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ORIGINAL RESEARCH

THE EFFECT OF CONTINUOUS VIGOROUS EXERCISE AND LIFESTYLE-EMBEDDED PHYSICAL ACTIVITY UPON ACUTE GLYCAEMIC REGULATION- A CASE STUDY

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Abstract

The purpose of this study was to investigate the effect of continuous exercise and lifestyle-embedded physical activity upon glucose regulation, and assess the feasibility of seven day continuous glucose monitoring (CGM) in a normoglycaemic individual. One physically active non-diabetic male [age: 22 y; mass: 71.5 kg; height: 181 cm] underwent 7 days CGM, performing 3 trial conditions: a sedentary control (< 2500 steps, pedometer controlled), a continuous exercise condition (2 x 30 min treadmill running at 70% HR_{max}), and a lifestyle-embedded physical activity condition (100 min fractionalized moderate activity). Diet was standardised and physical activity levels were monitored via accelerometry throughout. Results showed a significant difference of -0.24 $mmol.dL^{-1}$ in twenty-four hour mean glucose levels between the sedentary and continuous condition ($p = 0.00$), and a significant difference of -0.038 $mmol.L^{-1}$ in twenty-four hour mean glucose levels between the sedentary and lifestyle embedded physical activity condition ($p = 0.004$). Descriptive results displayed a post exercise decrease in glucose levels (2 h pre-6 h post (5.3 – 5.1 $mmol.L^{-1}$)) with a carryover effect for the following day (reduced mean glucose 24 h pre-post (5.5 ± 0.5 - 5.2 ± 0.3 $mmol.L^{-1}$)) in the continuous exercise condition. Physical activity counts ($c.min^{-1}$) during exercise were significantly related to blood glucose levels in the continuous exercise condition ($r = 0.51$, $p = 0.08$). Findings show that intra- and inter-day glucose homeostasis may be optimised through bouts of continuous vigorous exercise.
Key Words: Movement, Glucose, normoglycaemia, intervention.

Introduction

The economic and disease burden associated with diabetes is large and continues to escalate worldwide (1), approximately 1 million deaths were associated with diabetes worldwide as of 2002 (2). Thus the current climate of increasing prevalence provides strong rationale for developing preventative measures. A sedentary lifestyle is considered an important modifiable risk factor for type 2 diabetes. Indeed there is consensus that physical activity reduces the risk of developing insulin resistance and glucose intolerance (3), although the 'dose' a function of intensity, frequency, and duration, of physical activity required for optimal protection continues to be debated (4).

The effect of exercise upon glucose metabolism is well documented, exercise is known to increase the rate of glycogen uptake into the surrounding skeletal muscle (5). The majority of research upon blood glucose response to exercise is of a long-term experimental design, detailing chronic adaptations to exercise or physical activity interventions in primarily diabetic populations. However recent developments have enabled clinicians to reliably monitor plasma and/or interstitial glucose concentrations in an ambulatory and continuous manner (6). Continuous glucose monitoring (CGM) has recently emerged as a new tool for patients with type 1 diabetes mellitus to help maintain normal glucose levels.

CGM monitors provide information on ambulatory, postprandial and/or nocturnal glucose excursions (7). In contrast to intermittent self-monitoring of blood glucose (SMBG), CGM systems (e.g., Guardian RT, Minimed, Medtronic) allow glucose levels to be measured continuously from a small electrode inserted into the interstitial fluid of the subcutaneous tissue. The availability of such high resolution data permits investigation of the pattern of glucose in response to physical activity. Currently only two studies have utilised CGM within normoglycaemic populations (6, 8), and only two have explored glucose response to lifestyle related physical activity (8, 9).

Knowledge of acute glycaemic responses to physical activity and exercise will aid in the generation of evidence based physical activity interventions, and elucidate upon diurnal glucose regulation. Due to the paucity of physical activity and CGM related research literature within this field, the potential application of CGM is largely unknown. As yet no CGM studies have investigated differing physical activity conditions, and further utilised objective physical activity measurement in conjunction.

Therefore the aim of this study was to determine the role of continuous and lifestyle-embedded (intermittent bouts) physical activity (as measured by accelerometry) on the regulation of interstitial glucose (as measured by CGM). In addition a concurrent aim was to assess the feasibility and utility of CGM data collection alongside objective measures of physical activity.

Methods

Participants

This study was conducted as a case study of a single participant. The participant was a physically active male aged 22 years [mass: 71.5 kg; height: 181 cm]. The study was approved by the Ethics Committee of the School of Sport and Health Sciences at the University of Exeter, UK. The participant gave written informed consent before participating in the study.

