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Research Methods, Protocols, Procedures

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The effects of fasting compared to eating a meal or snack during simulated night shift on changes in metabolism associated with circadian misalignment: a protocol and methods paper

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Abstract

Study Objectives: This protocol paper outlines the methods that will be used to examine the impact of altering meal timing on metabolism, cognitive performance, and mood during the simulated night shift.

Methods: Participants (male and female) will be recruited according to an a priori selected sample size to complete a 7-day within and between participant's laboratory protocol. Participants will be randomly assigned to one of the three conditions: meal at night or snack at night or no meal at night. This protocol includes an 8-hour nighttime baseline sleep, followed by 4 consecutive nights of simulated nightshift (7 hours day sleep; 10:00–17:00 hours), and an 8-hour nighttime sleep (return to dayshift). During the simulated night shift, meals will be provided at ~06:30, 09:30, 14:10, and 19:00 hours (no eating at night); ~06:30, 19:00, and 00:30 hours (meal at night); or ~06:30, 14:10, 19:00, and 00:30 hours (snack at night). Meal composition will be strictly controlled throughout the study (45%–65% carbohydrates, 15%–25% protein, and 20%–35% fat per day) with daily energy provided to meet individual needs using the Harris-Benedict equation (light/sedentary activity). The primary outcome measures are serum concentrations of blood glucose, insulin, and free fatty acids area under the curve in response to the oral glucose tolerance test. Mixed-effect ANOVAs will be conducted.

Conclusions: This protocol paper describes a methodology to describe an innovative approach to reduce the metabolic disease impact associated with shift work.

Key words: meal timing; shiftwork; nightshift; metabolism

Approximately 15% of the Australian population currently work shift work [1] with numbers likely rising with increasing demand by companies to extend working hours, often to cover 24-hour work operations [2]. As a consequence of changes to the normal sleep–wake pattern, transitioning on and back off work shift schedules leads to circadian misalignment relative to normal solar day–night and sleep–wake cycles and is associated with performance and safety decrements and increased risk of obesity [3–6], metabolic diseases [7–9], gastrointestinal disturbances [10–12] and cardiovascular disease [13]. The incidence of poor health in the shift work population is not only important on an individual level, but also contributes to a financial costs for the organization and the broader healthcare system [14].

Until recently, the primary focus of most dietary interventions to reduce metabolic disease in shift workers, and indeed the broader community, has been restricting total energy intake and improving diet quality (macronutrient composition). By examining the dietary intake of shift workers, the interplay between circadian timing, metabolic physiology, and nutrition is evident. Many studies have found no significant differences in total daily

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energy intake when comparing night shift to day shift and/or day off conditions [15–19]. However, when shift workers eat at night their meal patterns are often out-of-phase with the underlying circadian regulation of metabolism [19–21]. At night, meal-induced secretion of insulin is impaired [22], and multiple studies have found elevated glucose responses with nighttime meals compared to daytime meals [23–29].

Research in rodents has suggested that limiting the window of eating to only the biological day, when working the night shift, may reduce the metabolic impacts associated with shift work. In these studies, the metabolic impairments associated with simulated "night shift" were reversed when food was withheld during the shift, with glucose levels maintained within control ranges [30, 31]. In addition, withholding food prevented fat and weight gain compared to animals that had free access to food [31]. Barclay et al. [30] suggested that these findings may result from limiting the peripheral circadian desynchrony caused by "night shift." However, there is limited data regarding the impact of completely withholding food intake across the night in humans.

A pilot study from our group suggests that not eating at night, during simulated night work may limit the adverse metabolic consequences of night shift, with increased glucose area under curve (AUC) in response to a standard breakfast meal observed when participants ate a large meal during the night shift but not when those calories were redistributed to the day on either side of the night shift [25]. These studies in humans and rodents all support reduced eating during the night shift. However, given many shift workers might find complete fasting on night shift difficult, there is a need to understand the impact of smaller meals or snacks on next-day glucose metabolism. Could a small meal be a suitable intermediate approach to increase uptake and adoption by shift workers while still protecting against metabolic disruption?

An additional factor that must be considered when changing night worker eating patterns, is how cognitive performance and safety might be impacted. There is research to suggest that energy intake preceding cognitive performance testing during the day reduces cognitive performance [32–34]. Our pilot data also support this, finding that eating at night increases sleepiness and impairs driving performance in the early morning hours compared to not eating at night [35, 36].

This protocol paper describes a study that will examine the impact of eating meals at night (snack or meal) compared to only eating during daytime hours on glucose metabolism after four nights of simulated shift work in healthy men and women. Secondary aims focus on understanding how cognitive performance and safety might be impacted by these conditions. Primary and secondary study outcomes of the proposed study are displayed in Table 1.

