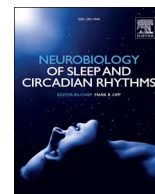




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## The impact of breaking up prolonged sitting on glucose metabolism and cognitive function when sleep is restricted

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## ABSTRACT

**Objectives:** To investigate the acute benefits of breaking up prolonged sitting with light-intensity physical activity on (i) glucose metabolism under conditions of sleep restriction, and (ii) cognitive deficits associated with sleep restriction.

**Methods:** This counterbalanced, crossover trial consisted of two five-day (5 night) experimental conditions separated by a two-week washout period. On the first night, participants were given a 9-h sleep opportunity to allow the collection of steady-state baseline measures the following day. This was followed by three consecutive nights of sleep restriction (5-h sleep opportunity). In the sitting condition (SIT), participants remained seated between 1000 and 1800 h. In the physical activity condition (ACT), participants completed 3-min bouts of light-intensity walking every 30 min on a motorised treadmill between 1000 and 1800 h. At all other times, in both conditions, participants remained seated, except when walking to the dining room or to use the bathroom (max distance = 32 m). Six physically inactive, healthy males were randomised to one of two trial orders, 1) SIT then ACT, or 2) ACT then SIT. Continuous measures of interstitial glucose were measured at 5-min intervals. A cognitive and subjective test battery was administered every two hours during wake periods. Analyses were conducted using a series of linear mixed-effect ANOVAs.

**Results:** No differences in interstitial glucose concentration or cognitive performance were observed between the SIT condition and the ACT condition. Participants reported higher levels of sleepiness, and felt less alert in the SIT condition compared with the ACT condition.

**Conclusions:** There were no observable benefits of breaking up prolonged sitting on glucose metabolism under conditions of sleep restriction. These findings have implications for behaviour change interventions. Future studies will need to include larger, less homogenous study populations and appropriate control conditions (i.e., 8–9 h sleep opportunities).

### 1. Introduction

To reduce the risk factors associated with cardiometabolic disease, research and public health interventions have traditionally centred upon improving physical activity and diet, and reducing tobacco use and alcohol intake (Cannon, 2007). However, there are other important modifiable risk factors for cardiometabolic disease that have received comparatively little attention, such as prolonged sitting (Bauman et al., 2013) and inadequate sleep (Schmid et al., 2015). Determining the optimal composition of a 24-h period to promote health and prevent chronic disease represents a new direction of behaviour change intervention research (Chastin et al., 2015; Tremblay et al., 2016), beyond conventional approaches that advocate improving any single behaviour

in isolation (e.g., increasing amount of moderate-vigorous physical activity). Thus, investigating how cardiometabolic disease risk factors interact with each other when they are combined is critical (e.g., prolonged sitting when sleep restricted).

Cross-sectional and prospective observational studies have indicated that prolonged sitting is a risk factor for diabetes, cardiovascular disease (CVD), and increased all-cause mortality (Wilmot et al., 2012), independent of physical activity levels (e.g., moderate-vigorous intensity physical activity such as brisk walking/jogging/sports) (Bankoski et al., 2011; Koster et al., 2012; Thorp et al., 2011; Wijndaele et al., 2014). However, a number of studies have demonstrated that breaking up prolonged sitting every 30 min, with 2–3 min of standing or short bouts of light-intensity physical activity, is associated with an

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improved metabolic profile (Chastin et al., 2015), reduced self-reported fatigue (Wennberg et al., 2016), and reduced all-cause mortality risk (Katzmarzyk, 2014). In addition, regularly breaking up prolonged sitting with short (1 min 40 s) bouts of light-intensity physical activity (Peddie et al., 2013) or standing (Benatti et al., 2017) is more effective than a single, continuous 30-min bout of moderate-vigorous physical activity in lowering postprandial glucose and insulin concentrations in healthy, normal weight adults. While there is good evidence that breaking up prolonged sitting is beneficial for cardiometabolic health, studies have not controlled for prior sleep duration, which is also a cardiometabolic disease risk factor.

To maintain optimal health and functioning, a typical adult should obtain at least 7 h of sleep per night (Watson et al., 2015). However, as many as 45% of adults do not meet this sleep duration recommendation (Adams et al., 2016; Centers for Disease Control Prevention, 2011). Inadequate sleep is associated with CVD, weight gain, obesity, inflammation, diabetes, and mortality (Knutson, 2010). A prospective study of healthy adults found that those who slept  $\leq 6$  h per night had a 15% higher risk of CVD compared with those who slept 7–8 h per night (Hoeveraar-Blom et al., 2011). Numerous well-controlled laboratory studies have observed impaired glucose metabolism with varying degrees of sleep loss (Broussard et al., 2012; Buxton et al., 2010; Nedeltcheva et al., 2009). For example, insulin sensitivity and disposition index (a marker of diabetes risk) were significantly impaired in individuals that were chronically sleep restricted (5 nights of 4 h time in bed per night) compared to those in the rested condition (5 nights of 12 h time in bed per night) (Spiegel et al., 1999). While there has been a recent move towards interventions that target breaking up prolonged sitting (e.g., implementing standing desks), any cardiometabolic benefit may be offset by sleep restriction. In essence, sleep restricted individuals may not benefit from breaking up prolonged sitting throughout the day. As a first step in exploring this hypothesis, the primary aim of this study was to determine the effects of breaking up prolonged sitting (with light-intensity physical activity) on acute cardiometabolic health outcomes under conditions of sleep restriction.

