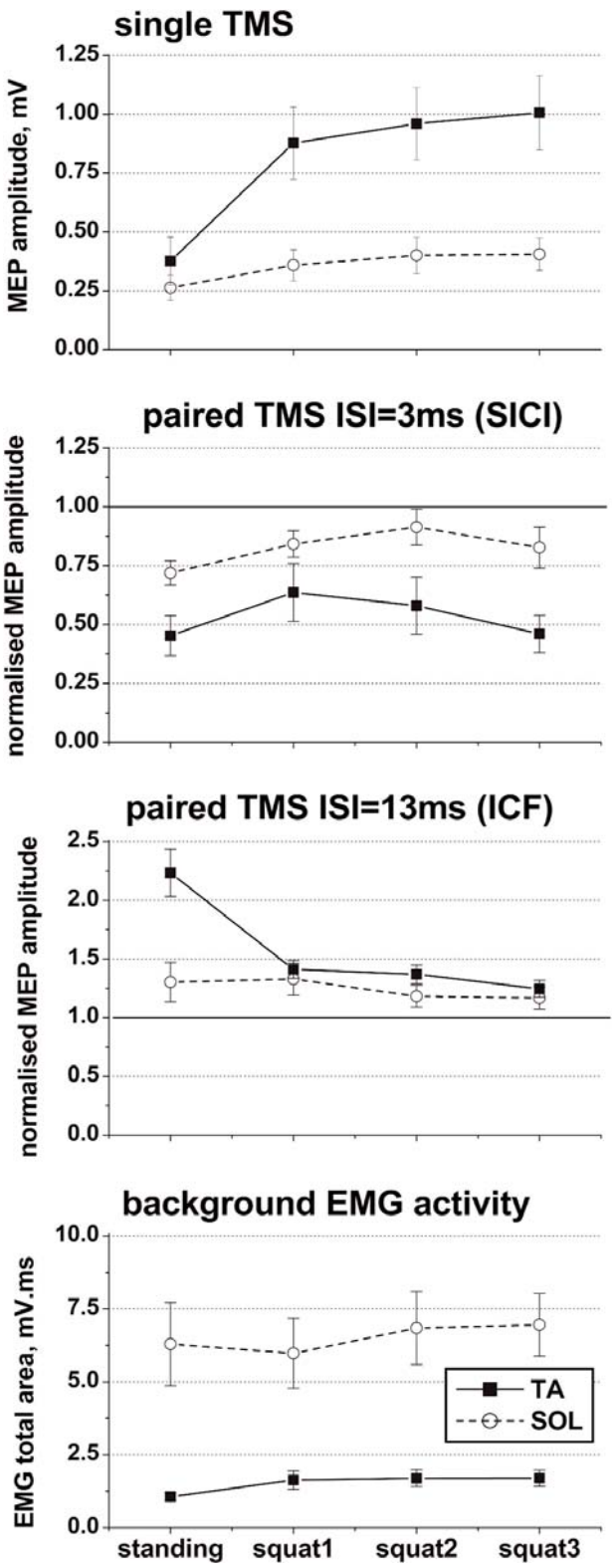


Figure 1: Tibialis anterior (TA) and soleus (SOL) motor evoked responses (MEP, mean±SEM, n=7) to single and paired TMS during standing and static squat at 30deg knee flexion angle.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC20

Muscle O_2 delivery-to-consumption matching at the limit of tolerance during ramp incremental exercise in men exhibiting a plateau in O_2 uptake

D.T. Cannon[1], S.R. Murgatroyd[1], T.S. Bowen[1], J.M. Kowalchuk[2,3] and H.B. Rossiter[1]

[1]Institute of Membrane and Systems Biology, Faculty of Biological Sciences, University of Leeds, Leeds, UK, [2]School of Kinesiology, Faculty of Health Sciences, The University of Western Ontario, London, ON, Canada and [3]Department of Physiology and Pharmacology, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, ON, Canada

The matching of muscle O_2 delivery (Q) to muscle O_2 consumption (mVO_2) is a key determinant of the ability to sustain exercise [1]. During exercise at VO_2max, respiratory muscle activity may necessitate redistribution of cardiac output from locomotor to respiratory muscles [2]. Near-infrared spectroscopy (NIRS) provides a non-invasive mVO_2/Q estimate via measurement of [deoxyhaemoglobin] change (Δ[HHb]), yet the relative contribution of VO_2 and Q to Δ[HHb] is typically not interpretable. However, a plateau in pulmonary O_2 uptake (pVO_2) during ramp-incremental exercise (RI) provides a scenario by which Δ[HHb] largely reflects changes in Q, assuming mVO_2 remains constant. Thus, the aim of this study was to examine mVO_2/Q matching in the vastus lateralis (VL) during a pVO_2 plateau. We hypothesised that, at VO_2max, Δ[HHb] would increase consequent to a redistribution of Q away from the locomotor muscles. Six healthy males (24 ± 4 yr; 185 ± 2 cm; 76 ± 6.3 kg), identified as exhibiting a pVO_2 plateau [cf. 3], completed RI cycle ergometry (20 W.min^{-1}) to the limit of tolerance. pVO_2 was measured breath-by-breath (mass spectrometry and turbinometry) and VL Δ[HHb] was measured using NIRS (NIRO-200). Δ[HHb]peak was determined from repeated maximal isometric contractions. The Δ[HHb] profile during RI was characterised by a sigmoid [4]: $\Delta[HHb] = A_0 + A / (1 + e^{-[-c+(d*t)]})$. The fitting window for Δ[HHb] spanned from RI onset to 60 s prior to the pVO_2 plateau, whence the model was projected forward to volitional exhaustion. This allowed comparison of the measured Δ[HHb] with the predicted value: A relative hypo- or hyper-perfusion state being estimated from an under- or over-prediction of the model, respectively. The pVO_2max plateau (4.08 ± 0.45 L.min^{-1}) averaged 69 ± 31 s (range 34 – 126 s) before termination. Ventilation (V_E) increased by 19.0 ± 10.6 L.min^{-1} during this time, reaching a peak of 178 ± 16 L.min^{-1}. The Δ[HHb] response to RI was well characterised by a sigmoid (R^2 = 0.92 - 0.99). At the limit of tolerance the predicted Δ[HHb] was 102 ± 4 % of the measured value, but with a Δ[HHb] 'reserve' demonstrated by Δ[HHb]peak (135 ± 21%). These data indicated mVO_2/Q matching in the VL during exercise at VO_2max, despite increased energetic demands from both the locomotor and respiratory muscles. The VO_2 requirement of the respiratory muscles at high V_E has been estimated to be >3 mL.min^{-1} VO_2 per L.min^{-1} V_E [5]. In the present investigation this equates to ~15% of the VO_2 increment in RI, which may be expected to manifest in a delivery-to-consumption mismatch in the locomotor muscles [2]. Conversely, these data suggest that in healthy young males mVO_2/Q in the VL is main-

tained at the limit of tolerance during cycling at pVO_2max despite the increased energetic demands of both locomotor and respiratory muscles.

Whipp BJ, Rossiter HB & Ward SA. (2002). Exertional oxygen uptake kinetics: a stamen of stamina? Biochem Soc Trans 30, 237-247.

Harms CA, Wetter TJ, McClaran SR, Pegelow DF, Nickele GA, Nelson WB, Hanson P & Dempsey JA. (1998). Effects of respiratory muscle work on cardiac output and its distribution during maximal exercise. J Appl Physiol 85, 609-618.

Day JR, Rossiter HB, Coats EM, Skasick A & Whipp BJ. (2003). The maximally attainable VO2 during exercise in humans: the peak vs. maximum issue. J Appl Physiol 95, 1901-1907.

Ferreira LF, Koga S & Barstow TJ. (2007). Dynamics of noninvasively estimated microvascular O2 extraction during ramp exercise. J Appl Physiol 103, 1999-2004.

Dempsey JA, Harms CA & Ainsworth DM. (1996). Respiratory muscle perfusion and energetics during exercise. Med Sci Sports Exerc 28, 1123-1128.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC21

The effect of contrast hydrotherapy following repeated Wingate tests on blood lactate clearance and subsequent exercise performance

D. Crampton[1], B. Donne[1], M. Egana[1] and S. Warmington[2]

[1]Department of Physiology, Trinity College Dublin, Dublin, Ireland and [2]School of Exercise and Nutrition Sciences, Deakin University, Melbourne, VIC, Australia

Contrast hydrotherapy comprises immersion in alternating cold and warm water baths during a period of recovery from exercise and is postulated to facilitate lactate clearance following high-intensity exercise by inducing fluctuations in muscle blood flow[1]. However, research has yet to identify the most effective duration, absolute temperature and time ratio of cold to warm water immersion. The present study compared a 30 min passive non-immersed recovery (PASS) with two separate cold (8□C) to warm (40□C) water contrast ratios (CON1=1:1 and CON2=1:4)to examine BLa clearance and subsequent performance following high-intensity exercise.

Eight active, male volunteers (25±3 yr; 82±6 kg; 180±9 cm) completed three trials separated by at least 7 days. For each trial, subjects completed three 30 s Wingate tests with 4 min rest interspersed, followed by a 30 min randomised recovery intervention. Post recovery, the Wingate tests (WAnT1, WAnT2, WAnT3) were repeated. Ethical approval for the study was granted by the Health Sciences Research Ethics Committee, Trinity College Dublin.

Data was analysed using a two-way repeated measures ANOVA and the Holm-Sidak method of *post-hoc* analysis (data presented as mean±SD). BLa concentration was significantly lower at 1 and 2.5 min of recovery in CON1 and CON2 compared with PASS (9.6±2.4, 9.7±2.3, 13.1±2.3 $mmol.l^{-1}$ and 9.8±2.3, 11.1±3.2, 13.1±1.8 $mmol.l^{-1}$ for CON1, CON2 and PASS at 1 and 2.5 min respectively; $P<0.05$). There were no differences in BLa between interventions at any other time during recovery. Post recovery, mean power (MP) was significantly higher ($P<0.05$) for WAnT1 in both CON1 and CON2 (669±71, 681±70W) compared with PASS (651±76W). For WAnT2, MP was significantly higher ($P<0.05$) in CON2 (657±52W) compared with CON1 and PASS (647±43, 628±57W). A similar finding was observed for WAnT3 (632±53W for CON2; 616±50 for CON1 and 602±45W for PASS).

In conclusion, lower BLa recorded at 1 and 2.5 min during recovery suggests that independent of the immersion protocol, contrast hydrotherapy affects immediate BLa kinetics following repeated Wingate tests. However, this effect was not sustained over the duration of the 30 min recovery period. Contrast immersion improved mean power output during subsequent high-intensity exercise with the 1:4 ratio of cold to warm water appearing more effective.