Materials and Methods

Study design

This study will be a single-site, single-blinded parallel three-arm group cluster randomized controlled trial (no meal at night, snack at night, and full meal at night), within- and between-group experimental study requiring a 7-day in laboratory stay. All participants will undergo a simulated shift work protocol, including one 8-hour nighttime baseline sleep, followed by 4 consecutive days of simulated shift work (7 hours sleep from 10:00 to 17:00 hours each day), followed by an 8-hour nighttime recovery sleep. The study protocol is illustrated in Figure 1.

Table 1. Study Outcomes

Outcome	Timepoint
Primary outcomes	
Glucose AUC derived from OGTT.	AUC post-OGTT on Baseline and Recovery
Insulin AUC derived from OGTT.	AUC post-OGTT on Baseline and Recovery
Free fatty acid AUC derived from OGTT.	AUC post-OGTT on Baseline and Recovery
Secondary outcomes	
Glucose during breakfast meal tolerance test.	AUC post-breakfast on days 3 and 6 (simulated night-work days).
Insulin during breakfast meal tolerance test.	AUC post-breakfast on days 3 and 6 (simulated night-work days).
Cognitive functioning is assessed by a battery of cognitive tests including psychomotor vigilance tasks and driving tasks.	Every 2 hours during wake periods on Baseline to Recovery (day 1 is used for acclimatizing to the laboratory setting and training).
Markers of sleep quality will be assessed using polysomnography.	Baseline, day 5, and recovery
Mood is assessed by a battery of cognitive tests including VAS scales and PANAS.	Approximately every 3 hours during wake periods Baseline to Recovery.
Salivary sample analysis to assess melatonin and cortisol in response to night shift.	Every hour during wake periods

AUC, area under the curve; OGTT, oral glucose tolerance test; VAS, visual analog scales; PANAS, positive and negative affect scale.

Study setting

This study, conducted at the University of South Australia's Sleep and Chronobiology laboratory, will recruit healthy individuals without obesity residing in Adelaide, Australia. Ambient room temperature will be maintained at 22(± 1)°C in the laboratory at all times. Light intensity will be set to 50 lux (slightly dimmed light), measured via vertical illuminance at the eye level, during scheduled wake periods and approximately <0.03 lux (darkness) during all scheduled sleep periods.

Randomization

Participants will be cluster randomized at the group level (participants will be tested four at a time), with each group undergoing the laboratory stay together. Participants will eat in isolation from one another in their allocated bedrooms. It is not possible to blind the research staff for logistical reasons. Analyses of primary outcomes will be done by an independent researcher who will not participate in data collection.

Ethics and dissemination

The study will be conducted according to the guidelines of the Declaration of Helsinki and was approved by the Institutional Review Board (or Ethics Committee) of University of South Australia (protocol ID: 0000033621, approved October 17, 2014)." Any modifications to the protocol will be submitted to the University of South Australia Human Ethics Committee and updates will be

made to the Australian New Zealand Clinical Trials Registry. The protocol has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN12616001556437). Informed consent will be obtained from all participants involved in the study prior to data collection. All authors will have access to the final de-identified dataset. No authors report any relevant conflicts of interest. The findings of this study will be disseminated via peer-reviewed publications and presentations at national and international conferences. The findings will also form part of student theses.

Recruitment and screening

Participants will be recruited via advertising flyers posted on notice boards and posting on web-based advertising platforms. Figure 2 displays screening process and participant cluster randomized to the study condition. Interested participants will initially be screened for eligibility via telephone screening to collect self-reported height/weight, age, smoking status, sleep patterns (sleep and wake times), general health status, daily/weekly alcohol consumption, and caffeine intake. Study inclusion and exclusion criteria are presented in Table 2. If interested participants remain eligible following initial screening, they will be invited to attend a face-to-face screening session to complete a more in-depth general health questionnaire (medical history), the Pittsburgh Sleep Quality Index to assess sleep quality (exclusion > 5) [37], the composite Morningness–Eveningness questionnaire to determine chronotype (exclusion < 31 or > 69) [38] and the Beck Depression Inventory to determine psychological health (exclusion > 14) [39]. A fasted blood sample will also be collected to determine general health, with levels assessed by the study physician to ensure they are within accepted normal ranges and determine whether the participant does not have indicators of any underlying condition that may affect metabolism. To control for the effects of menstrual phase on metabolism, female participants will only be scheduled to participate during the luteal phase of their menstrual cycle [40].

