PC1

Urea and creatinine clearances in the trimesters of pregnancy

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The aim of this study was to determine the glomerular filtration rate (GFR) in the three trimesters of pregnancy, using creatinine and urea clearances. A total of 108 healthy subjects between the ages of 18 and 37 years were divided into non-pregnant (28 ± 5 years, n = 30), 1st trimester of pregnant (28 ± 5 years, n = 18), 2nd trimester of pregnant (28 ± 4 years, n = 30), and 3rd trimester of pregnant (30 ± 4 years, n = 30) women. Serum and urine samples were collected in mid-trimester period. Creatinine and urea concentrations in serum and urine were determined using Jaffe's method (Bosnes et al. 1945) for creatinine, and the urease method (Martinek, 1964) for urea.

There was a significant increase (mean ± SD) in creatinine clearance, but a significant fall ($p < 0.001$) in blood creatinine concentration in the three trimesters of pregnancy when compared with the control value. The increases of 43 ± 26 ml/min (non-pregnant vs. 1st trimester), of 39 ± 21 ml/min (1st vs. 2nd trimesters) and of 42 ± 25 ml/min (2nd vs. 3rd trimesters) of were similar. Similarly, there was a significant increase in the Urea clearances in the 1st, 2nd and 3rd trimesters of pregnancy, and remained elevated during pregnancy. In contrast, blood urea concentration increased significantly ($p<0.01$) in the three trimesters, despite an increase in the 12 hour urine volume output.

The results in Table 1 show that Ccr and Cur increase and peak during the first trimester of pregnancy. Although there was a reduction in Ccr in the 3rd trimester compared to the 2nd trimester, the clearance remained significantly higher ($p<0.05$) than in the non-pregnant women. This study agrees with other workers (Logoglu et al. 1990; Susan & Donna, 1992), who showed similar increases of GFR during pregnancy.

It is concluded that GFR increases and peaks during the first trimester of pregnancy and remains relatively stable till term.

Table 1

	Non-pregnant, ml/min	Pregnant, ml/min		
		1st Trimester	2nd Trimester	3ed Trimester
Blood creatinine conc., mg/100ml	0.84 ± 0.21	0.52 ± 0.15	0.40 ± 0.12	0.50 ± 0.14
Creatinine clearance, Ccr, ml/min	97 ± 20	127 ± 18	162 ± 28	130 ± 28
Blood urea conc., mg/100ml	12.0 ± 4.0	16.1 ± 4.6	19.4 ± 4.8	16.7 ± 5.2
Urea Clearance, Cur, ml/min	62 ± 21	87 ± 10	96 ± 18	96 ± 12

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PC2

Slowed leg blood flow kinetics in type 2 diabetes

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OBJECTIVE: Exercise performance is impaired in people with type 2 diabetes even in the absence of cardiovascular complications. It appears that oxygen uptake (VO2) kinetics during submaximal exercise are slowed in diabetics, factor that is likely to be associated with the exercise impairment. However the mechanisms for this slowed response are far from clear although they might be related to slowed skeletal blood flow responses.

AIM: of this study was to compare calf blood flow kinetic responses in women with type 2 diabetes and age and activity-matched nondiabetic obese & lean women following a moderately high intensity (70%MVC) calf plantar-flexion exercise.

METHODS: Leg blood flow responses (venous occlusion plethysmography measured contraction by contraction) were measured in 9 diabetic, 8 nondiabetic obese and 8 nondiabetic lean women during three bouts of 6 minutes of isometric intermittent (6 s cycles, 2 s contraction, 4 s relaxation) one-leg plantar flexion exercise. To perform the kinetic analysis a biexponential equation was fitted to each subject's mean blood flow responses (averaged from the three trials).

RESULTS: The mean response time of the leg blood flow increase was prolonged in type 2 diabetic compared with lean and obese healthy subjects (43.5 ± 41.8, 16.3 ± 6.8 and 15.5 ± 10.1 s, respectively, $P < 0.05$). In addition, the time constant of the second phase of the kinetic response was significantly longer ($P < 0.05$) in the diabetic compared to the obese and lean groups (55.2 ± 36.8, 18.9 ± 10.4 and 18.9 ± 14.8 s, respectively). The rest of the kinetic parameters were not different among the three groups. Statistical significance was observed using one-way ANOVA.

CONCLUSIONS: The results suggest a slowed increase in calf blood flow in women with type 2 diabetes during high intensity plantar flexion exercise. A reduced vasodilatory capacity caused by vascular dysfunction during exercise might be related to this observation. Further studies are needed to study the mechanisms associated with the impaired muscle oxygen delivery in diabetes.