Fiscus KA *et al.* (2005). Changes in lower leg blood flow during warm, cold, and contrast water therapy. *Arch Phys Med Rehabil* **86**, 1404-1410.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC22

Expression of nucleoside transporters in the rat cardiac muscle: effects of streptozotocin-induced diabetes

S. Omar, A. Al-Turki, S. Malatiali and Z. Redzic

Physiology, Kuwait University, Kuwait, Kuwait

It has been shown in the rat that insulin affects expression of the rat equilibrative nucleoside transporter (rENT)2 and rat concentrative nucleoside transporter (rCNT)1 and 2 in cardiac fibroblasts (1) and adenosine uptake by cardiac myocytes (2). The aim of this study was to explore the effects of streptozotocin(STZ)-induced diabetes in rat on the expression of rENT1 and 2 and rCNT1, 2 and 3 in the heart. Diabetes was induced in Sprague-Dawley rats by an i.p. injection of STZ (60 mg/kg); controls were treated with vehicle. Diabetes was confirmed by plasma glucose >17 mM. Rats were sacrificed after 4 weeks, cardiac muscle samples were carefully collected and frozen in liquid nitrogen. Real time polymerase chain reaction was used to estimate the threshold cycles for target amplification (Ct) values. The difference between the Ct values for ENTs and CNTs and the Ct values for the housekeeping gene beta actin was calculated (ΔCt) and the difference between diabetic group and control group tested for significance as explained earlier (3). Data are presented as mean±S.D., n=3. Results revealed that the Ct value of beta actin did not differ significantly between the diabetic group (19.6±0.48) and control group (19.58±0.09, $p>0.05$), so, this gene was used as the endogenous control for the subsequent quantification of rENT1, rENT2, rCNT1, rCNT2 and rCNT3 gene expression. In the control group, the mRNA for rCNT2 and for rENT2 was abundant, with the ΔCt 2.4±0.4 and 4.3±0.3.7, respectively. The mRNA for rENT1 and the mRNA for rCNT1 were less abundant (ΔCt 7.4±0.6 and 8.1±0.1, respectively), while the mRNA for rCNT3 was either absent or of very low abundance. Four-week diabetes has caused significant decrease in the amount of mRNA for rCNT1 (ΔCt 9.19±0.31, $p<0.05$ vs control), while the ΔCt values for other nucleoside

transporters did not change significantly. The observed changes in rCNT1 mRNA amount may indicate a decrease in the amount of this pyrimidine-preferable transporter in the plasma-membrane, which in turn could reduce uptake of pyrimidines by cardiac muscle in diabetes.

Podgorska M et al. (2007) Arch Biochem Biophys 464: 344-9.

Podgorska et al., (2006) Basic Res Cardiol 101: 214-22.

Livak and Schmittgen (2001) Methods 25: 402-8.

This work was partially supported by the Kuwait University Research Administration grant No YM 04/07.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC23

Resistance training with blood flow restriction enhances the gains in calf strength parameters in older people

S. Patterson and R. Ferguson

School of Sport and Exercise Sciences, Loughborough University, Loughborough, Leicestershire, UK

Improvements in strength in older people can be brought about using progressive resistance training, using intensities in excess of 75% 1 repetition-maximum (1RM). Studies in young people have shown that low intensity (20–50% 1RM) resistance training with blood flow restriction enhances the gains in strength compared to resistance training alone (Takarada et al, 2000). However, the effect of resistance training with blood flow restriction in older people is not known. The purpose of this study was to determine the effect of resistance training combined with blood flow restriction on strength parameters of older people. 11 untrained participants (68(2)yr,170(7)cm,78(8)kg)volunteered for the study which had ethics approval. Participants trained 3 days per week for 4 weeks consisting of 3 sets of dynamic calf plantar-flexion to failure with 1 min rest. Both limbs were trained at 25% 1RM, one without and the other with blood flow restriction (110 mmHg) above the knee. 1RM, MVC and isokinetic torque (30, 60 & 120□.sec) were measured pre- and post-training. Statistical analysis were performed using a repeated measures two way (time x limb) ANOVA. Data are expressed as means ± standard deviation (SD). 1 RM was similar between limbs at baseline however the increase was greater in the restricted limb compared with normal blood flow (14 vs. 4%, respectively, P<0.01). MVC increased to a greater extent following resistance training with blood flow restriction compared to normal blood flow (18% vs. 4%, respectively P<0.01). Isokinetic torque at 30□.sec increased (P<0.01) by 20% compared to no change in restricted and normal, respectively. Isokinetic torque increased by 17% and 4% for the restricted and normal blood flow limbs at 60□.s-1 (main effect for time, P<0.01) and similarly by 11% and 3% at 120□.s-1 (main effect for time, P<0.01), for restricted and normal blood flow, respectively, with no differences between limbs at either speed. We have demonstrated that 4 weeks resistance training at 25% 1RM with blood flow restriction increases strength in older people by a greater extent compared to resistance training alone. Low intensity resistance training with blood flow restriction may be of benefit to individuals who cannot perform high weight loads, such as frail elderly people.

Changes in strength parameters following 4 weeks resistance training with (Restricted) and without (Normal) blood flow restriction.

Strength Parameter	Normal		Restricted	
	Pre	Post	Pre	Post
1RM (kg)	150(25)	155(25)	148(25)	168(25)*
MVC (N.m)	92(26)	95(25)	85(20)	100(26)*
30°.s (N.m)	92(25)	92(26)	83(27)	96(21)*
60°.s (N.m)	66(19)	69(20)	62(21)	69(18)
120°.s (N.m)	43(15)	44(15)	41(16)	45(16)

Values are means ± (SD). * significant (P<0.01) interaction between normal and restricted.

Takarada Y et al (2000). J. Appl. Physiol. 88: 2097-2106

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC24

ECG during the first helicopter underwater escape training (HUET) submersions of novice trainees

M. Tipton[1], P. Gibbs[2], C. Brooks[2], D. Roiz de Sa[3] and T. Reilly[4]

[1]Dept. Sport & Exercise Science, Univeristy of Portsmouth, Portsmouth, UK, [2]Survival Systems Training, Dartmouth, NS, Canada, [3]Institute of Naval Medicine, Gosport, Hants, UK and [4]Human Performance, PSP, National Defence, Ottawa, ON, Canada

Coincidental stimulation of the parasympathetic nervous system (face immersion and breath holding) and sympathetic nervous system with (anxiety and cooling) can cause "autonomic conflict" and consequent ECG abnormalities that are usually supraventricular and asymptomatic (Tipton et al, 1994). In theory, autonomic conflict could occur during HUET; the present study tested this possibility. Given the large number of people undergoing HUET training each year, and the absence of any reported cardiac problems, it was hypothesised that either ECG irregularities do not occur or, if they do, they are asymptomatic

Following ethical approval and informed consent, 26 naïve males completed a HUET submersion into water at 29.5□C. Each submersion was standardized: the participant entered the HUET helicopter and was secured into the seat with a four point harness. This plus the ditching briefing took 90s. At 3.5 minutes the dunker was submerged and rolled to the inverted position, this took 10s. Once inverted the participant escaped, this took an average of 10s during which they breath held. They then floated supine until 4.5 minutes had elapsed.

Participants wore a three lead (V5) telemetric ECG system (Sharktooth, MIE). They wore underclothing and immersion dry suit. Skin temperature was measured in one subject on the chest, forearm, scapula and forehead. The ECG trace was examined independently by a clinician and thermal physiologist.

Participants had raised heart rates prior to being submerged, indicating sympathetic activation. Heart rate increased during the HUET more probably due to anxiety and physical effort than cold shock as skin temperature did not fall. Participants demon-

strated a range of cardiac arrhythmias the most prevalent being: bradycardia; premature junctional escape; and ventricular ectopics. 26 of these arrhythmias were observed in 19 different participants; 23 of the arrhythmias occurred just after the cessation of breath holding.
Concurrent stimulation of the sympathetic and parasympathetic nervous system during HUET results in ECG abnormalities. The timings of these (after the release of a breath hold) is consistent with earlier findings (Tipton et al, 1994). These ECG abnormalities are asymptomatic and probably of little clinical significance in young, fit individuals. It remains to be seen if this is the case with an older, less fit cohort of people.

Tipton, M. J., Kelleher, P. & Golden, F. St.C. (1994) Supraventricular arrhythmias following breath-hold submersions in cold water. Undersea & Hyperbaric Medicine 21(3): 305-313.

The volunteers

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC25

Strength training affects the agonist-antagonist but not the force-agonist activation relationship

N.A. Tillin, M.T. Pain and J.P. Folland

School of Sport and Exercise Science, Loughborough University, Loughborough, UK

There is conflicting evidence for enhanced neuromuscular activation after strength training (Folland and Williams, 2007). Few studies have normalised agonist electromyography (EMG) to maximal M-wave (Mmax), which is recommended to improve reliability (Gandevia 2001), or measured antagonist activation relative to agonist activation. This study investigated the effects of unilateral isometric strength training of the knee extensors on agonist and antagonist neural activation in the trained and untrained leg. Nine previously untrained males, sat in a strength testing chair with knee and hip angles at 85□and 100□, respectively, and completed 4 sets of 10 isometric knee extensions at 75% of maximum voluntary force (MVF), 4 times a week for 4 weeks. The same apparatus was used for measurement trials pre and post training, which involved a series of involuntary and voluntary isometric contractions of the knee extensors. Force was measured with a strain gauge perpendicular to the tibia, and EMG was collected from the agonist (rectus femoris, vastus lateralis, and vastus medialis) and antagonist (bicep femoris) muscles (Bagnoli-4, Delsys, USA). The Mmax of each agonist muscle was established by supramaximal stimulation of the femoral nerve with single square pulses (100 μs; DS7AH, Digitimer Ltd, UK). MVF was determined as the peak force of four, 3-s maximal voluntary contractions. EMG root mean square (RMS) during a 200 ms epoch was measured at MVF and during a stable segment of voluntary contractions performed at 20, 40, 60 and 80% of MVF. Agonist and antagonist EMG was normalised to Mmax and maximal EMG during isometric knee flexions, respectively. MVF increased in both the trained (+20%; P = 0.001) and untrained leg (+8%; P = 0.007). There was no change in absolute agonist EMG at MVF in either leg, but agonist EMG normalised to Mmax increased in the trained leg (+26%; P = 0.046). There was no change in the quadratic relationship between normalised agonist EMG and absolute force for either leg. Despite a trend for antagonist neural activation to increase at MVF in the trained leg (+8%; P = 0.056), there was a downward shift in the linear relationship between agonist and antagonist neural activation (P = 0.014). This indicates that antagonist activation was lower for any given level of agonist activation post-training. In conclusion, strength and agonist activation increased by a similar magnitude after short term strength training, as reflected by no change in the entire agonist EMG-force relationship. Increased antagonist activation at MVF appears to be a response to greater force and agonist activation, as antagonist activation was lower for any given level of agonist activation post-training.

Folland JP, Williams AG. (2007). The adaptations to strength training: morphological and neurological contributions to increased strength. Sports Med, 37(2): 145-168.