One week prior to commencing the in-laboratory study, participants will be invited to tour the laboratory, test the driving simulator, and look through the menu to ensure all foods could be consumed without problems. At this visit, they will be given a take-home pack including a sleep diary and wrist actigraph and instructed to keep to a strict sleep schedule of going to sleep between 22:00 and 23:00 hours and waking between 06:00 and 07:00 hours for the following week (verified by the wrist actigraphy and sleep diary). Participants will also be asked to abstain from caffeine, alcohol, and napping in the week prior to the study commencing.

Laboratory protocol

Participants will enter the laboratory at 12:00 hours on training day and will be familiarized with the laboratory environment. All participants will then be given one sleep opportunity of 8 hours time in bed (TIB; 22:00–06:00 hours) before transitioning to the night shift protocol. During the subsequent 4 days of simulated night shift participants will be awake from 16:00 to 10:00 hours with a

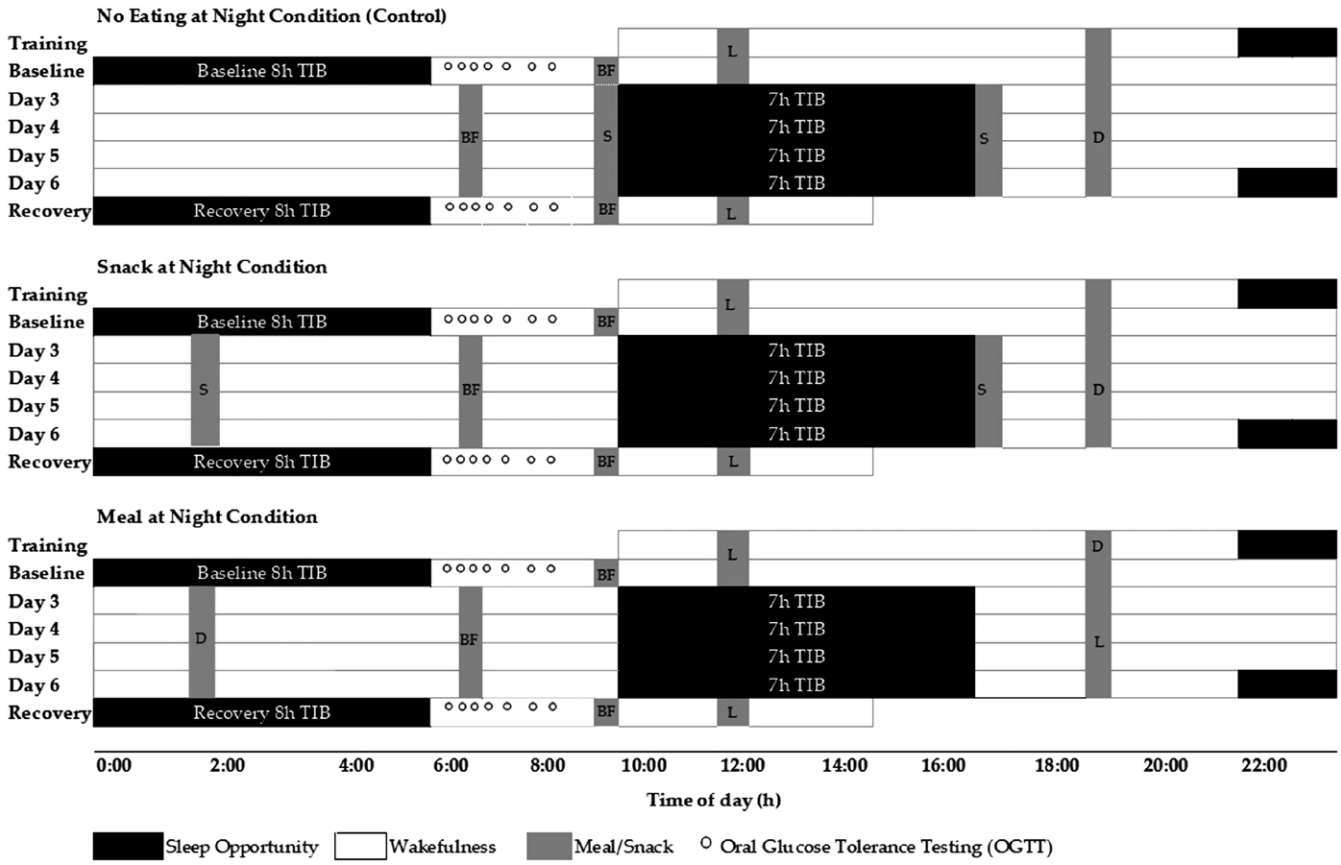

Figure 1. Study Design with Primary Outcomes. Black bar; sleep opportunities, white bar; wakefulness, grey box; meal or snack times, S; snack, BF; breakfast, L; Lunch, D; dinner, black circle; Oral Glucose Tolerance Testing (OGTT). Meal conditions will be divided into control; no eating at night, snack; a light snack served at night, and meal; a lunch-equivalent meal served at night.

