



RESEARCH TO
PRACTICE 2018

27-29 MARCH 2018
BRISBANE, QUEENSLAND

METABOLIC ORAL FREE PAPERS

Wednesday, 28 March 2018

11:00am – 12:30pm

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Effects of 4-week intermittent hypoxia intervention on insulin receptor phosphorylation and Akt activity in the liver and GLUT2 expression and GSIS in the pancreas islets of diabetic mice

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Introduction & Aims: Four weeks of intermittent exposure to moderate levels of hypoxia has been reported to reduce fasting blood glucose in mice with type 2 diabetes (T2D), and resulted in up-regulation in insulin-dependent signalling pathway and mitochondrial function in skeletal muscle. The aim of this report was to examine the associated changes in insulin receptor phosphorylation (IRP) and Akt activity (Akt-a) in the liver, and pancreatic beta-cell function, indicated by GLUT2 expression and glucose-stimulated insulin secretion (GSIS).

Methods: C57BL/6J mice with diet-induced T2D were allocated into 4 groups: rest in hypoxia (DH), exercise in hypoxia (DHE), exercise in normoxia (DE) and control (DC), plus a non-diabetic control group (NC) (n=7 each). The DH, DE and DHE were given the corresponding intervention 1 hr/session, 6 sessions/week, for 4 weeks. The DE and DHE exercised on a treadmill at ~75-90%VO₂max. Liver and pancreas islets samples were collected 72 hr after the last session. The targeted proteins were analysed by Western blot. The GSIS was determined by a 90 min incubation of isolated islets with various glucose concentrations.

Results: The DH and DHE showed an increased IRP and Akt-a in the liver compared to the DC (p=0.001). The DE also showed a higher Akt-a than the DC (p=0.001), but a lower IRP than the DH (p=0.015). The DH showed a lower GLUT2 than DC and DE (p=0.001 and 0.021, by one-way ANOVA). The insulin response to GSIS at the highest glucose concentration of 16.7mM was higher in the DH than other groups except DE (p<0.05 by repeated measures ANOVA).

Conclusion: Both DH and DHE resulted in improvement in the insulin-dependent signalling pathway as indicated by increased liver IRP and Akt-a. The lower basal level of islet GLUT2 in DH might relate to a reduced stress on beta-cell that could prevent further beta-cell failure. The DH and DE also resulted in increased insulin secretion in response to GSIS, indicating an improved β -cell function.





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Can exercise training provide additional health related quality of life benefits to dietary weight loss for women with severe obesity?

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Introduction and Aims: Women are twice as likely to have severe obesity (BMI > 35kg/m²) compared to men. Further, women are more likely to identify impaired health-related quality of life (HRQOL) in relation to severe obesity. Previous evidence reports that substantial weight loss following bariatric surgery can improve HRQOL to general population levels. Yet little is known regarding whether lifestyle interventions can achieve the same improvements. This study aimed to identify the degree to which modest weight loss with and without exercise training can improve HRQOL relative to healthy weight age matched controls.

Methods: 60 women with severe obesity (mean BMI = 40.4kg/m²) were recruited and randomised to a 12 month intervention of either energy restriction (ER) or energy restriction plus exercise training (EXER). Both groups followed an energy restricted, meal replacement diet under supervision of Accredited Practising Dietitians. EXER also participated in supervised (with an Accredited Exercise Physiologist) and unsupervised exercise training following a decreasing contact protocol targeting 300min/wk of exercise. HRQOL was assessed pre and post-intervention using the SF-36 and was compared to a community dwelling, age matched sample with healthy weight from the Australian Longitudinal Study of Women's Health (ALSWH).

Results: Following intervention, in comparison to healthy weight age matched women from the ALSWH, HRQOL was similar for all domains and summary scores of the SF-36 for women in the EXER group. However, women in the ER group scored lower for general health domain compared to healthy weight women ($p < 0.01$).