Instruments

The CGMS iPro

The CGMS iPro Continuous Glucose Recorder continuously collects and records patient interstitial glucose values at a 5 minute epoch. Values are registered as an electrical voltage known as an ISIG; these are converted into blood glucose concentrations upon calibration with time-matched fingerstick blood glucose samples in the download process. Firstly the glucose sensor (SOF-SENSOR, Medtronic, Northridge, USA) was placed into a spring loaded applicator, which fires the sensor into the chosen site. The applicator was pressed at a 45 ° angle against the skin and the sensor was fired into the skin. Following this the needle was removed from the skin leaving the sensory capillary located in the subcutaneous tissue. This was left for five minutes. The Solutions software was loaded and patient information entered. Following this the digital recorder was attached to the sensor.

Once the digital recorder was attached, the iPro was intialised by passing a magnetic wand (CGMS iPro Wand) along the edge of the recorder. Upon completion of this stage the digital recorder began recording and was covered by an occlusive dressing. The glucose sensor life is 72 h, thus on day 3 and 5 the expired sensor was removed and replaced. A different insertion site in the abdomen was used each time as. Following completion of the 8 day testing period, data was downloaded.

Experimental Protocol

Tables

Table 1. Experimental design

CGMs1*	CGMs1	CGMs1	CGMs2	CGMs2	CGMs2	CGMs3	CGMs3
Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Measurements	NCd1**	NPAd***	RBd1^	#CPAd	RBd2^	LPAd^^	RBd3^ (Finish)

***CGMs** Sensor number (life span 72 h). ****NCd1** (Nutrition control day 1): Participant diet standardised. *****NPAd** (No Physical activity day): Sedentary Control <2500 steps. #**CPAd** Continuous exercise day. ^**RBd 1, 2 & 3** (Return to baseline days 1, 2 & 3): 3 days of 'wash-out' after trial conditions to ensure no carry-over effects. ^^**LPAd** Lifestyle-embedded physical activity day. **Finish** Asses any last bout effect, download data, end of testing.

The participant initially reported to the laboratory upon which anthropometric data was gathered. In addition the participant underwent a maximal oxygen uptake test to determine the prescription of work rate during the ensuing trial conditions. The research design consisted of three experimental conditions (see table 1. below): a

sedentary control condition, a continuous vigorous exercise condition and a lifestyle-embedded physical activity condition. These conditions were embedded within an 8 day testing period, during which diet was standardised and physical activity levels were monitored via accelerometry throughout. At the start of the testing period the participant was fitted with a CGM (CGMS iPro, Medtronic, Northridge, USA) and an Actigraph GT1Ms accelerometer (Actigraph, USA).

Sedentary Control Condition

The participant completed an imposed sedentary condition (NPAd). During this 24hr period the participant was restricted to < 2500 steps, assessed via pedometery (Yamax Digi Walker SW-200).

Continuous Vigorous Exercise Condition

The participant completed 2 x 30 minute bouts of treadmill running at 70% of HR_{max} (144 $b.min^{-1}$) separated by a three hour transition period. Prior to and after the exercise bout, the participant was restricted to a daily total of < 2500 steps. This intensity was chosen on the basis of physical activity recommendations for glycaemic control (5).

Lifestyle-embedded Physical Activity Condition

The participant completed 100 min accumulated physical activity fractionalised into shorter bouts of treadmill walking, stair climbing, outside brisk walking and cycling on an ergometer, spread between the hours of 9am to 5pm. Treadmill walking was conducted at a set pace of 5 k $m.hr^{-1}$ to imitate a brisk walk. Stair climbing was undertaken in time with a metronome, set to dictate a moderate intensity. Outside brisk walking was conducted on a tarmac path, the participant was asked to maintain a pace they considered a brisk walk. A single bout cycling on a cycle ergometer was conducted at a cadence of 70 revolutions per minute (rpm) with a resistance set at 0.5 kg. Prior to and after the physical activity bouts, the participant was restricted to a daily total of < 2500 steps.

Statistical Analyses

Solutions software v. 2.0A (Solutions iPro, Medtronic, Northridge, USA) generated a table of summary statistics, daily glucose plots, and a database of recorded values. Statistical analysis was conducted using SPSS v.15.0 for Windows (SPSS, Chicago, IL, USA). A one- way repeated-measures ANOVA was used to determine differences in mean blood glucose values between conditions $p < 0.05$. Pearson's correlation coefficient was used to determine the relationship between glucose values and physical activity counts during exercise. Statistical significance was set at an alpha level of $p < 0.05$.