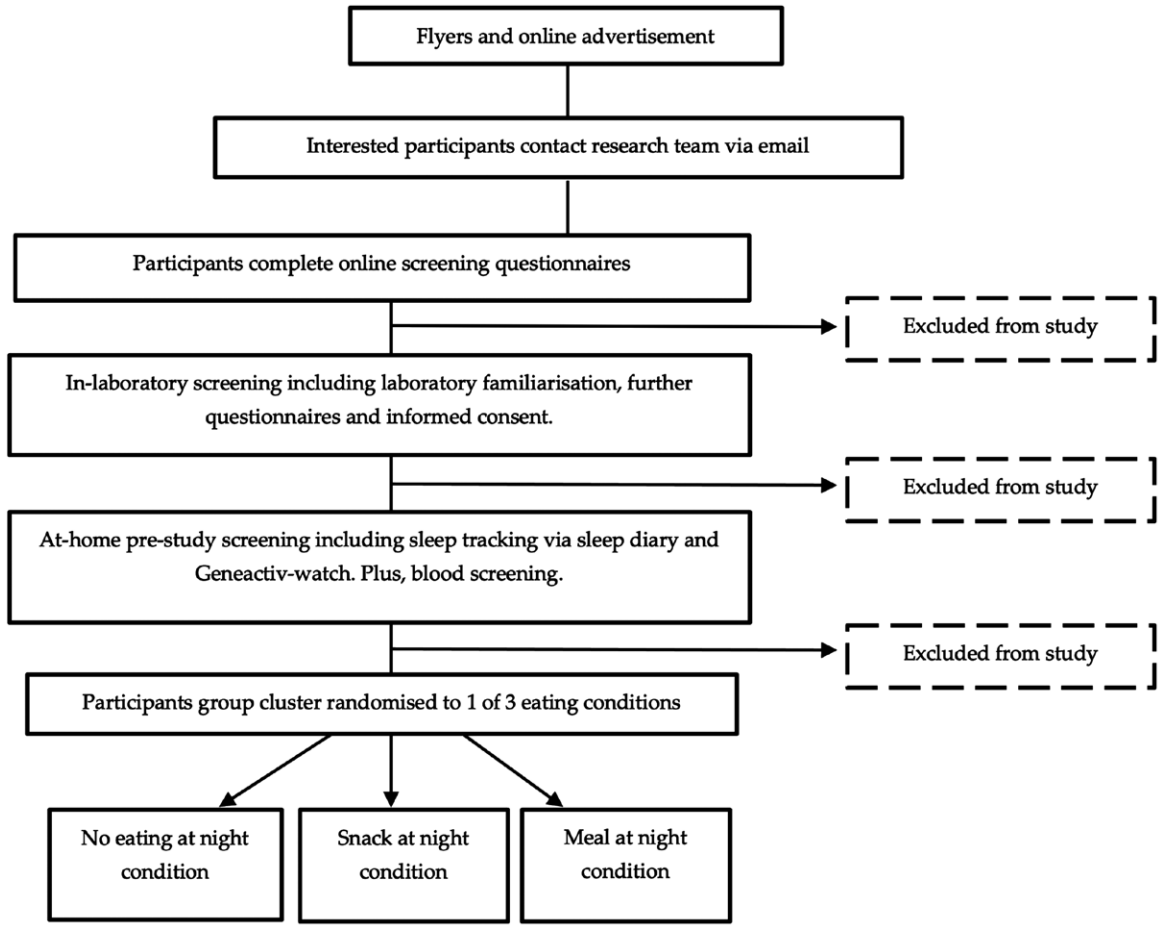

Figure 2. Consort diagram of the screening process and participant cluster randomized to study condition.

daytime sleep of 7 hours TIB (10:00–17:00 hours). Upon completion of the night shift schedule, participants will have a nocturnal recovery sleep of 8 hours TIB (22:00–06:00 hours). During wake periods participants will complete several physiological and cognitive tasks (The timing of these tasks is shown in Table 1).

Conditions

The diet will be standardized and fit within the Australian dietary recommendations for the percentage of daily energy from macronutrients; 45%–65% carbohydrates, 15%–25% protein, and 20%–35% fat per day [41]. The energy content of the meals will be based on individual daily dietary energy requirements (kJ) calculated using the Harris-Benedict equation with a light/sedentary activity level (laboratory condition). Energy intake will be consistent across conditions per 24-hour period, but the energy distribution of the meals differed by condition as shown in Figure 3. All food provided will be weighed and recorded pre- and post-consumption. Participants will be given a 30-minute eating window to consume all food within the given meal. Participants will not be permitted food outside these times; water will be accessed ad libitum.