Conclusion: It is possible for women with severe obesity to achieve HRQOL commensurate to their healthy weight, age-matched counterparts following EXER and ER. This was achieved using a lifestyle intervention and suggests that HRQOL should be a key outcome of weight loss programs beyond the bodyweight.





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Exercise Intensity does not Impact Positive Affect in People with Type 2 Diabetes

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Introduction: Exercise can result in positive affective responses, which can in turn promote exercise engagement and adherence. With the recent shift towards the use of high intensity interval training (HIIT) in people with chronic conditions, it is important to understand the impact of exercise intensity on positive affect (PA). The aims of this study were to assess the effects of HIIT and moderate intensity continuous training (MICT) on PA in people with type 2 diabetes (T2D) for a) changes in pre-exercise session PA after an 8-week intervention, and b) changes in pre- to post-exercise session PA.

Methods: 26 individuals (age 58.9±7.0y, BMI 33.4±7.2kg/m², 57.7% male) diagnosed with T2D (mean HbA_{1c} 7.5±1.3%) were randomly allocated to 8-weeks of either supervised low volume HIIT (1x4min high intensity aerobic @ 85-95% HRmax plus resistance training, 3times/week) or supervised MICT (22.5min @ 55-65% HRmax plus resistance training, 4times/week). PA was measured immediately before (pre) and after (post) each exercise session using the positive subscale of the Positive and Negative Affect Schedule. Changes in PA were calculated for each person as a) the difference between the first and final pre-exercise session assessments, and b) the difference between pre- and post-exercise session assessments for each session, averaged across all sessions.

Results: There were no between group differences ($p=.451$) in change in the pre-exercise PA scores (out of 50) following 8-weeks of HIIT (baseline 32.9±7.5, 8-weeks 36.6±9.6) or MICT (baseline 33.9±8.0, 8-weeks 35.2±10.8). There were also no between group differences ($p=.976$) in the changes in PA from pre- to post-exercise session (HIIT 4.1±7.4, MICT 4.0±4.5).

Conclusion: Exercise intensity did not impact positive affect in people with T2D, both with an acute bout of exercise and following an 8-week intervention. This has important implications for the psychological viability of HIIT to manage T2D and improve exercise adherence.





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High intensity interval training prior to assisted fertilization improved insulin sensitivity but did not increase pregnancy rate in overweight and obese women: A pilot study

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Introduction and aim: The risk of infertility is threefold higher in obese than in non-obese women. The exact pathophysiology of obesity-related infertility is unclear, but insulin resistance is proposed as an underlying factor. Our aim was to assess if high intensity interval training (HIT) prior to assisted fertilization would improve pregnancy rates in overweight and obese women.

Methods: This was a randomized controlled trial of HIT before assisted fertilization in women with a BMI ≥ 25 kg/m². Eighteen sedentary women (age 32.3 ± 5 yrs, BMI 30.2 ± 2.2 kg/m²) were randomly allocated to HIT ($n=8$) or control ($n=10$) for ten weeks prior to in vitro fertilization (IVF). The HIT group undertook three weekly sessions; two 4x4 min HIT sessions at an intensity corresponding to 85-95% of their heart rate maximum and one 10x1 min 'all out' session. Participants then underwent assisted fertilization using standard procedures. Our primary outcome was ongoing pregnancy, 7-8 weeks after embryo transfer. Secondary outcomes was insulin sensitivity (hyperinsulinemic-euglycemic clamp), oxygen uptake (VO_{2peak}) and body composition.

Results: The proportion of pregnancies after IVF was 50% in the HIIT group and 40% in the control group (no between-groups difference, $p=0.8$). Glucose infusion rate improved significantly after HIIT, from 264.1 mg/m²/min at baseline to 324.7 mg/m²/min after ten weeks, with no change in the control group (between-group difference 83.7 mg/m²/min, $p=0.04$). VO_{2peak} increased from 31.1 mL/min/kg at baseline to 33.7 mL/min/kg in the HIIT group, but this was not significant (between-group difference $p=0.09$). Body composition did not change in any group.