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with adjustment for age, sex and lean mass. tCys was the strongest plasma variable associated with fat mass, stronger than and independent of plasma lipids. Women in the highest tCys quintile had fat mass 6 kg greater than that of women in the lowest quintile (95% CI: 5, 7 kg), with adjustment for plasma lipids, physical activity, and dietary fat, protein, and total energy intakes. Corresponding values for men were 4 kg (95% CI: 3, 5 kg; P<0.001 for ANOVA across quintiles in both genders). A higher baseline tCys and a rise in tCys over 6 y were both associated with greater fat mass at follow-up (P<0.001 by linear regression), with no effect on lean mass.

Discussion

Literature evidence points to tCys as a powerful but ignored determinant of fat mass. Homocystinurics with genetic deficiency of CBS enzyme (and hence decreased cysteine synthesis) are thin and underweight [3], a feature not reported for other types of homocystinuria, in which cysteine synthesis is normal. In contrast, Down syndrome patients, having triple copies of the CBS gene and elevated tCys, are overweight. Dietary cysteine supplements enhance weight gain in cachectic AIDS and cancer patients [4]: an effect generally attributed to improved lean mass, but do we know? Dietary restriction of the cysteine-precursor methionine reduces visceral fat mass in rats [5]. Several early studies on rat adipocytes demonstrate potent antilipolytic and lipogenic actions of cysteine.

Conclusions

Overall, our data and literature evidence suggest that cysteine could be an important modulator of body fat mass in humans, and if so, provides an attractive anti-obesity target.

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C12 and PC22

Modulated skeletal muscle microRNA processing within the invariant transcriptional landscape of type 2 diabetes

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Global transcript abundance profiling is a powerful systems biology tool for mapping alterations in phenotype only when careful consideration of the physiological context is maintained. Herein we present the first robust global transcriptome analysis of human skeletal muscle (vastus lateralis) in type 2 diabetes from 118 subjects (type 2 diabetes (n=45), impaired glucose tolerance (n=26) and normal glucose tolerance (n=47)). The study and analysis was approved by the appropriate ethics committees and performed according to the Declaration of Helsinki. Patients were free from diabetic treatment for 1 week prior to assessment. RNA was isolated as previously described (Timmons et al., 2007) profiled on the Affymetrix™ platform covering >47,000 mRNA sequences. We also utilized the TaqMan microRNA (miRNA) real-time qPCR method, to determine the expression of the muscle specific microRNAs (miR-1, miR-133a and miR-206). Comprehensive microarray data analysis (SAM, GSEA, PCA) demonstrated that the global type 2 diabetes muscle transcriptome is invariant with respect to controls. Furthermore, the expression of the mitochondrial OXPHOS geneset was identical between groups. Profiling of the muscle specific non-coding RNAs, however, demonstrated substantial modulation of these post-transcriptional RNA molecules. In type 2 diabetes patients, miR-133a expression was reduced (unpaired t-test) by a robust 5-fold (p<0.001) and miR-206 (p=0.04) was reduced by 2-fold. Northern analysis demonstrated that only mature miRNA was readily detectable for miR-133a. Importantly, miR-133a expression correlated (pearson) with both short (fasting glucose R2=0.37, p<0.001) and longer term (hbA1c R2=0.29, p<0.001) indices of impaired insulin action. Transcript abundance from the genomic loci of miR-133a demonstrated that primary precursor miRNA (pri-miRNA) production in vivo varies distinctly between the co-located miR-133a and miR-1 genes, yet are unchanged with respect to metabolic status, suggesting that maturation of miR-133a is substantially altered in type 2 diabetes. Thus, contrary to recent claims (relying on smaller, less well controlled patient groups ((Mootha et al., 2003; Patti et al., 2003)) we find that the type 2 diabetes skeletal muscle transcriptome is not characterized by reduced OXPHOS gene expression, while it would appear that inhibition of miRNA molecule production may be a post-

transcriptional disease mechanism for altering muscle phenotype in human type 2 diabetes

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C13 and PC23

Increased energy intake in children with an obesity-associated FTO gene variant

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C14 and PC24

Illness, body mass index and leptin

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Introduction
There is anecdotal evidence that obese individuals suffer from poor wound healing and frequent minor illnesses such as upper respiratory tract infections (URTI) cf. lean individuals. The altered metabolic, psychological and endocrine status of obesity may lead to immunodepression. Our group has investigated URTI in fatigued athletes and military personnel (Castell, 2003); one study focused on the obesity hormone, leptin which regulates energy balance, and its role in immune function. Decreased circulating leptin can lead to hyperphagia in some genetically obese individuals (O'Rahilly, 2002). However, human obesity is usually characterized by excessive leptin, rather than deficiency. The leptin functional receptor is found in all immune response cell types: thus leptin may link nutritional status, energy balance and immune function. Sleep loss, partial or chronic, is linked to decreased immune function. Obesity is a factor in obstructive sleep apnoea, which significantly reduces sleep duration and quality.