Meal at night

Food intake for those in the meal at-night condition will be separated into breakfast, dinner, and a lunch-type meal at night. The schedule will be as follows, breakfast with 30% daily energy intake at 06:30 hours (toast, cereal, etc), dinner meal with 40% daily energy intake at 19:00 hours (mixed dishes, salad, vegetable, etc), and a lunch type meal 30% daily energy intake at 00:30 hours (sandwiches etc).

Snack at night

Food intake for those in the snack at night condition will be separated into breakfast, two snack meals, and a dinner meal. The schedule will be as follows: breakfast with 30% daily energy intake at 06:300 hours (toast, cereal, etc), an afternoon snack with 20% daily energy intake at 17:00 hours (sandwiches, etc), a dinner meal with 40% daily energy intake at 19:00 hours (mixed dishes, salad, vegetable, etc) and a snack at night 10% daily energy intake at 00:30 hours (fruit, crackers, etc).

No meal at night

Food intake for those in the no meal at night condition will also be separated into breakfast, two snack meals, and a dinner meal. The schedule will be as follows: breakfast with 30% daily energy intake at 06:30 hours (toast, cereal, etc), a morning snack with 10% daily energy intake at 09:30 hours (fruit, crackers, etc), an afternoon snack at 20% daily energy intake at 17:00 hours (sandwiches, etc), and a dinner meal 40% daily energy intake at 19:00 hours (mixed dishes, salad, vegetable, etc).

Data collection

Oral glucose tolerance test.

Blood will be collected via an in-dwelling cannula in the median cubital vein into Ethylenediaminetetraacetic acid (EDTA; for

Table 2. Study Inclusion and Exclusion Criterion

Criterion	Scale/assessment	Inclusion criteria	Exclusion criteria
Age	General Demographic Questionnaire	18–45 years	
Weight	General Demographic Questionnaire	BMI normal to overweight (20–29 kg/m^2), and stable weight over the preceding 3 months.	
Language ability	Verbal communication	Competent written and spoken English skills	
Smoking status	General Demographic Questionnaire		Current smoker
Alcohol consumption	General Demographic Questionnaire		>2 standard alcoholic drinks per day
Caffeine consumption	General Demographic Questionnaire		>2 standard cups per day
Dietary requirements and difficulties	General Demographic Questionnaire		Restrictive dietary requirements or difficulties including Gluten intolerance, restrictive eaters, allergies
Medications	Confidential medical screen		Regular medications that may impact outcome measures (e.g. Glucocorticoids, sleep aids, antidepressants, etc)
Drug use	Urine drug sample, and confidential medical screen		Positive urine drug result, and current or suspected use of illicit drugs, including but not limited to, benzodiazepines, amphetamine, cocaine, and marijuana.
Typical sleep–wake pattern	Sleep–wake survey	Habitual sleep duration between 7 and 8 hours a night, and self-reported nighttime lights out after 2100 and wake-up earlier than 0900 hours during weekdays.	
Typical napping	Sleep–wake survey		>1 nap per week
Sleep quality	Pittsburg Sleep Quality Index		Score > 5
Sleep disorder	Sleep–wake survey	No history of diagnosed sleep disorder	
Sleep apnea	Berlin Questionnaire, and Stop Bang Questionnaire	Defined as high risk for one or both questionnaires	
Chronotype	Morningness–Eveningness Questionnaire	Score < 31 or > 69	
Shiftwork status	General Demographic Questionnaire	Previous history of shiftwork in the 3 months preceding	
Trans-meridian travel	Sleep–wake survey	Overseas travel within 60 days prior to the study	
Physical health	Confidential medical screen	History of medical conditions; cardiovascular disease, neurological disorder, kidney dis ease, liver disease.	
Hematology	Pre-study blood test	Clinically significant values (as determined by the reviewing study physician) for any hematology or chemistry parameter.	
Psychological health	Clinical history, and Beck Depression Inventory.	Previous or current diagnosis of psychiatric concerns requiring hospitalization (including anxiety disorder). BDI score ≥ 14.	

<, less than; >, greater than; ≥, greater than or equal to.

measuring insulin and FFA) and sodium fluoride (for measuring glucose) tubes. Cannulas will be flushed with saline to ensure cannula patency and reduce heparinization. The cannula will be moved to other suitable veins if required. The gold standard oral glucose tolerance tests (OGTT) will be conducted at ~07:00 hours on baseline and recovery days. Blood samples will be collected at –15 and 0 minutes prior to consuming a 75 g glucose drink. Participants will be given 5 minutes to consume the drink and regular blood draws will be taken for the next two and a half hours (at 15, 30, 60-, 90-, 120- and 150 minutes post-drink) on each of these days. Blood samples will be centrifuged for 10 minutes at 4°C and plasma separated and stored at –80°C for later analyses. Glucose concentrations will be assayed using a commercial kit with a Konelab 20XT clinical chemistry analyzer (Thermo Fisher Scientific, Waltham, MA, USA). Insulin will be measured by enzyme-linked immunosorbent assay (ELISA; Mercodia, Uppsala, Sweden). FAA will be analyzed by photometric assay on the Roche Cobas c702 analyzer.

