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Objectively measured sedentary time and associations with insulin sensitivity: Importance of reallocating sedentary time to physical activity

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ABSTRACT

Objective. The aim of this study is to quantify associations between objectively measured sedentary time and markers of insulin sensitivity by considering allocation into light-intensity physical activity or moderate- to vigorous-intensity physical activity (MVPA).

Methods. Participants with an increased risk of impaired glucose regulation (IGR) were recruited (Leicestershire, United Kingdom, 2010–2011). Sedentary, light-intensity physical activity and MVPA time were measured using accelerometers. Fasting and 2-hour post-challenge insulin and glucose were assessed; insulin sensitivity was calculated by HOMA-IS and Matsuda-ISI. Isotemporal substitution regression models were used. Data were analysed in 2014.

Results. 508 participants were included (average age = 65 years, female = 34%). Reallocating 30 min of sedentary time into light-intensity physical activity was associated a 5% (95% CI 1, 9%; $p = 0.024$) difference in Matsuda-ISI after adjustment for measured confounding variables. Reallocation into MVPA was associated with a 15% (7, 25%; $p < 0.001$) difference in HOMA-IS and 18% (8, 28%; $p < 0.001$) difference in Matsuda-ISI. Results for light-intensity physical activity were modified by IGR status with stronger associations seen in those with IGR.

Conclusions. Reallocating sedentary time into light-intensity physical activity or MVPA was associated with differences in insulin sensitivity, with stronger and more consistent associations seen for MVPA.

Background

Over recent years, there has been mounting evidence suggesting that sedentary behaviour, defined as any sitting or lying time less than 1.5 METS during waking hours (Barnes et al., 2012), is an independent determinant of chronic disease and all-cause mortality (Yates et al., 2011; Owen et al., 2010). The most consistent and strongest associations have been with metabolic health and type 2 diabetes (Wilmot et al., 2012). However, there has been ongoing debate about whether the deleterious associations of sedentary behaviour are independent to the beneficial associations of greater physical activity. Studies that have employed accelerometer-based quantification of movement have drawn differing conclusions, even when reporting data from the same cohort (Healy et al., 2011; Maher et al., 2014).

During waking hours it is not possible to alter sedentary time whilst keeping time in other forms of physical activity constant; for example, reducing sedentary time by 30 min necessitates a 30 minute increase in some form of light-to-vigorous intensity physical activity. This fact is often overlooked in epidemiological research and may explain reported discrepancies in the literature.

Isotemporal substitution has been promoted as an appropriate model for investigating associations of health behaviours with finite boundaries, such as energy intake or time in physical activity during waking hours (Mekary et al., 2009). Isotemporal substitution can be used to model associations with health of reallocating one behaviour for another, which is particularly useful to sedentary behaviour research. In modern environments, humans spend the majority of their waking hours sedentary (Yates et al., 2011), therefore investigating the associations of reallocating this dominant behaviour into others is important. For example, analysis of accelerometer data from NHANES reported that reallocating 30 min of sedentary time to light-intensity physical activity was associated with 1.9% lower blood triglyceride levels and 2.4% lower insulin levels with stronger associations shown

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for reallocation into MVPA (Buman et al., 2014). Buman and colleagues also reported that reallocating objectively assessed sedentary time for light activity was associated with better physical health and well-being in older adults (Buman et al., 2010). We extend these observations in the general population to investigate the associations of reallocating sedentary time to light-intensity physical activity or moderate- to vigorous-intensity physical activity (MVPA) with markers of glucose regulation and insulin sensitivity in a primary care population at increased risk of type 2 diabetes.

Methods

Participants

This study reports baseline data from the Walking Away from Type 2 Diabetes study, the methods of which have been published elsewhere (Yates et al., 2012). A total of 833 participants at increased risk of type 2 diabetes were recruited through 10 primary care practices in Leicestershire, UK, in 2010–2011; the analysis was conducted in 2014. Individuals with an increased risk of impaired glucose regulation (IGR) (composite of impaired glucose tolerance (IGT) and/or impaired fasting glycaemia (IFG) and/or undiagnosed type 2 diabetes) were identified using a modified version of the Leicester Risk Score (Gray et al., 2012a). Those individuals scoring within the 90th percentile in each practice were invited to take part in the study. This approach has reasonable sensitivity and specificity for identifying participants with IGR (Gray et al., 2012a, 2012b). Individuals were unaware of their diabetes risk status before entering the study. We excluded those who had previously diagnosed type 2 diabetes, were currently taking steroids or were unable to take part in any walking activity.

Ethics

Ethical approval was obtained from the Nottingham Research Ethics Committee, UK. Written informed consent was provided by all participants.

Objective sedentary and physical activity time assessment

Participants were asked to wear a tri-axial accelerometer (Actigraph GT3X, Pensacola, FL, USA), for a minimum of seven consecutive days during waking hours. Data were recorded in 15 second epochs. Previously used cut-points were employed to categorise time spent in sedentary behaviours (<25 counts per 15 s), time in light-intensity physical activity (≥25 to <488 counts per 15 s) and time in MVPA (≥488 counts per 15 s) from the vertical axis (Freedson et al., 1998).