Gandevia, SC. (2001). Spinal and supraspinal factors in human muscle fatigue. Physiol Rev, 81(4): 1725-1789.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC26

Biodynamic and neuromuscular responses to whole-body vibrations of different frequencies and amplitudes

L.N. Zaidell, K.N. Mileva and J.L. Bowtell

Sport and Exercise Science, FESBE, London South Bank University, London, UK

Myoelectric activity has been shown to increase during whole-body vibration (WBV) in a frequency (1,2) and amplitude (2) dependent fashion, which may be related to the propagation of vibration through the body. We have therefore explored the relationship between vibration transmission and muscle activity during WBV of different frequencies and amplitudes. Surface electromyography (EMG) was recorded from the Soleus (SOL) and Vastus Lateralis (VL) of 8 healthy men during isometric squat exercise (150□knee joint angle). 30s squats were performed on a WBV platform during 1.5mm and 3mm p-p amplitude vertical WBV of 20, 25, 30 and 35Hz (8 squats) in pseudorandom order interspersed with 60s rest. To quantify WBV transmission, vertical acceleration was measured via skin-mounted tri-axial ±10G accelerometers placed at the segmental centre of mass of the shank and thigh, and on the platform. Data were analysed by 2 way repeated measures ANOVA (amplitude vs frequency), and regression analysis to determine any relationship between segmental accelerations and EMG activity. Shank (p=0.003) and thigh (p=0.007) vertical acceleration were significantly greater at 3 than 1.5mm. There was a main effect of frequency on shank acceleration (p=0.001) with the highest at 25Hz (1.5mm amp: 1.41± 0.68; 3mm amp: 2.07±1.11; root mean square, RMS G; mean ±SD) and the lowest at 35Hz (1.5mm: 0.78 ± 0.49; 3mm: 1.08±0.84; RMS G).

Shank was greater than thigh vertical acceleration ($p<0.001$), however only a weak relationship existed between these segment accelerations ($R^2=0.28$, $p<0.001$). There was no significant effect of WBV frequency on SOL or VL RMS EMG amplitude, although SOL RMS EMG amplitude was greatest at 25Hz (1.5mm: 0.012±0.005; 3 mm: 0.015±0.007 V) and lowest at 35 or 30 Hz for 1.5 and 3 mm amplitude WBV respectively (0.008±0.004, 0.011±0.007 V). There was no relationship between shank acceleration and SOL RMS EMG amplitude ($R^2=0.02$,$p=0.215$), and a positive relationship ($R^2=0.36$,$p<0.001$) between thigh acceleration and VL RMS EMG amplitude. Both shank and thigh acceleration were greater at the higher WBV amplitude but only shank acceleration exhibited WBV frequency dependency. There was significant attenuation of vibration between shank and thigh, presumably due to passive and active damping via joint compliance and muscle activation, respectively. There was significant inter-individual variation in segmental acceleration and muscle activity, which may be indicative of individualised strategies for vibration damping.

1. Cardinale M & Lim J (2003). *J Strength Condit Res* **17**(3) 621-624.

2. Hazell TJ *et al.* (2007). *Appl Physiol Nutr Metab* **32**(6) 1156-63.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC27

Failure of the QT interval of the electrocardiogram to prolong during a diving response-induced bradycardia in human subjects

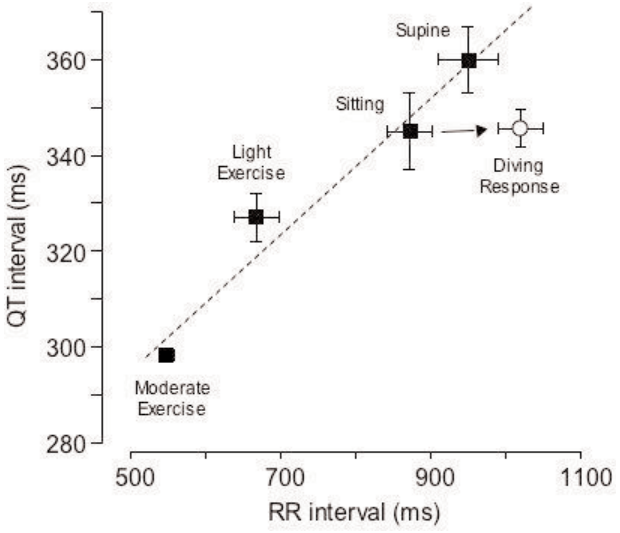
G. Wong, J.E. Clark and M.J. Shattock

Cardiovascular Division, King's College London, London, UK

The QT interval of the electrocardiogram (ECG) reflects the underlying duration of the ventricular action potential. In most species, including man, as heart rate slows the action potential (and hence QT interval) prolongs and, conversely, on an increase in heart rate, the QT interval shortens. The aim of the present study was to investigate changes in the QT interval during a diving response-induced bradycardia in healthy human subjects. Male (n=10) and female (n=9) subjects aged between 18 and 50 were instrumented with ECG electrodes placed on the right clavicle and lower left margin of the ribs (equivalent to limb lead II). ECGs were digitised (at 1kHz) and recorded using a PowerLab recorder and LabChart Pro 6.0 software (AD Instruments, Australia). Measurements were made under five conditions (i) supine at rest, (ii) sitting at rest, (iii) light exercise, (iv) moderate exercise and (v) during a 30s facial immersion in cold (♠ 12oC) water with breath-hold. For (i) to (iv) measurements were made after 10min of steady-state recording. Exercise involved cycling on a friction-loaded cycle ergometer. All data are presented as means±SEM (n=10 for males and 9 for females). There were no differences in responses between males and females. In male subjects the RR intervals during light exercise, moderate exercise, sitting and supine were: 668±30, 547±10, 872±30 and 950±40ms. QT intervals were respectively 327±5, 298±1, 345±8 and 360±7ms and all fell on a straight line described by QT (ms) = (0.14*RR)+225 (see figure). However, during bradycardia induced by the diving response (30s), the QT interval did not prolong (in males, Diving Response RR=1018±30 and QT=346±4ms) (see figure).

Since the QT interval was measured under non-steady state conditions after only 30s of facial immersion, the failure of the QT interval to adjust to the prevailing slower heart rate could be due to the slow time-constant of the QT response to an abrupt heart rate change(1). Lau et al (1) have described fast and slow components of the QT response to a rapid change in heart rate. However, their data would predict that changes in heart rate equivalent to those induced here by 30s facial immersion should prolong the QT interval by approximately 80ms. Possible other explanations include the co-activation of parasympathetic and sympathetic limbs of the autonomic nervous system to simultaneously slow heart rate while preventing QT prolongation(2).

The mechanism underlying this phenomenon requires further investigation, however, it is clear that a failure of the QT interval to match a prevailing diastolic interval during facial immersion would leave the heart vulnerable to re-entrant arrhythmias and, for example, may contribute to the dangers of swimming and diving as known triggers for lethal arrhythmias in genetically-vulnerable individuals(3).



Relationship between the QT interval of the ECG and prevailing heart rate (RR interval) in healthy male subjects during mild and moderate exercise, while sitting, supine or after 30s of facial immersion with apnoea (Diving Response). Data are expressed as means±SEM (n=10) and r2 for the regression line (see text) is 0.9592.

Lau CP, Freedman AR, Fleming S, Malik M, Camm AJ, Ward DE (1998) Hysteresis of the ventricular paced QT interval in response to abrupt changes in pacing rate. Cardiovasc Res. 22(1):67-72.

Paton JF, Nalivaiko E, Boscan P, Pickering AE (2006) Reflexly evoked coactivation of cardiac vagal and sympathetic motor outflows: observations and functional implications. Clin Exp Pharmacol Physiol. 33(12):1245-50.

Ackerman MJ, Tester DJ, Porter CJ (1999) Swimming, a gene-specific arrhythmogenic trigger for inherited long QT syndrome. Mayo Clin Proc. 74(11):1088-94.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC28

Effects of reductions to rapid-acting insulin on blood glucose responses before, during and after aerobic exercise in people with Type 1 diabetes

D.J. West[1], R. Morton[1], G.J. Dunseath[3], S. Luzio[3], J.W. Stephens[2], S. Bain[2] and R.M. Bracken[1]

[1]Sport and Exercise Science Research Centre, Swansea University, Swansea, UK, [2]School of Medicine, Swansea University, Swansea, UK and [3]Diabetes Research Unit, Llandough Hospital, Swansea, UK

Reducing pre-exercise exogenous insulin may be an effective way to combat hypoglycaemia in exercising people with type 1 diabetes (T1DM; Rabasa-Lhoret et al., 2001; Mauvais-Jarvis et al., 2003). However there are conflicting views on the best insulin reduction strategy to perform prior to exercise to preserve blood glucose after exercise. This study examined changes in insulin isoforms (Lispro/Aspart) and blood glucose in T1DM individuals before, during and after exercise following reductions in self-administered insulin dose. With ethical approval, eight T1DM individuals (7 males, 1 female, 34±13 years, 84±16 kg, Hb_{A1c} 8.3±0.6%, VO_{2peak} 44±7 ml.kg^{-1}.min^{-1}) volunteered for this study. In randomised order and on separate occasions after an overnight fast, participants self-administered 100%, 75%, 50% or 25% of their rapid-acting insulin dose subcutaneously into the abdomen prior to consuming a 1121 kJ meal (60g carbohydrates, 2g protein, 2g fat). After a 2 h rest, participants performed 45 min of treadmill running at 70±1% VO_{2peak}. Blood glucose (BG) and insulin were measured for 2 h pre and 3 h post-exercise. Data were analysed using repeated-measures ANOVA and presented as mean±SD. Results are expressed as changes from resting values. In the 2 h before exercise peak insulin values under 100% were greater than 50% and 25% (P<0.05). Consequently, there was a trend for lower peak BG under 100% (6.1±2.6 mM.l^{-1}) than 75% (7.6±2.3 mM.l^{-1}, P=0.09), 50% (7.2±3.1 mM.l^{-1}, P=0.09) and 25% (8.5±4.2 mM.l^{-1}, P=0.05). After 2 h, insulin under 100% (112±97 nM.l^{-1}) tended to be greater than 75% (86±65 nM.l^{-1}, P=0.08), 50% (56±47 nM.l^{-1}, P=0.09) and 25% (70±55 nM.l^{-1}, P=0.06) with BG under 100% (3.9±2.7 mM.l^{-1}) lower than 75% (6.5±2.4 mM.l^{-1}, P=0.01), and tending to be lower than 50% (5.9±3.0 mM.l^{-1}, P=0.07), and 25% (7.4±4.6 mM.l^{-1}, P=0.06). BG decreased under all conditions following exercise with the reduction under 100% (6.3±3.1 mM.l^{-1}) similar to 75% and 50% and greater than 25% (4.0±3.3 mM.l^{-1}, P<0.05). Insulin concentrations did not change after exercise during 100% and 75% but tended to increase after 25% and 50% (P=0.07). In the 3 h following exercise, insulin decreased to resting values under all conditions (100% 15±61, 75% 8±76, 50% 7±76, 25% 22±37 nM.l^{-1}, P<0.05) with the drop in insulin under 100% greater than 25% (P<0.05). Although BG did not change over 3 h post-exercise, the decline from rest was greater under 100% (-2.5±5.2 mM.l^{-1}) compared with 75% and 25% (0.4±5.3 and 3.6±4.2 mM.l^{-1}, respectively, P<0.05) but similar to 50% (-1.5±6.0 mM.l^{-1}, NS). The findings demonstrate a 75% reduction to rapid-acting insulin two hours before exercise best preserves blood glucose concentrations during and after aerobic exercise in T1DM individuals and may offer a useful strategy in the prevention of hypoglycaemia.