Aims
This pilot study surveyed the incidence and severity of URTI, psychological and sleep profiles in sedentary participants of different ages, and body mass indices (BMI). The aim was to observe whether mild obesity (BMI 30-35) predisposed people to an increase in URTI cf. individuals with a lower BMI. The survey was a precursor to a more detailed study.
Methods
Eight lean, 2 overweight, 8 obese sex matched, sedentary participants were recruited for this ethically approved survey. Anthropometrics (ht, wt, waist, hips) were taken; A resting blood sample measured plasma leptin; Daily questionnaires were given for 6 wks to monitor URTI; POMS (depression, stress, fatigue, motivation); Sleep (duration, quality); Dietary diaries. A multiple regression General Linear Model was used to explain the "illness score".
Results
A higher BMI was significantly associated with higher symptoms of illness ($p<0.01$). Calorie consumption was associated with BMI ($p<0.05$). BMI correlated with plasma leptin concentration. Poor sleep quality predisposed individuals to an increase in URTI symptoms ($p<0.032$); in addition it was associated with higher levels of depression ($p<0.005$) and stress ($p<0.005$). Sleep duration did not have any effects.
There was an apparent link between smoking and increased URTI symptoms.
Discussion
The study showed links between increased BMI, poor sleep quality and the incidence of self-reported URTI. It is suggested that obesity is associated with an increase in URTI cf. normal or lean weight. BMI was linked with blood leptin concentration, and it is tempting to speculate that there might be a link between leptin and increased URTI.

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We are grateful to the volunteers for their cheerful participation

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C15 and PC25

Extremely short duration high intensity training substantially improves insulin action in young healthy males

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Introduction: The prevalence of type 2 diabetes is increasing in western societies resulting in increased healthcare/economic costs. However, the risk of developing T2D is positively modified by regular physical activity. Despite this, there is a lack of consensus on the ideal strategies for ensuring adult participation in exercise. Current recommendations involve performing moderate intensity exercise for several hours per week; however, the general population fails to adhere to such regimes typically stating time as a major barrier. Recently an extremely low volume high-intensity training paradigm (HIT), ~7.5 minutes of exercise per week, has been proposed as a novel, time-efficient exercise regime for inducing aerobic adaptations[1]. This has challenged our understanding of aerobic adaptation in humans. Aerobic training has been demonstrated to improve insulin action in humans and we sought to establish if HIT can enhance insulin sensitivity in sedentary younger male subjects.
Methods: 25 young men (21±5 y) were randomly assigned to control (n=9) or HIT (n=16) groups. Subjects underwent an oral glucose tolerance test (OGTT), a VO_{2peak} test and 2x250kJ cycling time trials. The control group adhered to their normal routine for 2 weeks prior to a second OGTT. HIT comprised of 15 min exercise over 2 weeks, consisting of 4-6 x 30-second cycle-sprints per session. At 48 or 72 hr post training, subjects underwent a second OGTT followed by a third time trial 24h later.
Results: Following 2 weeks of HIT, the area under the plasma glucose, insulin and NEFA concentration-time curves were all reduced (12%, 37%, 26% respectively, all $P<0.001$). Insulin sensitivity (Cederholm index) was markedly improved following 2 weeks of HIT (23%, $P<0.001$). Fasting plasma NEFA concentration was also reduced (pre: 350 ± 36 v post: 290 ± 39 $\mu mol.l^{-1}$, $P<0.05$) while fasting plasma insulin and glucose concentrations remained unchanged. There were no changes in the control group.

Conclusions: These results demonstrate the remarkable efficacy of HIT to improve insulin action in young healthy men. Therefore, there is a need to reappraise the current trends in exercise prescription for increasing energy expenditure, to focus on strategies that are both preventative and more likely to be adhered to by young and middle-aged people.

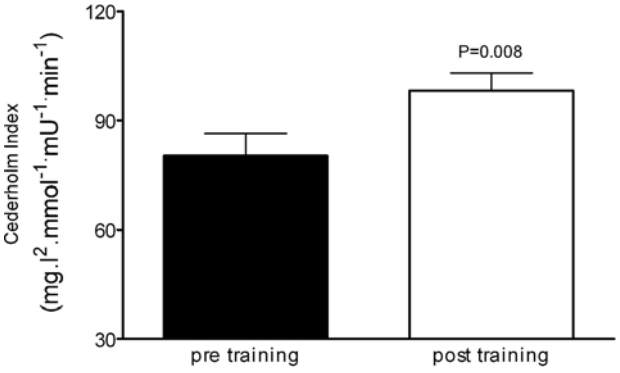

Figure 1: insulin sensitivity pre and post HIT

Burgomaster KA, Hughes SC, Heigenhauser GJ, Bradwell SN, Gibala MJ. Six Sessions of Sprint Interval Training Increases Muscle Oxidative Potential and Cycle Endurance Capacity in Humans. J Appl Physiol 2005; 98: 1985-90.

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