Non-wear time was defined as a minimum of 60 min of continuous zero counts. At least 600 min of wear time per day was considered valid. For inclusion in these analyses, participants were required at have at least four days of valid accelerometer data (Trost et al., 2005). A commercially available data analysis tool (KineSoft version 3.3.76, Kinesoft, New Brunswick, Canada; www.kinesoft.org) was used to process accelerometer data.

Demographic, anthropometric, lifestyle and biochemical measurements

Medication, ethnicity and smoking status were obtained following an interview-administered questionnaire conducted by a healthcare professional. Social deprivation was determined by assigning an Index of Multiple Deprivation (IMD) score to the participant's residential area. IMD scores are publically available continuous measures of compound social and material deprivation. Body weight (Tanita TBE 611, Tanita, West Drayton, UK), waist circumference (midpoint between the lower costal margin and iliac crest) and height were measured to the nearest 0.1 kg and 0.5 cm respectively.

All participants underwent a standardised oral glucose tolerance test. Participants were asked to fast from 10 pm on the evening before the test and to avoid vigorous-intensity physical activity in the preceding 24 h. Fasting and 2-hour post 75 g glucose challenge (2-h) samples were measured within the same laboratory at the Leicester Royal Infirmary, Leicestershire, UK, using a glucose oxidase method on the Beckman Auto Analyzer (Beckman, High Wycombe, UK). Plasma samples for fasting and 2-h insulin analysis were frozen within a −80 °C freezer and analysed at the end of baseline data collection using an enzyme immuno-assay (80-INSHU-E01.1, E10.1 Alpco Diagnostics 26G Keewaydin Drive, Salem, NH 03079, USA). Insulin analysis was undertaken within a specialist laboratory by Unilever R&D, Bedfordshire, UK. Due to the cessation of bleeding or insufficient plasma volumes, both fasting and 2-h insulin samples were available for 583 (70%) participants.

Measures of insulin sensitivity

HOMA-IS and Matsuda-ISI were used to calculate insulin sensitivity (Matthews et al., 1985; DeFronzo and Matsuda, 2010):

$$\text{HOMA-IS } [15] = 1/\text{HOMA-IR} = 22.5/(G_0 \cdot I_0)$$
$$\text{Matsuda-ISI } [16] = 10000/\text{sqrt}(G_0 \cdot I_0 \cdot G_{120} \cdot I_{120})$$

These models are commonly used indexes of insulin sensitivity in epidemiological research and have been shown to correlate reasonably with gold standard measures of insulin sensitivity and/or progression to type 2 diabetes (Otten et al., 2014; Muniyappa et al., 2008). Matsuda-ISI is more likely to reflect factors related to insulin release and peripheral insulin resistance whereas HOMA-IS may be a better measure of hepatic insulin resistance (Abdul-Ghani et al., 2006).

Statistical analysis

Linear regression modelling employing an isotemporal substitution approach was used to quantify the association of substituting sedentary behaviour for light-intensity physical activity or MVPA on markers of glucose regulation and insulin sensitivity. Isotemporal substitution specifically takes into account that, in behavioural terms, time is not infinite; spending more time in one kind of activity requires less time spent in other activities during waking hours. Consequently it has been recommended for use in observational research employing time based measures of physical activity (Mekary et al., 2009, 2013; Buman et al., 2014).

In order to investigate the association between sedentary behaviour and insulin sensitivity, isotemporal substitution requires that average wear time, time in light-intensity physical activity and time in MVPA are simultaneously entered into a linear regression model; the resulting regression coefficient for light-intensity physical activity and MVPA represents the association of substituting a given unit of sedentary time into each category, respectively (Mekary et al., 2009). Each model was further adjusted for measured potential confounding variables defined as age, sex, ethnicity, social deprivation, smoking status, and beta-blocker and statin medication status. In addition, results were further adjusted for BMI. Interaction terms were fitted to assess whether the association of light-intensity physical activity or MVPA with measures of insulin sensitivity was modified by sex or IGR status; for the purposes of this analysis IGR was defined as: fasting glucose ≥ 6.0 mmol/l and/or 2-hour glucose ≥ 7.8 mmol/l and/or HbA1c ≥ 6.0%. The derived indexes of insulin sensitivity displayed non-parametric distributions, therefore all dependent variables were log-transformed with resulting regression coefficients back transformed; displayed coefficients consequently represent the value by which the dependent variable is multiplied by for a given unit of time in light-intensity physical activity or MVPA. We display results per 30 minute difference for ease of interpretation.

We undertook a sensitivity analysis to establish whether associations of light-intensity physical activity with measures of insulin sensitivity were affected if a lower definition of MVPA was used. Whilst the primary definition of MVPA used in this analysis has been extensively employed in epidemiological research across a wide range of populations (Buman et al., 2014; Healy et al., 2007; Cooper et al., 2012; Ekelund et al., 2007), lower cut-points for older adults have been suggested (Copeland and Esliger, 2009). Given the older nature of our cohort, for the sensitivity analysis we used an MVPA cut-point specifically developed in older adults (≥260 counts per 15 s) (Copeland and Esliger, 2009). Others have also used this threshold in epidemiological research (Buman et al., 2010). This lower threshold is likely to include