Rabasa-Lhoret R et al. (2001). *Diabetes Care*, **24**, 625-630

Mauvais-Jarvis F et al. (2003). *Diabetes Care*, **26**, 1316-1317

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC29

Metabolic changes following a heart rate prescribed, laboratory-supervised walking training programme in individuals with Type 2 diabetes

R.D. Morton[1], D.J. West[1], J.W. Stephens[2], S.C. Bain[2] and R.M. Bracken[1,2]

[1]Sports and Exercise Research Centre, Swansea University, Swansea, UK and [2]Diabetes Research Group, School of Medicine, Swansea University, Swansea, UK

Walking is commonly employed as a non-pharmacological therapy for people with type 2 diabetes (T2DM) and has been shown to improve glycaemic control, lipid metabolism and insulin sensitivity (Di Loreto et al., 2005). However, other research has not shown these findings (Gray et al., 2009). The factors responsible for the differences in these studies are unclear hampered by ill-defined characteristics of the walking training programmes. This study examined changes in fasting glucose, insulin and non-esterified fatty acid (NEFA) concentrations following a 7-week heart rate prescribed, laboratory-supervised walking programme in individuals with T2DM. With ethics approval, twenty-eight people with complication free T2DM (age 60±10 years, mass 91.1±23.5 kg, HbA_{1c} 7.0±1.4%, VO_{2peak} 20.9±3.9 ml.kg^{-1}.min^{-1}) were randomly assigned to WALK or CONTROL groups. Participants attended the laboratory on two occasions in a fasted state having abstained from physical activity for the prior 24 h. Resting blood samples were obtained from an antecubital vein and were analysed for blood glucose (GEM Premier 3000, Instrumentation Laboratories), serum insulin (Roche Diagnostics Ltd) and non-esterified fatty acid (Roche Diagnostics Ltd) concentrations. WALK then completed a 7-week (4 sessions.wk^{-1}, ~ 135 min weekly walking) heart rate intensity-prescribed, laboratory-supervised, walking training programme, while CONTROL continued normal daily activities. A Homeostasis Model Assessment (HOMA-IR) and revised Quantitative Insulin Sensitivity Check Index (QUICKI) were used to assess changes in insulin sensitivity. Data are presented as mean±SD and analysed using independent samples T-test's with p<0.05. Training sessions over 7 weeks elicited a mean heart rate of 78±8 %HR_{peak} and an RPE of 11±1. Fasting insulin and glucose concentrations were not different between groups following training (Insulin: WALK Δ-1.4±10.9 vs. CONTROL Δ-5.2±19.7 μU.ml^{-1} & Glucose: WALK Δ-0.5±1.9 vs. CONTROL Δ0.9±3.0 mmol.L^{-1}, *NS*). NEFA was similar between WALK and CONTROL following walking training (WALK Δ-0.3±0.3 vs. CONTROL Δ-0.2±0.3 mmol.L^{-1}, *NS*). HOMA-IR (WALK Δ-1.2±3.6 vs. CONTROL Δ-0.5±6.3, *NS*) and QUICKI (WALK Δ 0.02±0.03 vs. CONTROL Δ 0.01±0.04, *NS*) index's were not different between WALK and CONTROL following training. A 7-week heart rate prescribed, laboratory-supervised walking programme performed four times a week at 78±8 % of heart rate peak had no significant effect on fasted, resting glucose, insulin or non-esterified fatty acid concentrations. Insulin sensitivity was not

improved following training when calculated using either HOMA-IR or QUICKI models. These findings demonstrate that the intensity of walking in this programme may not have been sufficient to alter resting metabolism or influence insulin sensitivity in individuals with T2DM.

Di Loreto, C., Fanelli, C., Lucidi, P., Murdolo, G., De Cicco, A., Parlanti, N., Ranchelli, A., Fatone, C., Taglioni, C., Santeusanio, F., and De Feo, P., (2005). Make your diabetic patients walk: long-term impact of different amounts of physical activity on type 2 diabetes. Diabetes Care, 28(6), 1295-302.

Gray, S.R., Baker, G., Wright, A., Fitzsimons, C.F., Mutrie, N., and Nimmo, M.A.; Scottish Physical Activity Research Collaboration. (2009).The effect of a 12 week walking intervention on markers of insulin resistance and systemic inflammation. Preventive Medicine, 48, 39–44.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC30

Lower leg artery and vein responses to venous distension and head up tilt in healthy men and women

M.D. Brown, C. Phillips, K. Whitham and R. Lawler

Sport and Exercise Sciences, University of Birmingham, Birmingham, UK

In healthy men and women, increases in muscle sympathetic nerve activity, circulating catecholamines and total peripheral resistance during upright tilt are similar (Fu et al. 2005). Reflex vasoconstriction when upright protects against excessive lower body pooling, and decreases in ultrasound femoral artery blood flow during tilt (~ 40%) correlate with those of plethysmographic lower limb blood flow (~46%) in healthy subjects of mixed gender (Kooijman et al. 2007). We used ultrasound to investigate whether tilt responses of the popliteal artery and long saphenous vein are also the same in men and women. Young healthy subjects age 18-23 years, 14 men and 15 women (tested in their menstrual phase) participated in a study approved by the University of Birmingham Local Research Ethics Subcommittee. Mean arterial pressure (MAP) and heart rate (HR, Portapres), calf volume (strain gauge plethysmography), popliteal artery diameter and velocity and long saphenous (LS) vein diameter (ultrasound) were measured during supine rest and either 5 min of non weight-bearing 60º head up tilt (HUT) or 5 min supine venous distension (thigh cuff inflated to 50 mmHg). Responses during tilt or venous distension were compared to supine rest by repeated measures Anova with gender and intervention as factors. During tilt, MAP did not alter in either group while men showed bigger increases in HR than women (17 ± 3 beats.min^{-1} v. 9 ± 2, mean ± S.E.M., $p<0.01$). During venous distension, neither MAP nor HR altered. Calf volume increased to a similar extent in men and women during venous distension (2.5 ± 0.3 %, 2.5 ± 0.2 %, ns) but during tilt, calf volume increased significantly more in men than it did during distension (4.0 ± 0.2 %, $p<0.001$) while in women, tilt-induced increases in calf volume were not different (2.6 ± 0.3 %). Conductance of the popliteal artery was calculated from flow (cross sectional area x velocity) and mean arterial pressure (corrected for venous distension pressure, and for height difference during tilt). Popliteal conductance did not change significantly during tilt (men +6 %, women +9 %) or distension (men +15 %, women +8 %). LS vein diameter increased 70-80% during tilt and was greater in men than women (3.5 ± 0.3 mm v 2.3 ± 0.2, $p<0.01$). It increased 50-60% during distension and was similar in size in the groups (men 2.5 ± 0.2 mm v. 2.1 ± 0.2, ns). We conclude that, unlike the femoral artery, the popliteal artery does not show postural vasoconstriction. The larger increase in calf volume in men than women during tilt despite similar estimated hydrostatic pressures at the level of the strain gauge (men 69 ± 4 mmHg, women 65 ± 2) is associated with greater vein distensibility. This may be related to different gender proportions of lean and fat tissues in the lower leg segment.

Fu Q *et al.* (2005) *Am J Physiol* **289**,109-116

Kooijman M *et al.* (2007) *Clin Auton Res* **17**,106-111

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC32

Strength and neural activation of the knee joint musculature in Parkinson's Disease: Effects of medication

J.P. Folland[1], B. Haas[2] and P.C. Castle[3]

[1]School of Sport & Exercise Sciences, Loughborough University, Loughborough, UK, [2]School of Health Professions, University of Plymouth, Plymouth, UK and [3]School of Physical Education and Sports Science, University of Bedfordshire, Plymouth, UK

The muscle weakness that occurs with Parkinson's disease (PD) appears to be largely attenuated with medication (principally dopaminergic agonists; Brown et al. 1997), but the specific neuromuscular mechanisms for compromised muscle strength with PD, and the improvement that occurs with medication, have not been clearly delineated. This study compared the knee extension and flexion strength of PD patients on and off medication, and assessed the associated changes in agonist and antagonist neural activation. Ten patients with idiopathic PD (8 men, 2 women. Mean ± SD: age, 63 ± 15 yr; body mass, 76 ± 14 kg, Hoehn-Yahr scale, 1.9 ± 0.8) completed a familiarisation session and two main trials randomly assigned as, on medication (ON) and off medication (OFF, 12 hours after drug withdrawal). Knee joint muscle function of both legs was assessed unilaterally with an isometric strength testing chair at knee and hip joint angles of 90□. Force was measured with a strain gauge perpendicular to the tibia, and surface electromyography (Bagnoli-4, Delsys, USA) was collected from the rectus femoris, vastus lateralis, biceps femoris and semitendinosus. Peak knee extension and flexion force was determined with a series of maximal voluntary contractions (MVCs). EMG root mean square (RMS) was measured during a 500 ms epoch around peak force and during a stable segment of sub-

maximal knee extensions at 20, 40, 60 and 80% of peak force. The interpolated twitch technique was applied to a second series of knee extension MVCs with single square-wave pulses (constant current, 50 μs duration; DS7AH, Digitimer Ltd, UK) delivered percutaneously to evoke supramaximal twitches before and during each MVC. Impaired locomotory performance ('Up and Go' and '5 m walk' times) confirmed a greater severity of movement disorder when off medication. Isometric strength of the knee extensors (ON, 410 ± 103 vs OFF, 381 ± 86 N; Paired t, P=0.03) and flexors (ON, 165 ± 37 vs OFF, 149 ± 37 N; Paired t, P=0.09) was reduced without medication. Maximum voluntary activation of the knee extensors, assessed with the interpolated twitch technique, was reduced by a similar magnitude (7.5%) after withdrawal of medication (ON, 86.7 ± 10.2 vs OFF, 80.3 ± 12.6%; Paired t, P=0.005). Without medication, maximum agonist EMG amplitudes for knee extension and flexion were 13 and 7% lower, respectively, but these effects were not significant (Paired t, 0.59≤P≤0.77). During knee extension contractions the agonist and antagonist EMG-force relationships, and the maximum antagonist EMG, were unaffected by medication withdrawal. In conclusion, the decrease in knee extension strength when PD patients were off medication was entirely due to reduced neural drive to the agonist muscle, rather than any change in antagonist activation, and these changes were associated with reduced locomotory performance.