Results

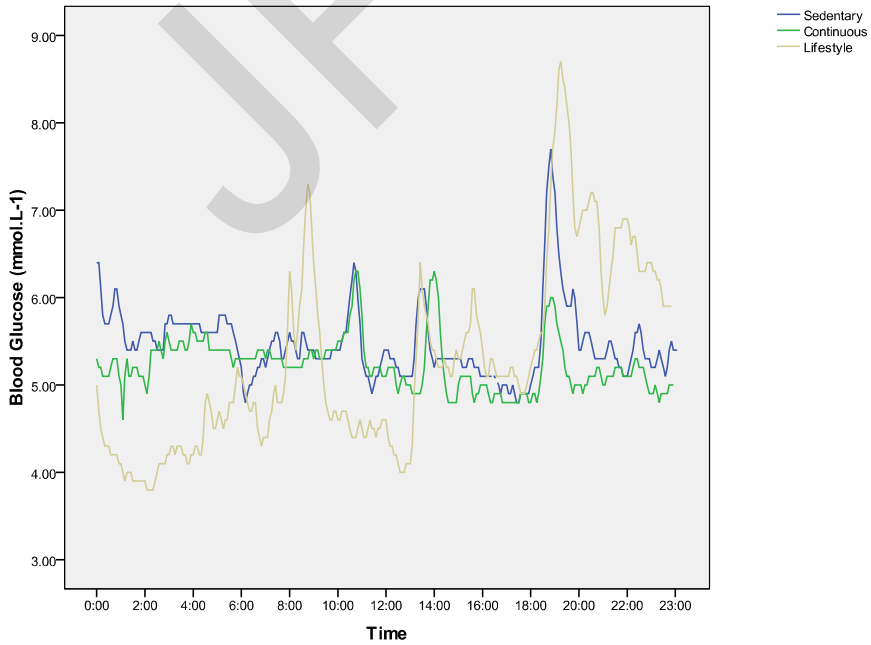

Figure 1. Twenty-four blood glucose profiles for sedentary, continuous and lifestyle embedded-physical activity condition.

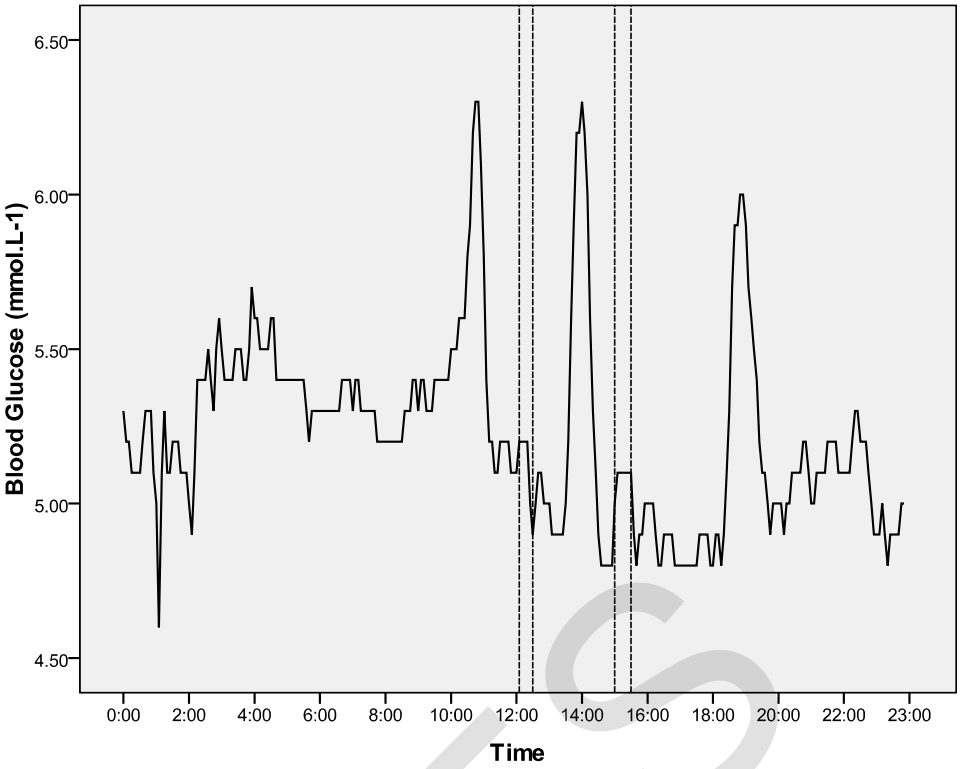

Figure 2. Twenty-four hour blood glucose profile for the continuous exercise condition. Dashed lines represent times of 30 min exercise bouts.