In addition to the effects on cardiometabolic health, breaking up prolonged sitting may also benefit other aspects of waking function, such as cognitive performance. Restricted sleep can result in multiple neuro-behavioural deficits, including lapses in attention, slow working memory, reduced cognitive throughput, and depressed mood (Belenky et al., 2003; Van Dongen et al., 2003). Beneficial effects of exercise on cognitive performance have been observed following a single bout of exercise (Chang et al., 2015), suggesting that at least light-intensity physical activities may mediate pathways involved in mental fatigue and cognition. Indeed, a recent pilot study found that breaking up prolonged sitting with light-intensity walking breaks may be an effective acute fatigue countermeasure, though sleep duration prior to experimentation was not reported (Wennberg et al., 2016). As such, it is unknown whether physical activity can counteract the adverse impact of sleep restriction on cognitive function by acting as a fatigue countermeasure. Therefore, a secondary aim of this pilot study is to determine whether breaking up prolonged sitting with light-intensity walking breaks can counteract the acute cognitive deficits associated with sleep restriction.

## 2. Methods

### 2.1. Study design

The study was a laboratory-based, randomised, counter-balanced, crossover trial with two experimental conditions – a sitting condition (SIT) and an active condition (ACT). Participants were required to attend the laboratory on two occasions separated by a 2-week washout period. On each occasion, participants lived in the laboratory for five consecutive days and nights. An overview of the experimental protocol is shown in Fig. 1.

### 2.2. Participants

Healthy adult males ( $n = 6$ ) were recruited from the Adelaide (Australia) region. Participant characteristics are reported in Table 1. Participation was voluntary and ethical approval was obtained from the Human Research Ethics Committee of Central Queensland University (H16/11-298). Participants provided written consent and were compensated financially for their time at the conclusion of the study (AU \$1200).

Participants were screened using a general health questionnaire to determine their eligibility to participate in the study. Inclusion criteria were: age 20–35 years, non-smoker, non-shiftworker, caffeinated beverage consumption  $\leq 120$  mg/day ( $\sim 2$  cups of coffee); consumption of  $\leq 2$  standard alcoholic beverages/week; habitual bedtimes between 2200 and 0000 h; rise times between 0600–0800 h; absence of previous diagnosis of psychiatric and/or neurological problems; no trans-meridian travel in the previous four weeks; free from medication and drugs acting on the central nervous system, known to interfere with sleep or glucose- and/or lipid-lowering medication; and no history of habitual napping. Participants were also required to have a waist circumference  $< 100$  cm, an Epworth Sleepiness Scale score  $< 10$  (Johns, 1991), a global Pittsburgh Sleep Quality Index  $\leq 5$  (Buysse et al., 1989), a low or moderate score on the International Physical Activity Questionnaire (IPAQ Research Committee, 2005), normal scores on the 21-item Depression Anxiety Stress Scale (Lovibond and Lovibond, 1995), and moderately morning/evening or neither chronotype on the Horne-Ostberg Morningness/Eveningness Questionnaire (Horne and Ostberg, 1975).

### 2.3. Randomisation

Participants were randomised to one of two possible trial orders, 1) SIT then ACT, or 2) ACT then SIT. Three participants performed trial order 1 and three participants performed trial order 2. A computerised randomisation list of participant and order were allocated into envelopes and kept by an independent third party. The envelopes were opened once informed consent was obtained for all participants. Participants were told of their trial order upon entering the laboratory for the first trial.

### 2.4. Pre-experimental procedures

Following screening, participants attended a familiarisation visit at the research laboratory. During this visit, participants were given the opportunity to ask questions about the experimental protocol, underwent training on cognitive tests, and completed practice questionnaires. In the week prior to the study, participants were instructed to maintain their normal sleep behaviour to reduce the likelihood of sleep debt upon entering the study. To minimise the potential carry over effects of physical activity, participants were also instructed to avoid any moderate and/or vigorous physical activity for at least 48 h prior to each trial. To ensure fidelity of participants' habitual sleep and physical activity levels and the aforementioned pre-experimental requirements, participants wore an activity monitor (Actical MiniMitter/Respironics, Bend, OR) on their non-dominant wrist and completed a sleep diary. Activity monitors are a useful and valid means for estimating total sleep time and wakefulness (Marino et al., 2013).

### 2.5. Experimental procedure

Participants lived in a sound-attenuated and temperature-controlled ( $21 \pm 2$  °C) laboratory on two separate occasions for five consecutive days and nights. On the arrival day, participants arrived at 1400 h, performed training on the cognitive performance tasks and were familiarised with walking on a motorised treadmill on a level incline. Following a baseline sleep (BL; 2200–0700 h) participants were sleep

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