Brown P, Corcos DM & Rothwell JC (1997). *Brain*, **120**: 401-408.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC33

Leg vascular conductance kinetics in older *versus* young women during high intensity calf plantar plexion exercise

H.N. Reilly[1], S. Green[2] and M. Egana[1]

[1]Physiology, Trinity College, Dublin, Ireland and [2]University of Otago, Dunedin, New Zealand

Older women exhibit blunted vascular conductance (VC) responses to incremental leg extension exercise compared to active young women[1]. However, the age-related effects on the rate at which the vascular conductance response increases at the onset of constant load exercise (VC kinetic response) has not yet been examined.

The aim was to investigate leg VC kinetic responses during a high intensity constant-load calf plantar-flexion exercise.

Sixteen older (60-75 years) and ten younger (20-35 years) sedentary women were tested. Ethical approval was obtained from the Trinity College Dublin Faculty Research Ethics Committee. Subjects performed three constant load exercise bouts (6 min long) of intermittent calf plantar flexion exercise (6s duty cycle: 2 s contraction, 4 s relaxation) at an intensity of 70% maximum voluntary contraction (MVC) on a custom-built calf ergometer at a tilt of 67 degrees. Calf blood flow was measured contraction by contraction using venous occlusion plethysmography. Kinetic analysis was performed by fitting a biexponential function to the mean (3 bouts) of the vascular conductance (BF/MAP) data. Student t-tests were used to detect differences between groups.

The time constant of the fast component was significantly shorter in the young (1.6 ± 1.4 s) compared to the older (3.1 ± 1.7 s) group but the rest of the VC kinetic parameters, the mean response time of the complete response and the end exercise value (amplitude) were not different between both groups.

This study showed that the rate at which vascular conductance responses increase during high intensity static calf exercise is similar in young and older women, suggesting similar vasodilatory function in the two groups. These novel findings disagree with a recent study showing reduced VC responses in older active women following a graded static leg-extension exercise[1]. The different exercise modalities used in the two studies (calf versus quadriceps muscle exercise) and different fitness levels of the participants (active versus sedentary) may in part explain these differences.

Parker BA, Smithmyer SL, Pelberg JA. Sex-specific influence of aging on exercising leg blood flow. J. Appl. Physiol 2007; 104: 655-664.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC34

Acute resistance exercise results in increased leucine transport and amino acid transporter expression

M.G. MacKenzie, D. Hamilton, P. Taylor and K. Baar

Molecular Physiology, University of Dundee, Dundee, UK

Following an acute bout of resistance exercise in either humans or rodents intramuscular levels of amino acids ([aa]i), for example leucine, lycine and glutamine, increase. This increase is associated with both accelerated protein synthesis and degradation and we hypothesize that the increased [aa]i levels are a direct consequence of high force muscle contractions. The mechanism as to how this increase in [aa]i is induced is currently unknown; conceivably, it could be the result of increased protein breakdown, increased amino acid transporter level/activity, or a combination of both. Since the Na2+-independent (LAT1) and Na2+-dependent (SNAT2) amino acid transporters carry leucine and glutamine respectively, we hypothesized that they would be responsive to resistance exercise. To investigate this hypothesis, rats underwent a unilateral bout of resistance exercise where the right sciatic nerve was electrically stimulated (under isoflurane anaesthesia) using a Grass stimulator at a frequency of 100 Hz, 6-12 V, 1 ms duration, 9ms delay for 10 sets of 6 repetitions. Each repetition lasted 2s, a 10s recovery was permitted between repetitions, and a 1min recovery was allowed between sets resulting in a 20 min stimulation protocol. 0.5, 1.5, 3, 6, 18 and 48 hours following the acute bout of contractions, stimulated and contralateral control muscles were rapidly removed and

snap frozen in liquid nitrogen. mRNA and protein levels of LAT1 and SNAT2 as well as 5 other amino acid transporters were determined by RT-PCR and western blotting throughout the time course. LAT1 transcription increases 5.15±0.84 fold 3h after exercise and stays high for up to 48h (2.56±0.19 fold). SNAT2 expression increases at 30mins (1.73±0.11 fold) and peaks at 6h (2.56±0.19 fold). The other transporters did not change. LAT1 protein increased 32±12% in the exercised muscle 90mins after contraction while SNAT2 protein levels were unchanged. In addition, c-Myc, a key transcription factor involved in control of cell growth and connected to the nutrient-sensing signalling network, precedes LAT1, increasing immediately after exercise (2.05±0.2 fold), peaking at 3h (7.47±0.43 fold) and staying high for 48h (1.87±0.43 fold). Interestingly we have identified a potential c-myc binding site in the LAT1 promoter. As c-myc activity is known to be increased by mTOR, through the degradation of MAD1, this may provide a mechanism for increased LAT1 expression and the positive effects of amino acids on protein synthesis following resistance exercise.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC35

Satellite cell number and fibre size with disuse atrophy, a case study

T.E. George, C.P. Velloso, N. Haamedi and S.D. Harridge

Division of Applied Biomedical Research, Kings College London, London, London, UK

Disuse atrophy of skeletal muscle is a phenomenon commonly associated with prolonged periods of inactivity resulting in reduced cross sectional area of the myofibres. Satellite cells are mononucleated cells closely juxtaposed to myofibres that are required for the repair and hypertrophy of skeletal muscle (Adams, 2006). In humans, the number of myofibre associated satellite cells can change, increasing following resistance training and decreasing following a period of detraining (Kadi et al., 2004). However, the association between disuse atrophy and satellite cell number has not been closely investigated. We aimed to determine whether atrophy associated with long term disuse leads to loss of satellite cells. Following local anaesthesia (2% lignocaine), needle biopsies were taken from the left and right vastus lateralis muscles of a young male volunteer (aged 25 yrs) who had suffered a knee injury six years prior. Visible connective and adipose tissue were dissected and the biopsies split into two parts, one for histology to determine muscle fibre composition and fibre size and one for satellite cell isolation. For histological analyses, the tissue was mounted in OCT medium, and frozen in iso-pentane cooled to -80□C. Serial cross-sections (10μm) were cut and ATPase histochemistry was performed for the determination of type I and II fibre size and relative composition. Rather than counting a limited number of satellite cells in cryosections, we aimed to measure all satellite cells by extracting them from the biopsy sample. For satellite cell isolation, tissue was weighed and digested in a solution containing trypsin (5mg/ml). Cells were harvested by centrifugation and cultured in skeletal muscle cell growth medium supplemented with 10% foetal calf serum. After 10 days the total number of cells was counted. The proportion of muscles cells was determined by expression of desmin using immunofluorescence. The mean fibre area of Type I and II fibres was 5206 (3377-7361)μm2 and 6248 (4430-7449)μm2 respectively in the uninjured leg, but were on average 16% and 32% lower in the injured leg. The proportion of Type II fibres was slightly higher (60%) in the injured verus the uninjured (54%) leg. The total yield of cells extracted from muscle tissue was 9834 cells/mg in the uninjured versus 7081 cells/mg in the injured leg. The proportion of desmin positive cells in the extracts was 97% in the uninjured and 89% in the injured leg. The data suggests that there is a concurrent loss of satellite cells with the reduction in myofibre area.

Adams GR (2006). Appl Physiol Nutr Metab 31,782-790

Kadi F et al (2004). J Physiol 558,1005-1012

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC36

Individual variability in skeletal muscle metabolic response to endurance training in humans

J.S. McPhee[1], H. Degens[1], D.A. Jones[1], K. Baar[2] and A.G. Williams[1]

[1]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK and [2]Division of Molecular Physiology, University of Dundee, Dundee, UK

Regular endurance training increases skeletal muscle aerobic capacity, but there is considerable variability between individuals in the magnitude of the training response. The present study investigated inter-individual variability in adaptations of enzymes involved in fatty acid and glucose metabolism. The local ethics committee approved the study and 20 untrained young women gave written informed consent to participate. Biopsies were obtained from the vastus lateralis muscle before and after six weeks of endurance cycle training (3 x 45 min sessions/wk). Western blot analyses were used to measure the expression of a) the mitochondrial enzymes succinate dehydrogenase (SDH), cytochrome C oxidase (COX1) and ATP synthase (ATPsyn); b) the proteins involved in fatty acid metabolism 3-hydroxyacyl CoA dehydrogenase (HAD) and transporter CD36 (CD36) and c) those involved in glucose metabolism; phosphofructokinase (PFK) and glucose transporter 4 (GLUT4). As the data were not normally distributed non-parametric statistical tests were used. The maximal oxygen uptake (10%) and protein expression of SDH (47%), COX1 (52%), ATPsyn (63%), HAD (69%) and CD36 (86%) were all significantly elevated (all $P < 0.05$), while PFK (29%) and GLUT4 (18%) did not change with

training. There was, however, considerable inter-individual variability in training response of each protein and this was examined in relation to the delta SDH, since fatty acid and glucose metabolism converge in the mitochondria. Delta SDH correlated with the training-induced changes in COX1 (r = 0.63), HAD (r = 68), CD36 (r = 0.85), PFK (r = 0.86) and GLUT4 (r = 0.80) (all P < 0.01), but not with delta ATPsyn (r = 0.38, P = 0.099). High and Low groups (n = 6 per group) were classified as those individuals having a delta SDH in the upper or lower third, respectively, of the mean of the group as a whole. The absence of a significant group x protein interaction (repeated measures ANOVA) indicated that the changes in expression of enzymes involved in fatty acid and glucose metabolism showed similar responses within groups, but different responses between groups (Fig. 1). This was also true if delta COX1 was used instead of delta SDH as a marker of mitochondrial adaptations. In conclusion, the data indicate a coordinated response of mitochondrial enzymes and proteins associated with fat metabolism in response to endurance training. The variable response between individuals may indicate genetic differences in the coordinating signal(s).