Table 2. Whole day mean blood glucose and physical activity levels for all conditions

	Sedentary	Continuous	Lifestyle
Mean Blood Glucose ($mmol.L^{-1}$)	5.4 ± 5.4*^	5.2 ± 0.3*	5.2 ±1.1^
Mean Physical Activity Count *($c.min^{-1}$)	63.7 ± 252.1	496.2 ± 1716.0	324.0 ± 999.5

*Significant difference between continuous and sedentary ($p<0.05$).
^Significant difference between lifestyle and sedentary ($p<0.05$).

A repeated measures ANOVA showed that there were significant differences in twenty-four hour mean blood glucose levels between conditions F (1.2, 568) = 11.394, p =0.00. Post hoc tests using a bonferroni corrected alpha ($p<0.05$) revealed a significant difference of -0.24 mmol.dL-1 in twenty-four hour mean glucose levels between the sedentary and continuous condition (p = 0.00), and a significant difference of -0.038 mmol.dL-1 in twenty-four hour mean glucose levels between the sedentary and lifestyle embedded physical activity condition (p = 0.004).

Descriptive results showed in the sedentary condition there was no change in mean glucose levels 24 hours pre and post trial conditions (Mean ± SD: 5.5 ± 0.4 $mmol.L^{-1}$). In the continuous exercise condition, blood glucose concentration decreased (5.5 ± 0.5 - 5.2 ± 0.3 $mmol.L^{-1}$). In the lifestyle-embedded activity condition, glucose concentration increased (5.2 ± 0.3 – 5.4 ± 0.6 $mmol.L^{-1}$). In the continuous exercise condition glucose levels decreased in the first two hours post last exercise bout, and then maintained a steady state (5.3 ± 0.5 – 5.1 ± 0.08 $mmol.L^{-1}$).

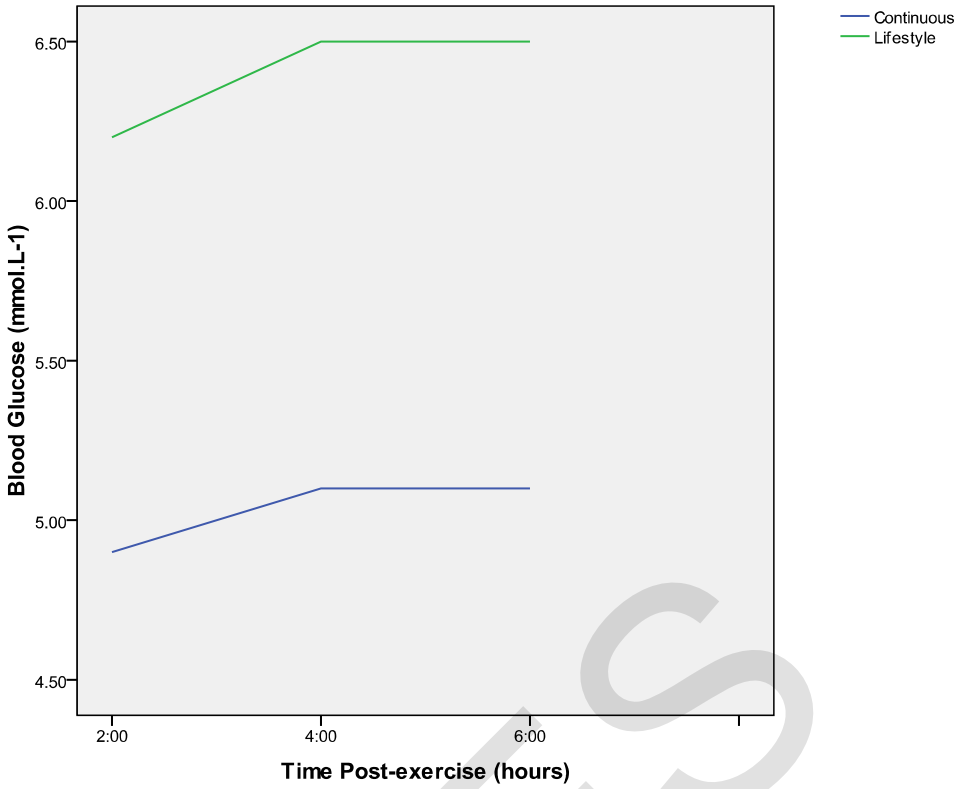

Figure 3. Mean blood glucose, 2,4 and 6 hours post final exercise bout for continuous exercise and lifestyle-embedded physical activity conditions.

