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Intermittent walking, but not standing, improves postprandial insulin and glucose relative to sustained sitting: A randomised cross-over study in inactive middle-aged men

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ABSTRACT

Objectives: Interrupting prolonged periods of sitting may improve postprandial insulin and glucose although it is unclear whether interruptions need to involve physical activity or simply a change in posture (from sitting to standing) to benefit adults without metabolic impairment. This study examined effects of interrupting sitting with intermittent walking, and intermittent standing on dynamic insulin and glucose responses in men without known metabolic impairment.
Design: A randomised three-arm, cross-over experimental study comprising three seven-hour days of sustained sitting.
Methods: Twenty-five inactive men (aged 40.2 ± 12.2 years) took part. The three interventions were; SIT-ONLY (uninterrupted sitting), SIT-STAND (sitting interrupted with 2 min standing bouts every 20 min) and SIT-WALK (sitting interrupted with 2 min light-intensity walking bouts every 20 min). An oral glucose tolerance test was administered at baseline and a standardised mixed test meal at hour three. Comparisons of Matsuda Index, and area under the curve (AUC) for insulin and glucose were made between interventions using generalised estimating equation models.
Results: Matsuda index was 16% higher (mean difference 1.2 [95%CI 0.1, 2.2] $p = 0.02$), AUC for glucose 9% lower (−2.5 mmol/L × 7 h [−3.7, −1.3 mmol/L × 7 h] $p < 0.001$) and AUC for insulin 21% lower (−546.5 pmol/L × 7 h [−723.6, −369.3 pmol/L × 7 h] $p < 0.001$) in SIT-WALK compared to SIT-ONLY. There were no significant differences between SIT-STAND and SIT-ONLY in any main outcome measure.
Conclusions: Interrupting sustained sitting with brief repeated bouts of light-intensity walking but not standing reduced insulin demand and improved glucose uptake during a simulated sedentary working day. The benefits of such minor behavioural changes could inform future workplace health interventions.

1. Introduction

Poor glycaemic control is an important contributor to global morbidity and mortality,[1] both directly through microvascular complications and through the associated 2–3 fold increase in cardiovascular disease risk.[2] Physical activity provides a valuable tool in reducing diabetes and cardiovascular risk but advancements in technology and the social and built environments, have reduced necessity for physical activity, and increased our propensity for sitting.[3] Adults spend up to 10 h per day sitting,[4] including over 75% of working hours,[5] as the proportion of people in largely sedentary occupations increases.[6] Observational studies report positive associations between daily sitting time and risk for diabetes,[7] and insulin resistance[8] that are independent of moderate to vigorous intensity physical activity (MVPA) participation.

Interrupting sustained periods of sitting with regular bouts of walking of at least light intensity[9–11] can reduce circulating glucose and insulin. However, it is unclear whether these beneficial effects are due to interrupting sitting per se (a change in posture) or the increase in muscle contraction resulting from walking, a difference which is important for any future workplace health promotion. To address this question it is necessary to examine the effects of interrupting sitting with standing (a posture change only), and with a change in physical activity (through walking). Evidence regarding the effectiveness of intermittent standing is lacking. A recent study observed that short standing breaks improved postprandial insulin and glucose in overweight and obese postmenopausal women with impaired glucose regulation,[12] but it is unclear whether such

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effects would also be observed in men without known metabolic impairment by at least reducing insulin demand, in the control of glucose homeostasis, which has so far not been addressed.[11] This would establish the value of standing breaks in the prevention of metabolic disease, rather than treatment. This study aimed to address these questions by examining the dynamic responses of both insulin and glucose in men without metabolic impairment, during sustained sitting and when sitting is interrupted by (1) intermittent standing and (2) intermittent walking. Specifically the present study tested the hypothesis that intermittent standing and walking would improve glucose and insulin responses relative to sustained sitting.

2. Methods

A three-intervention experimental study with a cross-over design was approved by the University of Exeter departmental ethics committee (approval number 2013/410). Written informed consent was obtained from all participants prior to their involvement.

Participants were recruited from a research volunteer database, the 'Exeter Ten-thousand' (Extend – http://www.exeter.crf.nihr.ac.uk/node/155) held by the NIHR Clinical Research Facility in Exeter, and from advertisements sent to University employees. Participants were male, non-smokers aged 30–65 years, who were weight stable. Exclusion criteria were: regular physical activity (>3 occasions per month), contraindications preventing standing or walking, hypertension (resting BP ≥140/90 mmHg; or use of antihypertensive medication), diabetes or known metabolic dysfunction, cardiovascular or endocrine disorders, previous gastric surgery, requirement of any medication or nutritional supplements known to effect lipid or carbohydrate metabolism, antidepressants, a history of heavy alcohol use (>20 units a week) or recreational drug use.