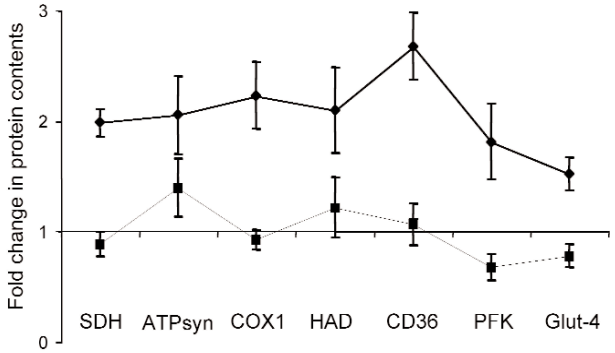


Fig. 1

Within-group similarity in training responses of separate proteins. Groups defined by High or Low delta SDH training response. Mean (SEM), both n = 6.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC37

The effect of cutaneous electrical stimulation of the sole of the foot on peak femoral vein velocity and mean blood pressure during protracted sitting

S. Hunter[1], D.A. Green[2] and P. Sumners[1]

[1]Sport and Exercise Science, London South Bank University, London, UK and [2]Department of Physiology, King's College London, London, UK

Protracted sitting with limited or no mobility can increase the risk of blood pooling and coagulation which increase the risk of thrombosis. A decrease in venous return due to pooling can result in hypotension, dizziness or actual fainting. Folkow et al (1970) reported that dynamic exercise i.e. rhythmic contraction of skeletal muscle can evoke elevated venous outflow that may act to ameliorate pooling. Furthermore, Shoemaker & Hughson (1999) suggest that such a 'muscle pump' is an important mechanism of increased blood flow. Electrically-evoked, is considered inferior to voluntary evoked contractions in producing venous flow whilst requiring high currents and can be painful. Therefore, the aim of the study was to determine if rhythmical non-painful electrical stimulation applied to the sole of the foot could activate the muscle pump evidenced by increased peak femoral venous blood velocity. Eighteen healthy volunteers gave informed consent to participate in the study, which had received local ethical committee approval. Quantification of the subjective pain threshold and peak blood velocity (BV) at 10% plantar flexion maximal voluntary contraction (MVC) was determined prior to the protocol. Subjects then sat in a chair resting for 5 mins. In the final minute, recordings (PRE) of femoral vein velocity (Doppler) and digital blood pressure (BP; mmHg) were obtained. Subjects then sat still for a further 40 minutes (STASIS) in order to produce pooling in the lower limbs. Following this period, electrical stimulation of the sole (50% of pain threshold) of both feet was performed for 10 min (STIM). Measurements of BV and BP were made in the final minute of STASIS and STIM. Students paired t-test were performed between conditions and corrected for multiple comparisons (Tukey). BV was significantly greater during STIM (52.9±4.3 cm/s; P<0.001) and 10% MVC (32.0±5.0 cm/s; P<0.001) compared to PRE (7.0±0.6 cm/s). The increase in peak venous BV between PRE and 10% MVC was greater than that between PRE and STIM. Mean blood pressure (MBP) showed no change during STASIS (106±3 mmHg) vs. PRE (105±4 mmHg) but showed significant elevation during STIM (112±3 mmHg) vs. PRE (P<0.001) and STASIS (P<0.001). Thus, cutaneous stimulation of the sole of the foot produced a muscle contraction equivalent to 54.6% of a 10% MVC in terms of BV. Hence, non-painful electrical stimulation delivered to the sole was adequate to evoke an increase in BV and MBP that may relate to the degree of pooling amelioration.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC38

Effect of 5-weeks high-frequency airway occlusion training on respiratory function and breathlessness

T.A. Morris[1], D.P. Sumners[2] and D.A. Green[1]

[1]Division of Applied Biomedical Research, King's College London, London, UK and [2]Sport and Exercise Research Centre, London South Bank University, London, UK

High frequency airway occlusion (HFAO) increases maximal inspiratory mouth pressure generation (Sumners et al., 2008) but as yet the chronic training effects have not been investigated. Therefore the aim of this study was to investigate the effects of 5 weeks training with high frequency airway occlusion on lung function, respiratory function, autonomic function and sensation in healthy subjects. The study had local ethical approval and informed consent was obtained. The protocol

consisted of a pre-training testing session, followed by five weeks training (60 breaths/day, 5 days/week) with a HFAO device (youbreathe®), followed by an identical post-testing session. Pre and post-testing sessions consisted of breath-by-breath analysis during 3 conditions: 3 minutes tidal breathing, 1 minute inspiratory resistive-loaded breathing (19 $cmH_2O.l^{-1}.s^{-1}$) and 1 minute maximum voluntary hyperventilation. In addition a battery of lung function tests, maximal dynamic and static mouth pressures, maximal dynamic inspiratory flow and maximal dynamic inspiratory volumes were determined (mean±SEM). Dypnoea was rated during HFAO and resistive-loaded breathing on a BORG scale (0-10). Physiological parameters were tested PRE vs. POST with Student's paired t-test and dyspnoea with a Wilcoxon Signed Rank test with significance assumed at $p<0.05$. Following 5 weeks HFAO training significant improvement in maximal dynamic mouth pressures (-6.27±0.42 to -8.58±0.63 mmHg; $p<0.05$) and maximal static mouth pressures (-71±3.01 to -79.44±3.78 mmHg; $p<0.05$) were observed. In addition, mouth pressure (-4.16±0.32 to -4.76±0.35 L/sec; $p<0.05$) was increased during maximal voluntary hyperventilation. Furthermore HFAO training resulted in significant reductions in dyspnoea both during HFAO (2.74±0.28 to 2.21±0.27; $p<0.05$) and inspiratory resistance (4.42±0.34 to 3.21±0.21; $p<0.05$). Therefore, 5 weeks of HFAO training evokes significant improvements both in dynamic and static maximal respiratory mouth pressure generation, and a reduction in dyspnoea during loaded breathing in young healthy individuals. Such findings suggest that transient inspiratory vibratory stimulus may provide a useful training stimulus for individuals whom experience respiratory-related limitations.

Sumners, D. P., Green, D. A., Mileva, K. N., Bowtell, J. L. (2008). Increases in inspiratory neural drive in response to rapid oscillating airflow braking forces (vibration). Respir Physiol Neurobiol. 29;160(3):350-2.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC39

Age does not affect the proliferation or differentiation of human myoblasts

T.E. George, C.P. Velloso and S.D. Harridge

Division of Applied Biomedical Research, Kings College London, London, London, UK

Ageing is characterised by a loss of muscle mass (sarcopenia). The mechanisms contributing to this loss are not known. One theory is that sarcopenia results from impaired regeneration after contraction-induced injury. Muscle repair is mediated by satellite cells and there is evidence that satellite cells from both young and old donor animals are equally able to proliferate *in vitro* and populate the regenerating, damaged muscles of young animals *in vivo* (Collins et al., 2007). This suggests that the satellite cells themselves are not affected by age, although their responses are impaired by the aged systemic milieu (Conboy et al., 2005). The aim of this study was to determine whether satellite cell derived myoblasts extracted from elderly and young humans differ in their ability to proliferate and differentiate in culture. Needle biopsies were taken under local anaesthesia (2% lignocaine) from the vastus lateralis muscles of 6 young (aged 23-26 yrs, 3 males 3 females) and 5 older (aged 80-81 yrs, 3 females, 2 males) subjects. Serum was obtained from one young male (aged 24 yrs). Visible fat and connective tissue was removed from the biopsy sample and the remaining muscle was digested with trypsin (5mg/ml). Cells were collected by pelleting and cultured in skeletal muscle cell growth medium (SMCGM) supplemented with 10% foetal calf serum in 96 well dishes. After 24 hours the SMCGM was replaced with basal skeletal muscle medium supplemented with 15% serum for proliferation or 2% serum for differentiation experiments. Cells were fixed after 46 hours (proliferation experiments) or 11 days (differentiation experiments) in 4% paraformaldehyde + 0.2% triton. Proliferation was determined as the number of desmin (muscle cell marker) positive muscle cells that also stained for Ki67 (a proliferation marker). Differentiation capacity was determined by counting the number of nuclei (counterstained with Hoechst) in myosin heavy chain positive cells relative to the total number of nuclei in the culture. Two wells were studied per condition and the mean value used for analysis, counting at least 500 cells per well. The data revealed no differences (unpaired t-test) in proliferation of myoblasts obtained from the elderly (33.0+/-6.9%, mean +/-SEM) compared to the young (32.1+/-6.9%) subjects. Likewise, the differentiation of myoblasts from the elderly subjects (54.8+/-22.4%) was no different compared to that of young subjects (59.6+/-10.4%). The data suggest that age does not affect the ability of human myoblasts to proliferate or differentiate in culture.

Collins et al (2007). Stem Cells 25,885-894

Conboy et al (2005). Nature 433,760-764

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC40

Nandrolone: a doping agent! Ophthalmic therapy or therapy for the ageing musculoskeletal system?

M.R. Graham[1], P. Ryan[1], P.J. Evans[2], B. Davies[3] and J.S. Baker[4]

[1]The Newman Centre for Sport and Exercise Research, Newman University College, Birmingham, UK, [2]Department of Diabetes, Royal Gwent Hospital, Newport, UK, [3]Health and Exercise Science Research Unit, University of Glamorgan, Cardiff, UK and [4]Division of Sport, University of the West of Scotland, Glasgow, UK

Nandrolone (19-Nortestosterone) is an androgenic-anabolic steroid, known to increase muscle mass and strength, thereby enhancing sporting performance, in injectable or oral presentation (Lambert and Gibson, 1995). The metabolites of Nandrolone are 19-Norandrosterone (19-NA), 19-Noretiocholanolone (19-NE) and 19-Norepiandrosterone. Their urinary detection by gas chromatography-mass spectrometry, forms the basis of doping. Nandrolone still has therapeutic use in specified disease processes, including osteoporosis, but is rarely used (BNF, 2009). The International Olympic Committee (IOC) prohibited its use in sport in 1976. A doping offence occurs

when the critical concentration for Nandrolone metabolites in the urine exceeds 2 ng/ml. In a doping control situation, the excretion kinetics of labelled Nandrolone, show inter-individual variability, in 2 individuals treated with the same dosage at the same time (Baume et al., 2004).

An international athlete recently presented with metabolites of urinary Nandrolone >2 ng/ml. There was a variation in levels in A (19-NA: 6.2 ± 0.18 ng/ml; 19-NE: 2.6 ± 0.08 ng/ml) and B (19-NA: 5.6 ± 1.1 ng/ml; 19-NE: not measured) samples. The medico-legal defence prepared a defence: that he had been prescribed "Keratyl" eye drops (containing Nandrolone sodium sulphate) for an anterior uveitis and corneal abrasion. A WADA-accredited laboratory study administered therapeutic levels of Keratyl eye drops to subjects which produced positive urinary Nandrolone metabolites >2ng/ml (Avois et al., 2007). The urinary concentrations reached 450 ng/mL and 70 ng/mL for 19-NA and 19-NE, respectively. The study demonstrated that concentrations >2ng/ml could be found in samples, 15 days after the last administration of the drug, depending on individual metabolism. Due to poor bioavailability of ophthalmic solutions, it was not expected to obtain such high urinary concentrations and such discrepancies between individuals. Poor bioavailability of ocular drugs has been documented in the literature (Kaur et al., 2004). Quantification indicated a great variability in terms of inter- and intra-individual excretion of Nandrolone metabolites, with respect to this medication. Ophthalmic pharmaceuticals are often considered "harmless". Sport's Physicians have not always been aware they can lead to a "positive" urine, even several weeks after the last administration and do not warn athletes against using this kind of medication. Can an ophthalmic delivery elevate the serum levels of Nandrolone to an extent where they increase muscle development? Further research is required to quantify if Keratyl can be used for therapeutic medical management of the ageing musculoskeletal system.

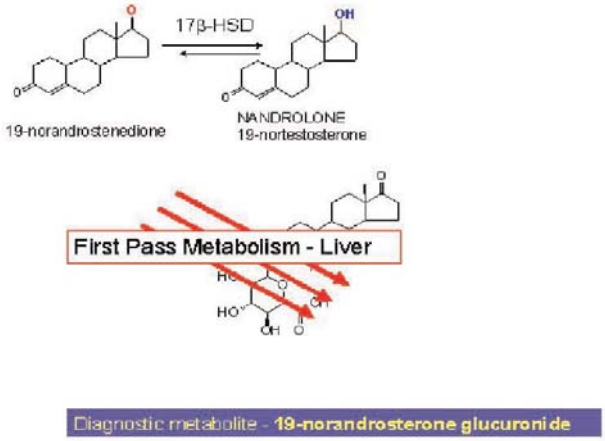


Figure 1. Nandrolone and its main diagnostic metabolite.