In the lifestyle condition glucose levels increased until four hours post exercise, then maintained a steady state (5.3 ± 0.3 – 6.5 ± 0.3 mmol.L^{-1}). Pearson's correlation revealed a significant correlation between physical activity counts and glucose values during exercise in the continuous condition (r = 0.51, p = 0.08). No significant correlation was found during activity bouts in the lifestyle condition (r = -0.13, p = 0.75).

Discussion

Mean 24 hour Glucose Levels

Clearly exercise bouts in both the continuous and lifestyle conditions down-regulated 24 h mean glucose levels. The lower glucose levels reported during the exercise condition is in keeping with the majority of published data, which indicates that aerobic exercise reduces acute blood glucose levels. (10). Decreased mean glucose levels may be explained by an increase in glucose transport and phosphorylation as a result of a greater number of GLUT4 transporter proteins in the plasma membrane; through exercise stimulated translocation from intracellular storage (11,12). However as this was a normoglycaemic individual, the extent to which the exercise conditions aided glucose clearance from the blood is unclear.

Mean Glucose Levels: Pre-Post Condition

The purpose of this outcome was to ascertain any lasting effect of the trial condition upon glucose levels. A positive effect was found in the continuous exercise condition only (5.5 ± 0.5 - 5.2 ± 0.3 mmol.L^{-1}). This may be explained by the participant's current level of fitness (Peak VO_2 = 62 mL.kg.min^{-1}). Whilst lifestyle-embedded activity modulates whole day glucose levels, it is postulated that the metabolic cost (set as moderate intensity) was not sufficient to stimulate a lasting effect. Previous findings show that muscle glucose uptake at 85% of VO_{2max} is twice that at 65% of VO_{2max}, supporting this hypothesis (13).

Mean Glucose Levels: Pre-Post Last Activity Bout

Results showed a marked difference in post-exercise glucose response between conditions. The continuous exercise condition displayed a last bout reduction in mean glucose, which decreased from 2 h prior to 6 h post the final exercise bout (5.3 ± 0.5 – 5.1 ± 0.08 mmol.L^{-1}). Numerous mechanisms may explain the transient post-exercise decrease in glucose levels and more importantly the carry over effect upon the ensuing 24 h. Exercise leads to diverse adaptations that have significant impact on glucoregulation, even after the cessation of exercise (5). These adaptations largely share the common purpose of replenishing fuel stores, particularly muscle and liver glycogen. Stimulation of muscle glucose uptake persists well after exercise. The added glucose uptake post-exercise is stored as glycogen, this is characterised by a marked and persistent increase in insulin action and sensitivity (14), which can persist post-exercise despite glycogen levels returning to baseline. Therefore the

decrease in glucose levels observed 2 hours post the final activity bout in the continuous condition may result from increased insulin sensitivity.

The Relationship between Physical Activity and Glucose Regulation

The relationship between physical activity counts and glucose values was assessed during exercise only. Lifestyle-embedded physical activity bouts, were not significantly related to blood glucose levels (r = -0.13, p = 0.75). During the continuous exercise bouts, a medium positive correlation was identified (r = 0.51, p = 0.08). This suggests that for a transient period glucose levels are raised in the blood. This is in agreement with some research that state during exercise at a high workload; liver glucose output may be regulated by a feed-forward mechanism, whereby motor centers in the brain activate, in parallel, locomotion and neuroendocrine responses increase glucose production (15). It would be churlish however to conclude that on the basis of this relationship a causal link is apparent. It is believed there may be a significant time lag (of up to 5 minutes) between interstitial glucose CGM readings and current blood glucose levels (16). Future studies may wish to explore this time lag to elucidate upon the true relationship between time matched physical activity data and glucose levels.

Conclusions

It is concluded that improved intra-and inter day glucose regulation in a normoglycaemic individual may be achieved through undertaking bouts of vigorous intensity aerobic exercise. In accordance moderate lifestyle-embedded physical activity may provide a beneficial alternative to those who cannot or are unwilling to partake in regular aerobic exercise. The utilisation of CGM in exercise protocols and prolonged data collection is deemed a feasible proposition; however larger scale studies may pose logistical problems. This study was limited by its single subject design and specificity to normoglycaemic populations, future studies should look to include a greater sample size and characterise glycaemic regulation in pre-diabetic and diabetic populations.

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