Participants attended preliminary testing prior to the main experimental visits. Height, weight and body fat percentage (BF-350, Body Composition Analyser, Tanita, Tokyo, Japan), waist circumference (at the midaxillary line midway between the lower rib cage and the iliac crest), and resting blood pressure using an automated sphygmomanometer (in duplicate according to AHA specifications,[13] Omron M6, Omron Healthcare, Netherlands) were recorded. Baseline blood samples were analysed for, glucose, insulin, triglycerides, cholesterol (total, and both low and high density lipoproteins [HDL and LDL]), urea, creatinine, alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Homoeostatic model assessment of insulin resistance (HOMA-IR) and Total/HDL cholesterol ratio were computed.

Steady-state energy expenditure (EE) values for sitting, standing and walking were obtained using indirect calorimetry (Cosmed K4b^2, Cosmed. Rome, Italy). Participants remained seated for 30 min after which they completed 5 min periods of standing and walking (at 2 mph) separated by a 5 min seated rest period. Mean energy expenditure in metabolic equivalents (METs; 1 MET = 3.5mlO_2/kg/min)[14] from minutes 27–30 of the sitting period and minutes 2–5 of the standing and walking periods represented steady state values.[15]

Participants wore a wrist-mounted accelerometer (GENEActive, ActivInsights, Kimbolton, UK), and refrained from any physical activity (other than day to day activities) for 48 h, and from consuming alcohol and caffeine for 24 h prior to experimental visits. Participants completed a 24 h food diary on the day prior to their first visit and this diet was repeated in the 24 h prior to subsequent visits. Participants were randomised to six possible experimental orders (as shown in Supplementary Figure) by an impartial third party using sealed envelopes. Experimental visits began within 30 days of the preliminary visit and were separated by a minimum of six days.

For the main experimental visits participants attended the laboratory at 08.30 following a 12.5 h overnight fast, arriving either by private car or taxi. Upon arrival, an indwelling cannula was inserted into an antecubital vein. Participants were then seated at a desk in a simulated office equipped with telephone and computer with internet access. Forty-eight hour activity data was uploaded using GENEActiv software (http://www.geneactiv.org/resources-support/downloads-software/) and minutes of MVPA derived using established data cutpoints.[16] Participants remained seated until 10.00 (to achieve a steady state) when a baseline blood sample was collected and they received a glucose drink for an oral glucose tolerance test (OGTT). Participants consumed a mixed test meal of standardized macronutrient composition at 13.00 in the form of a meal replacement drink. Blood samples were collected (while seated) at 10 min intervals for 30 min following the OGTT and test meal, and then at 30 min intervals until 17.00.

During the study participants were subject to 3 interventions:

Uninterrupted sitting (SIT-ONLY): participants remained seated. They were free to work at the computer, read, watch television or listen to the radio.

Interrupted sitting 1 (SIT-STAND): as described for SIT-ONLY. In addition participants were instructed to stand upright and still for 2 min at 20 min intervals.

Interrupted sitting 2 (SIT-WALK): in an identical pattern to the standing intervals in SIT-STAND, participants completed 2 min bouts of light intensity walking at 2 mph on a motorized walking platform (FitWork^{TM} Walkstation, Details, New York) placed adjacent to their chair in order to minimize the transition between activities. An overview of the interventions is described in Supplementary Fig. 1.

With the exception of standing and walking intervals participants remained seated, rising only to void (facilities <15 m from the desk). The time and duration of comfort breaks was recorded during their first visit and replicated in the subsequent two visits. Water was consumed ad libitum during the first visit and the volume and timing of water consumption was recorded and replicated in the subsequent two visits. Participants were observed throughout to ensure adherence to experimental protocols.

The OGTT consisted of 435 ml of a standardised glucose drink (Lucozade Ribena Suntory Ltd, UK) containing 75 g glucose (1244.74 kJ) consumed within 2 min. The mixed test meal was a meal replacement shake (Fortisip, Nutricia, UK) providing protein (6.0 g); fat (5.8 g), carbohydrates (18.4 g) and 150 kcal per 100 ml. This was prescribed so as to provide 0.3 g protein, 0.4 g fat, 1.2 g carbohydrate, and 39 kJ per kilogram body mass (as used in previous studies)[17] and closely represents the average diet composition of the UK adult population (17% protein, 36% fat, and 47% carbohydrate).[18] No additional snacks or drinks other than water were permitted.

Blood samples were collected while participants were seated. Plasma insulin concentrations were determined using an immunoenzymetric assay (ILB International, Hamburg, Germany). Plasma glucose concentrations were determined using an enzyme based colorimetric assay (Cayman Chemical Co., Ann Arbor, MI, USA). Intra-assay coefficient of variation was 2.4% for glucose and 7.6% for insulin.

Outcome measures were Matsuda index, and area under the curve (AUC) for plasma glucose and insulin. Glucose and insulin values at baseline and at 30, 60, 90 and 120 min were used to compute Matsuda index[19] and AUCs for glucose and insulin were computed using the trapezoidal method for 7 h observation periods.

Data regarding glucose and insulin responses to an OGTT in inactive adults were used to determine required sample size. Short et al.[20] observed a mean (±SD) Matsuda index value of 9.3 ± 1.2

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