Lambert MI and St Clair Gibson A. (1995). Anabolic-androgenic steroids: effects on muscle size and strength. SA J Sports Med 2, 6-9.

British National Formulary. A joint publication of the British Medical Association and the Royal Pharmaceutical Society of Great Britain. BMJ Group and RPS Publishing, 2009 [online]. Available from URL: http://www.bnf.org [Accessed 2009 Jan 28].

Baume N et al. (2004). 13C Nandrolone excretion in trained athletes interindividual variability in metabolism. Clin Chem 50, 355-364.

Avois L et al. (2007). Concentrations of nandrolone metabolites in urine after the therapeutic administration of an ophthalmic solution. J Pharm Biomed Anal 44, 173-179.

Kaur IP et al. (2004). Vesicular systems in ocular drug delivery: an overview. Int J Pharm 269, 1-14.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC41

Myokine responses to an acute bout of resistance exercise in rat

D.L. Hamilton, A. Philp, G. Hardie, K. Baar and M. Towler

Molecular Physiology, University of Dundee, Dundee, UK

Skeletal muscle has recently been identified as an important endocrine organ, which independently produces a group of cytokines, now termed myokines. Recent work from our lab identified that an acute bout of unilateral resistance exercise can systemically modulate the responsiveness of skeletal muscle insulin signalling to an IP bolus of insulin (10mU/g BW). To investigate this further we exposed rats to a single bout of unilateral resistance exercise via sciatic nerve stimulation under inhaled anaesthetic (2.5% Isoflourane vaporised in 100% oxygen at 1.5L/min) followed by an insulin tolerance test under inhaled anaesthetic 48hrs later. The exercised animals had a trend to lower post-prandial blood glucose compared to the sham operated controls (Sham = 7.55 ± 0.22 mmol/L, Ex = 7.15 ± 0.22 mmol/L) and there was a trend for blood glucose to be lower at all other time points. In the livers of exercised animals, S6K1 Thr389 phosphorylation was significantly elevated [Con = 0.18 ± 0.04, sham = 0.47 ±0.09, Ex = 1.01 ± 0.09 (n=4, Tukey's HSD test)] there was also a trend for PKB Thr308 phosphorylation to be elevated in the Ex group above that of the Sham group. We profiled a range of myokines at the mRNA level using qPCR over a time course following a single bout of unilateral resistance exercise. IL18 was significantly elevated at 18 [200.47 ± 50.50% (t-test)] and 48hrs [121.95 ± 56.58% (t-test)] and the caspase responsible for cleaving pro-IL18, Caspase-1, was also significantly elevated at 48hrs [48.04 ± 14.12% (t-test)] following exercise. Treatment of C2C12 cells with IL18 for 24hrs significantly elevated insulin (100nM) stimulated PKB Thr308 [vehicle + con = 0.84 ± 0.09, vehicle + Ins = 3.97 ± 0.34, IL18 + con = 0.68 ± 0.32, IL18 + Ins = 5.18 ± 0.10 (n=3, Tukey's HSD test)] phosphorylation and led to increased insulin stimulated glucose uptake [vehicle + Ins = 2.94 ± 0.17, IL18 + Ins = 3.61 ± 0.45 (n=4, Tukey's HSD test). To conclude resistance exercise recruiting approximately 2% of the animal's body mass leads to a systemic modulation in insulin stimulated signalling, which may be mediated by the myokine IL18.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

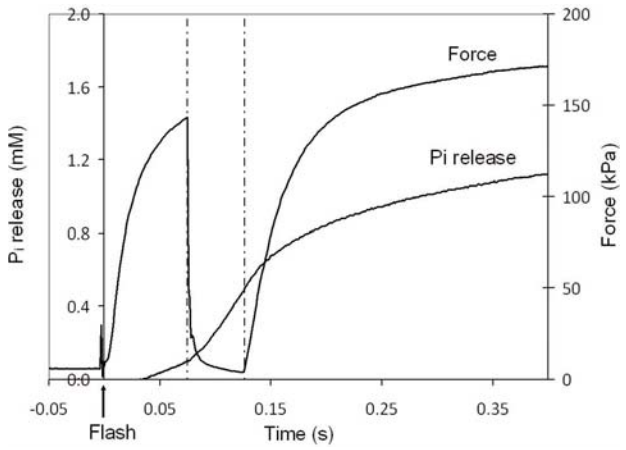
PC43

Rate of inorganic phosphate release by permeabilised dogfish fibres

S. Park-Holohan, M. Caremani, T. West, R. Woledge, M. Ferenczi and N. Curtin

Molecular Medicine Section, Imperial College London, London, UK

Muscle contraction depends on actomyosin interaction fuelled by ATP. The rate of consumption of ATP can be monitored by the time-resolved phosphate release detected with the fluorescent protein MDCC-PBP, N-(2[1-maleimidyl]ethyl)-7-diethylamino-coumarin-3-carboxamide phosphate binding protein. The aim of this study was to measure in permeabilised dogfish fibres the time course of inorganic phosphate (Pi) released during and after fibre shortening. Dogfish (Scyliorhinus canicula) were anaesthetised with MS-222, ethyl 3-aminobenzoate methanesulfonic acid (2g dissolved in 10 litre artificial seawater) followed by decapitation and destruction of the brain and spinal cord in accordance with Schedule I of the UK Animals (Scientific Procedures) Act 1986. Single fibres were dissected and stored as reported previously1. At 2.4μm sarcomere length the Triton X-100 permeabilised fibre was transferred through a sequence of solutions: (1) pre-rigor, (2) Ca2+-free, (3) Ca2+-rigor, (4) loading solution, (5) silicone oil. The fibre was activated from rigor state by flash photolysis of NPE-caged ATP (P3-1-(2-nitrophenyl)ethylester of adenosine 5'-triphosphate) to release 1.5mM ATP in silicone oil. Ramp release or step-ramp release was applied either early (start of release <50ms) or delayed (start of release 50 ms< t<100 ms) from the time of activation. The epifluorescence microscope and photomultiplier were used to record fluorescence time course2 for up to 3s after start of activation. Fibres were activated only once at physiological temperature of dogfish, 12C. Typical records of tension and Pi release during step-ramp fast shortening are shown with the start and end of fibre shortening indicated (-.-). Force trace: Following the photolytic release of ATP (t=0), tension increased with a biphasic profile. When tension nearly reached a plateau the fibre was allowed to shorten at a constant velocity, and tension decreased to a lower level. At the end of the shortening tension redeveloped to reach a new plateau. Pi release trace: After correction, for aci-nitro decay, and calibration, fluorescence record yielded a measure of Pi release during the fibre shortening. Saturation of the signal is shown when Pi release approached 1mM. The two important features to notice are the delay before the rate of Pi release reached a steady rate and the duration after the end of shortening for which this rate is maintained. The rate of Pi release increased during fibre shortening. This observation is in agreement with a previous publication by He and colleagues3. Further experiments are needed to explain the apparent shift in the steady Pi release rate with respect to the duration of fibre shortening.



1 Timothy West et al. J Physiol (2005), 567.3, pp 989–1000.

2 Zhen-He He et al. J Physiol (1997), 501.1, pp. 125-148.

3 Zhen-He He et al. Biophy J (2000), 79, pp 945-961.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC44

Sodium bicarbonate increases glucose uptake and mitochondrial biogenesis in C2C12 myotubes potentially via the transcriptional co-activator PGC-1α

J. Perez-Schindler, A. Philp and K. Baar

Division of Molecular Physiology, University of Dundee, Dundee, UK

Ingestion of Sodium Bicarbonate (NaHCO3) during short-term interval training has beneficial effects on cellular metabolism and metabolite transport in both rodents (Thomas et al, 2007) and humans (Edge et al (2006). However, the cellular mechanism for this additive effect remains unclear. The aim of this study was to examine the effect of NaHCO3 administration in C2C12 myotubes. Five days following differentiation, C2C12 myotubes were treated for 72h with either NaHCO3 (5-50mM) or sodium chloride (50mM) as an osmotic control. Following treatment, cells were collected in lysis buffer (50mM Tris pH 7.5; 250mM Sucrose; 1mM EDTA; 1mM EGTA; 1% Triton X-100; 1mM NaVO4; 50mM NaF; 0.10% DTT; 0.50% PIC), centrifuged for 5 mins at 8,000 RPM and the supernatant removed for protein determination. Protein content was determined via western blotting using commercially available antibodies. Total RNA was isolated from 35mm plates using phenol/chloroform. Real time quantitative PCR was performed to measure relative mRNA expression using an Eppendorf Light Cycler PCR machine, SYBR green PCR plus reagents (Sigma Aldrich, Dorset, UK) and custom designed primers. Ten μl PCR reactions were assayed in triplicate on a 96 well heat sealed PCR plate (Thermo Scientific, Leicestershire, UK). Each reaction contained 5μl SYBR green taq, 1μl of forward and reverse primers and 3ul of cDNA (1:2 dilution). Differences between groups were assessed by students paired t-tests (SPSS version 10) whilst all results are expressed as Mean ± SEM. NaHCO3 treatment increased the expression of PGC-1α (302%), GLUT4 (266%) and cytochrome-c (291%) whilst increasing the protein content of GLUT4 (37%), MCT1 and the respiratory chain subunits COX-2 (63%) and COX-4 (42%). Both basal and insulin stimulated glucose uptake were increased following NaHCO3 treatment (68% and 73% respectively) as was basal cell oxygen consumption (10%). Finally NaHCO3 increased the abundance of membrane bound GLUT4 (68%) and MCT1 (73%). Taken together, these findings suggest that NaHCO3 induced chronic alkalosis promotes up-regulation of PGC-1α and its downstream targets COX-2, COX-4, Cytochrome-c and MCT1. Further, NaHCO3 also increases basal and insulin stimulated glucose uptake via increased GLUT4 expression, content and membrane localisation. Further research should assess whether PGC-1α is the specific target for NaHCO3 mediated adaptation and how chronic alkalosis effects PGC-1α signalling.

Edge J, Bishop D, Goodman C (2006) J Appl Physiol 101(3):918-25.