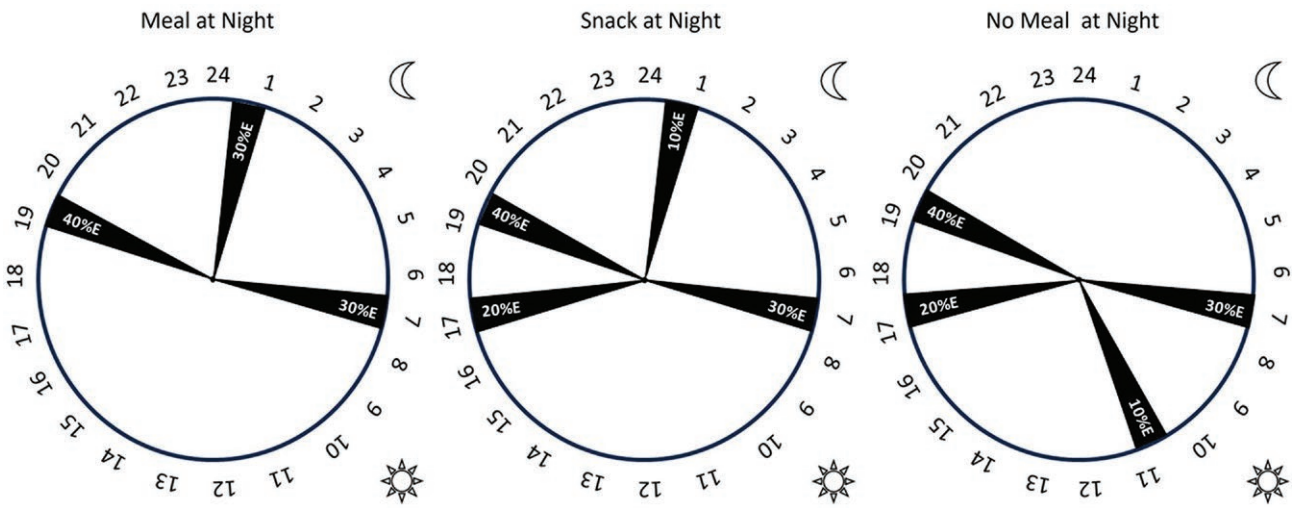

Figure 3. Representation of energy distribution by condition. %E; percentage energy, Sun symbol; day, Moon symbol; night.

Table 3. Breakfast Meal Macronutrient Composition

Foods (quantity)	Energy (kJ)	Total Fat (g)	Protein (g)	Carb (g)	Fiber (g)
White bread toasted (35 g)	305.0	0.6	3.1	13.1	1.0
Margarine (5 g)	140.2	3.8	0.0	0.0	0.0
Strawberry jam (5 g)	74.1	0.0	0.0	4.5	0.1
Reduced fat milk (200 mL)	428.0	2.5	7.7	12.1	0.0
Orange Juice (200 mL)	340.2	2.0	1.2	18.0	0.4
Cornflakes (57 g)	884.9	0.3	4.9	45.7	1.8
Total	2171.9	9.2	16.9	93.5	3.2

g, grams; ml, milliliters; kJ, kilojoules; Carb, carbohydrate.

Figure 4. Diagram showing the order of testing in the cognitive test battery. PVT, Psychomotor Vigilance Task; VAS, Visual Analogue Scale; PANAS, Positive and Negative Affect Schedule. This testing battery will be conducted for all conditions at 13:00, 20:00, 22:30, 01:30, and 04:00 hours during wake times.

Breakfast meal tolerance test.

On all other study days participants will consume "breakfast" between 06:30 and 07:00 hours. The breakfast meal will be a high carbohydrate, high glycaemic index meal designed to challenge the metabolic system and will be identical between participants each day. The contents of the breakfast meal are listed in Table 3. On days 3 and 6 a cannula will be inserted, and blood samples will be collected at -15 and 0 minutes prior to and 15, 30, 60-, 90-, 120- and 150-minute post-breakfast on each of these days. Blood samples will be handled as for the OGTT.

Cognitive testing

Cognitive testing will occur at 13:00, 20:00 22:30, 01:30, and 04:00 hours for all conditions during wake times using the measures outlined below. Figure 4 shows the proposed order of testing.