Conclusions: Pregnancy rate did not increase after ten weeks of HIIT prior to IVF in overweight and obese women, probably due to an underpowered sample size. We observed a significant improvement in insulin sensitivity after HIIT, possibly of clinical relevance for IVF success rates in this population.



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The association between hepatic enzymes, sedentary behaviour, physical activity and cardiorespiratory fitness in a large population based-cohort

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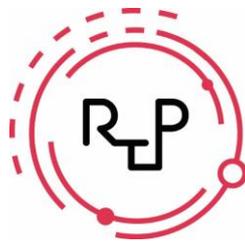
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Introduction and Aims: Elevated hepatic enzymes alanine aminotransaminase (ALT) and gamma glutamyl transferase (GGT) are associated with non-alcoholic fatty liver disease (NAFLD), and independently predict incident type 2 diabetes and cardiovascular disease (CVD). Prolonged sedentary time (ST) is a risk factor for cardio-metabolic diseases and elevated ALT and GGT, independent of physical activity (PA). Recent studies have shown that high cardiorespiratory fitness (CRF) attenuates the negative association between ST and CVD risk independent of PA. However, whether high CRF has a similar protective effect on hepatic health is not known. This study examined the effects of CRF and PA on the association of ST with markers of hepatic disease (elevated ALT and GGT).

Methods: A cross-sectional analysis of 16'640 adults (52% female) was conducted. Self-reported ST during a regular day was divided into three tertiles. CRF was estimated (eCRF) using a previously validated non-exercise model. Elevated ALT and GGT were defined as the highest sex- and age- specific tertiles. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression analyses.

Results: For each additional 1h of ST, the likelihood of having elevated ALT and GGT was significantly increased (by 2% and 4%, respectively). For each 1MET decrement in eCRF, it was increased by 11% and 27%. In combined analyses, compared to the reference group [high eCRF, PA \geq recommendations(rec), and ST<4h/d], individuals with low eCRF had higher likelihood of having elevated ALT (by 84%; OR, 1.84; CI 1.2-2.8) and GGT (2.08; 1.4-3.2), even if they had ST<4h/d and PA \geq rec. In contrast, high-eCRF was protective even in those sedentary and below PA \geq rec (ALT:1.18; 0.96-1.44).

Conclusions: High sex- and age-specific eCRF attenuated the adverse effects of ST on liver enzymes, even in individuals not meeting PA \geq rec. Guidelines for the management of NAFLD should incorporate recommendations to improve CRF.



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Heat Treatment and Exercise Prevents Skeletal Muscle Insulin Resistance in Wistar Rats Fed High-Fat Diet

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Background: Insulin resistance (IR) is associated with many related health complications. Previous studies demonstrated that heat and exercise could have positive function on IR separately. Earlier our study in IR rats induced by high-fat diet showed that exercise combined with high temperature had more effective on IR.

Methods: Male Wistar rats were randomly divided into five groups: exercised (NE; n=10), heat (HC; n=10), exercised and heat (HE; n=10), sedentary (NC; n=10), and normal diet sedentary (CC; n=10). The subjects were fed a high-fat diet (60% calories from fat) for 10 weeks and treated heat and/or exercise for 8 weeks. Protein expression of soleus and extensor digitorum longus (EDL), serum, and brown fat was analyzed using Western blotting.

Results: Our results show that heat treatment accompanying exercise shifts the metabolic characteristics of rats on a high-fat diet toward those on a standard diet. Eight weeks of heat accompanying endurance exercise increased PGC-1 α , CnA, CaMKIV and p38 MAPK protein expression in the soleus ($P < 0.01$ or $P < 0.05$), Insulin protein expression in the serum ($P < 0.05$), and UCP1 protein expression in the brown fat ($P < 0.05$) compared to the sedentary group.

Conclusions: Exercise combined with high temperature treatment mitigates the development of IR from Irisin pathway. The study also provides potential "green" methods for therapeutic treatment of insulin resistance.