Thomas C, Bishop D, Moore-Morris T, Mercier J (2007) Am J Physiol Endocrinol Metab 293(4):E916-22.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC45

Aerobic fitness, activity levels and heart rate variability in young adults

A.J. Connorton, V.F. Gladwell and G.R. Sandercock

Essex University, Colchester, UK

Poor autonomic control of the heart is associated with increased risk of cardiovascular disease. Previous research indicates that increasing aerobic capacity induce positively autonomic control of the heart (Aubert et al. 2003) regardless of present training load (Buchheit and Gindre 2006). Current training load, however, influences heart rate recovery (HRR) from maximal exercise (Buchheit and Gindre 2006). Previous studies have used middle aged or highly fit populations. Therefore, the aim of the study was to examine the relationship between aerobic capacity, training load, heart rate variability (HRV) and HRR in young, healthy adults. Institutional ethics approval was granted and forty-six healthy non-smoking individuals free from cardiovascular disease participated in the study (age: 21+2.3 years; BMI: 22.8+2.7 kg/m2; %bodyfat: 20.8+7.7%). Autonomic control of the heart was measured non-invasively using HRV analysis of a five minute resting supine electrocardiogram. A physical activity questionnaire assessed training load (Baecke et al. 1982). VO2peak was determined by a maximal incremental cycling test. To determine HRR, seated HR 60 seconds post exercise termination was subtracted from the maximal HR at the end of the maximal test. Correlations were used to determine relationships between Baecke score, VO2peak, HRV variables and HRR. VO2peak was converted to z scores to adjust for sex. Pearson's correlation was used

where data were normally distributed otherwise Spearman's rank correlation was adopted. A positive relationship was established between Baecke score and sex-adjusted VO2peak (r=0.355, p<0.05). No relationships, however, were found between Baecke score and HRV variables or with HRR. Additionally, VO2peak (z score) was not correlated to HRV variables or HRR. Furthermore, no relationship was found between HRV and HRR. These findings contradict previous studies conducted in older or more highly fit populations suggesting that in a young moderately fit population other factors such as genetic predisposition or prior training may have more influence on HRV and HRR than training load or fitness.

Aubert A, Seps B, Beckers F (2003) Heart rate variability in athletes. Sports Med 33: 889-919

Baecke JA, Burema J, Frijters JE (1982) A short questionnaire for the measurement of habitual physical activity in epidemiological studies. Am J Clin Nutr 36: 936-942

Buchheit M, Gindre C (2006) Cardiac parasympathetic regulation: respective associations with cardiorespiratory fitness and training load. Am J Physiol Heart Circ Physiol 291: H451-458

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC46

Region-specific adaptations in determinants of rat skeletal muscle oxygenation to chronic hypoxia

H. Degens[1], L.J. Hoofd[3], W.J. Van der Laarse[4], R.T. Jaspers[5], A.F. van Heijst[6] and R.C. Wüst[1,2]

[1]Institute for Biomedical Research into Human Movement and Health, Manchester Metropolitan University, Manchester, UK, [2]Institute of Membrane and Sytstems Biology, University of Leeds, Leeds, UK, [3]Department of Physiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [4]Department of Physiology, VU University Medical Centre, Amsterdam, Netherlands, [5]Research Institute MOVE, VU University Amsterdam, Amsterdam, Netherlands and [6]Department of Paediatrics, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

Chronic exposure to hypoxia is often seen in patients with lung and heart failure and is generally associated with muscle atrophy (i.e. reduction in muscle fibre cross-sectional area), reduced oxidative capacity and capillary growth. As some controversy still exists in the literature to what extend these changes are muscle and fibre type specific, we hypothesize that different regions of the same muscle would respond differently to severe chronic hypoxia. To investigate this we compared the deep (oxidative) and superficial (glycolytic) region of the plantaris muscle of 8 male rats exposed to 4 weeks hypobaric hypoxia (410 mm Hg) with those of 9 normoxic rats. The haematocrit was higher in chronic hypoxic than control rats (59 vs. 50%; P<0.001). Using histochemistry, we observed a 10% fiber atrophy (P<0.05, multilevel analysis) in both regions of the muscle, but no shift in fibre type composition and myoglobin concentration of the fibres. In hypoxic rats, the succinate dehydrogenase (SDH)-activity was elevated in fibres of each type in the superficial (25%, P<0.05), but not in the deep region, while in the deep, but not the superficial region, the number of capillaries supplying a fibre was elevated (14%, P<0.05). Model calculations (Krogh model) showed that the region-specific alterations in fibre size, SDH-activity and capillary supply to a fibre prevented the occurrence of anoxic areas in the deep region, but not in the superficial region. Interestingly, the acclimatization-induced increases in mean capillary oxygen pressure (from 25 to 36 mm Hg, [1]) counteracted the impaired tissue oxygenation in the glycolytic region and further improved the tissue oxygenation in the deep region. We conclude that the determinants of tissue oxygenation show region specific adaptations, resulting in a marked differential effect on tissue oxygen tension.

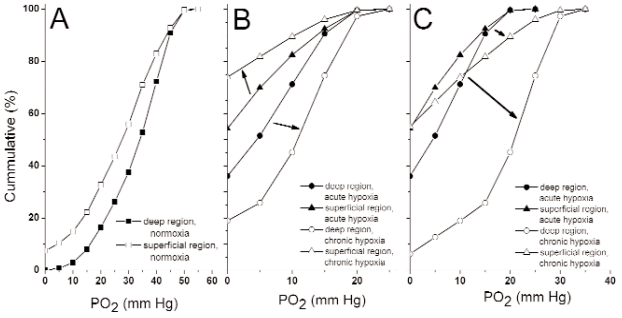


Figure 1: Muscle tissue oxygenation during (A) normoxia, (B) acute hypoxia and when taking into account tissue adaptations to chronic hypoxia and (C) chronic hypoxia when also taking into account

adaptations in blood flow and haematocrit.

Calbet, JA et al. (2009). J Physiol. 2009 587: 477-90.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC47

Physical activity can offset the obesogenic effect of an *FTO* gene polymorphism in adolescents

R. Scott[1], C.N. Moran[1], M.E. Bailey[1], R.H. Wilson[1], N. Fuku[2], M. Tanaka[2], A. Tsiokanos[3], A.Z. Jamurtas[3] and Y.P. Pitsiladis[1]

[1]Integrative and Systems Biology, University of Glasgow, Glasgow, UK, [2]Genomics for Longevity and Health, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan and [3]Department of Physical Education and Sports Science, University of Thessaly, Trikala, Greece

Obesity is a leading risk factor for type 2 diabetes and cardiovascular disease. Recent data suggest that one in three children in the UK is overweight or obese, and the prevalence is increasing. The discovery of the FaT mass and Obesity associated (*FTO*) gene has provided compelling evidence of genetic variation in the general population that influences fat levels and risk of obesity (1). Individuals carrying certain variants of this gene are at increased risk of obesity and have greater measures of fatness than non-carriers. The interaction of genetic and environmental factors requires investigation to understand how environment can modulate genetic contributions to risk of obesity. 949 11-18 year old Greek adolescents from the EUREKA study (Males: N=499; Females: N=450) were genotyped at the *FTO* rs17817449 polymorphism, and their weight, BMI, triceps and subscapular skinfolds were measured. Those reporting more

than the compulsory 2hrs of school-based physical activity by questionnaire were classified as active, while others were classified as inactive. Age and gender sub-groups were transformed and z-scores applied in each sub-group. Data are presented reverse-transformed based on 17-18 year old male values. The population was in Hardy-Weinberg Equilibrium. ANOVA analysis in all subjects showed an effect of *FTO* genotype on weight (P=0.017), with a T-dominant model explaining 99% of the genetic variance. All subsequent analyses were performed using this model and showed that *FTO* genotype influenced weight (P=0.005), BMI (P=0.012), triceps (P=0.02) and subscapular skinfolds (P=0.028). Homozygotes for the G-allele (GGs) had a 3kg increase in weight relative to T-carriers, and higher BMI and skinfolds. Gender sub-group analysis revealed effects on weight (P=0.01) and BMI (P=0.027) in males but not females. GLM-ANOVA analysis of weight in males revealed an interaction between physical activity and *FTO* genotype (P=0.01). The influence of *FTO* genotype was more pronounced in inactive males, and effects were found on weight (P=0.001), BMI (P=0.002), triceps (P=0.013) and subscapular skinfolds (P = 0.045). Inactive GG carriers displayed the equivalent of an almost 10kg increase in weight ((Data are mean (95% C.I) GG = 80.9kg (75.29-86.95), T-carriers = 70.99kg (68.3-73.78)), and 3 BMI units (GG = 25.68 (24.24-27.31), T-carriers = 22.92 (22.17-23.72)). Post-hoc analyses revealed that inactive GGs had higher adiposity than active GGs and all T-carriers; but that physically active GGs did not differ from T-carriers in any phenotypic measurement. It is concluded that *FTO* genotype at rs17817449 influences variation in obesity-related measures, and that GG individuals display higher levels of adiposity than T-carriers. However, a key finding of this study is that physically active carriers of the "fat variant" display the same levels of adiposity as non-carriers.

1. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science 2007;316: 889-94.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC48

Muscle function in cancer cachexia: Influence of systemic inflammation

N.A. Stephens, C.D. Gray, K.C. Fearon and C.A. Greig

School of Clinical Sciences and Community Health, The University of Edinburgh, Edinburgh, UK

Muscle wasting and loss of function are key features of cancer cachexia. Systemic inflammation (SI) is believed to play a central role in driving muscle loss and is also associated with poor survival in cancer (Deans et al, 2009). We hypothesized that muscle strength and power would be lower in cancer patients at the time of diagnosis compared with UK population data (Skelton et al 1994; 1999), and that strength, power and muscle quality (defined as strength per unit muscle volume Nl,$^{-1}$) would be influenced by the presence of systemic inflammation (defined as C-reactive protein (CRP) > 10mgl,$^{-1}$).

Twenty five patients with a new diagnosis of upper GI (UGI) cancer, (15 men, 10 women; mean age 66y), (mean) weight loss 8% and CRP 22mgl^{-1} participated. Lower limb power output (Nottingham power rig) and maximum voluntary isometric knee extensor strength were measured pre-operatively. In a sub-group of patients (n=12), sequential T1 weighted axial magnetic resonance (MR) images were acquired using a 1.5T MR scanner and analysed off-line for quadriceps muscle volume and derived measures of muscle quality. Statistical analysis to determine group differences was by Mann-Whitney and independent t-tests.

Mean (SD) maximum voluntary isometric knee extensor strength was 3.68Nkg^{-1} (1.15) in males and 3.36Nkg^{-1} (0.96) in females. Mean lower limb power output was 1.53Wkg^{-1} (0.43) in men and 0.98Wkg^{-1} (0.28) in women. Muscle power output and isometric strength were 42% ($p<0.001$) and 35% ($p<0.001$) below UK age- and sex-matched reference values. The differences between measured and reference values of power and strength were significantly greater ($p<0.008$; $p<0.047$ respectively) in the presence of SI. Muscle quality was also significantly reduced in patients with SI compared to those without SI, (147.8Nl^{-1} vs 268.1Nl^{-1}, p=0.017).

We conclude that at the time of diagnosis, muscle function in UGI cancer patients is already impaired. The magnitude of the impairment appears to be greater in the presence of SI. These data provide a rationale for targeting early therapeutic intervention to improve muscle function in cancer cachexia.

Deans DA, Tan BH, Wigmore SJ et al. Br J Cancer 2009; 100(1):63-9

Skelton DA, Greig CA, Davies JM et al. Age & Ageing 1994; 23(5):371-377.

We thank Cancer Research UK for financial support.

Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.