Psychomotor vigilance task.

The psychomotor vigilance task (PVT) is a test designed to objectively evaluate sustained attention and vigilance via response times to visual stimuli. Participants respond to a stimulus as quickly as possible by pressing a button on a hand-held device with the thumb of their dominant hand. They will be instructed to react immediately and make the least number of false starts (responding before the stimulus appears) as possible. Participants will complete both the 3- and 10-minute versions of the PVT. The inter-stimulus interval varies from 1000 to 4000 ms (3-minute PVT) and 2000–10 000 ms (10-minute PVT). The PVT has been found to be a reliable and valid test of sustained attention in various settings. For both the 3- and 10-minute versions of the PVT, measures of sustained attention will include reaction time (stimulus to pressing button latency) and number of lapses (reactions over 500 milliseconds). False starts will be defined as reactions prior to 100 milliseconds.

Driving task.

A computer-based driving simulation task will be performed as a measurement of cognitive functioning (York Computer Technologies Inc., 2018). To simulate a realistic driving experience, a steering wheel, accelerator, and brake will be installed on the computers. Participants will experience a monotonous 40-minute country drive of a standard motorway road scene with lane markings but not traffic or street signage. Participants will be instructed to stay within the left-hand lane and keep their hands on the steering wheel at the 10 and 2 clock position at all times. They will be instructed to maintain the speed limit as closely as possible, 100 km/h on straight roads and 80 km/h around the bends. The York Driving Simulator has good convergent validity regarding its sensitivity to other cognitive performance measures which are sensitive to sleep loss, including self-reports, vigilance tests, and sleep latency tasks [42]. As previously used in the pilot study, the variables derived from this task will be lane deviation, speed deviation, and number of crashes [36].

Mood testing

Visual Analogue Scales.

Visual Analogue Scales (VAS) will be used to assess mood and associated symptoms which are commonly altered during periods of shiftwork [43]. These include hunger, fullness, desire to eat, thoughts about food, headache, dizziness, stomach disturbance, and bloating. Participants will be asked to rate the extent to which they experience each symptom by placing a vertical line on a 100 mm horizontal scale anchored with extremes of each symptom. For example, participants describe their experience of hunger from "not at all hungry" to "as hungry as I've ever felt." Scales and respective anchors include hunger ("not at all hungry" to "as hungry as I've ever felt"), fullness ("not at all full" to "as full as I've ever felt"), desire to eat ("very weak desire to eat" to "very strong desire to eat"), thoughts of food ("no thoughts of food" to "very preoccupied with food"), headache ("no headache at all" to "extremely bad headache"), dizziness ("no dizziness" to "a lot of dizziness"), stomach disturbance ("no stomach upset" to 'extremely upset stomach) and bloating ("I don't feel bloated" to 'I feel very bloated). VAS have been found to be a valid and reliable measure to assess mood [44].

Positive and Negative Affect Schedule.

The Positive and Negative Affect Schedule (PANAS) will be employed as a subjective measure of the two primary dimensions of mood, positive and negative affect [45]. Two PANAS subscales each comprising of 10-items (one positive and one negative). Participants will rate their experience of each effect in the last week on a 5-point Likert scale ranging from 1 (very slightly) to 5 (extremely). Positive affects include "proud" and "excited," while negative affects include "irritable" and "ashamed." Both subscales show high internal consistency largely uncorrelated with one another [45]. Particularly within sleep literature, the PANAS is considered sensitive to the fluctuations in mood commonly experienced with the alteration of habitual sleep patterns [46]. Composite scores for each scale range from a minimum of 10 to a maximum of 50, with a larger score reflecting a greater presence of affect.

Physiological testing

Sleep.

Baseline, day 5 and Recovery sleep will be recorded, using Compumedics GRAEL hardware and Profusion Version 5 software (Melbourne, Australia). Electroencephalography (EEG) data will be collected from sites F3, F4, C3, C4, O1, and O2 and will be referenced to a contralateral mastoid (M1, M2). Electrooculography (EOG) and Electromyography (EMG) will also be recorded. On the first night of the study, respiratory signals will be collected to ensure participants do not have any undiagnosed sleep conditions including OSA. Participants will be monitored via an infrared camera overnight by an experienced sleep technician. Studies will be scored according to Rechtschaffen and Kales [47] sleep staging criteria. Sleep variables analyzed will include TIB, total sleep time, wake after sleep onset, sleep efficiency, sleep onset latency, and time in minutes of rapid eye movement, stages 1, 2, 3, and 4.

Melatonin and cortisol.

Approximately every 2 hours during the study(baseline, day 3–6, and recovery) saliva samples will be collected using Salivettes® (Sarstedt, Numbrecht, Germany). The Salivettes® tubes containing the plugs will then be stored at –80°C, thawed, and centrifuged prior to analysis. Saliva melatonin will be assayed by the Adelaide Research Assay Facility at the University of Adelaide by double antibody radioimmunoassay, using standards and reagents supplied by Novolytix (RKDSM-2, Novolytix, Witterswil, Switzerland). This assay is based on the Kennaway G280 anti-melatonin antibody [48] and uses [125I]2-iodomelatonin as the radioligand. The assay will use the protocol provided by Novolytix and the samples (200 µL) assayed in duplicate. Saliva cortisol will be analyzed at the Adelaide Research Assay Facility by Enzyme-Linked Immunosorbent Assay (ELISA; 1-3002, Salimetrics, State College PA, USA).

Data management and analysis

For the primary outcomes, area under the curve (AUC) will be calculated from samples taken between 0 and 150 minutes post-glucose drink administration for plasma glucose, insulin, and FFA from the OGTT at baseline and recovery. Differences in response to day and night eating versus day eating only will be examined using mixed effects modeling for longitudinal data, which accounts for inter-individual differences at baseline and as a response to treatment. Models for glucose and insulin will specify fixed effects (main and interaction) of condition (meal at night/snack at night/no meal at night), and day (baseline/recovery), with a random effect of participant.

Sample size and power

Sample size calculations are focused on achieving sufficient power to detect the condition effect in this study. Our previous published pilot data [25] from participants (night eating $n = 4$, day only eating $n = 7$) undergoing the same protocol found a post-prandial mean AUC glucose of 734.1 ± 210.6 (*SD*) mmol/L for meal at night group and 883.6 ± 160.5 (SD) mmol/L for no meal at night group (large effect size $d = 0.78$) after four nights of simulated shiftwork. Based on this effect size for the difference between conditions, the proposed study would require 52 participants to be sufficiently powered ($\alpha = 0.05$, $1–ß = 0.80$).

The current study also requires sufficient power to detect the condition (meal at night/snack at night/no meal at night) by day (baseline/recovery) interaction. For glucose, our published pilot data [25] from participants (night eating $n = 4$, day only eating $n = 7$) undergoing the same protocol, yielded large effect size estimates for the day (baseline/recovery; partial $\eta 2 = 0.54$) and the condition*day interaction (partial $\eta 2 = 0.53$). To be sufficiently powered for this condition*day interaction, we would require a total of 9 participants ($\alpha = 0.05$, $1–ß = 0.80$).

Given that participants will be required to stay in the laboratory for 7 days, we expect an attrition rate of ~15%. Participants will be run in groups of four and allowing for attrition we plan to recruit $n = 60$ participants, for $N = 52$ in the final sample to be sufficiently powered to detect the effects of primary interest.

Discussion

The rates of obesity and diabetes are increasing. Over 60% of Australians are overweight or obese, and approximately one in 20 have diabetes [49, 50]. In 2020–21, Australians processed over 16.5 million scripts for diabetes medications attributing to an estimated $3.4 billion on the Australian health system [50]. Preventative strategies to reduce the incidence of metabolic disorders are timely and important. Rates of type 2 diabetes and obesity are elevated among shift workers, compared to the general population, even after controlling for lifestyle and socioeconomic status [51, 52]. In this way, studying shift workers may provide a "magnifying glass" to identify potentially modifiable risk factors for metabolic disease. Our preliminary data [25, 53] show that shift workers eat more at night and that this meal timing plays an important role in metabolic disturbance. The public and private health costs of not acting to curb the metabolic effects of shift work will be very high; added to this are the likely reductions in work performance and productivity by those with these conditions.

This study will use an innovative approach to reduce the metabolic disease impact associated with shift work. Not eating at night while working the night shift is a straightforward intervention that could be readily translated to existing dietary guidelines. This simplicity may provide significant advantages over more complex lifestyle prescriptions in terms of compliance. Given the 1.5 million Australian shift workers [1] who are likely to eat during the night, as well as those chronically awake and eating at night for other reasons, including feeding an infant or suffering a sleep disorder, such dietary manipulation could provide significant improvements in health.

Primary study outcomes will be (1) A detailed characterization of the changes in glucose metabolism when a meal or a snack versus no meal is consumed at night and how this impairment accumulates over multiple night shifts; (2) Description of an intervention to reduce the negative metabolic impact of shift work. This intervention has a straightforward message that simply changes one behavior rather than trying to limit certain macronutrients e.g. carbohydrates or overall kilojoules; and (3) An evidence base to potentially change industry recommendations and workplace policy to improve the health costs of millions of workers.

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Author Contributions

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