

# The Influence of Split Sleep-Wake Schedules and Daytime Sleep Strategies on Neurobehavioural Performance

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*BPsych(Hons)*

Dissertation submitted in fulfilment of the requirements for the degree of  
Doctor of Philosophy

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4<sup>th</sup> May, 2017

## Summary

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Demand for 24-h access to services and goods has led to an increase in the number of employees engaged in shiftwork. However, while shiftwork has become necessary to meet community expectations, it has serious consequences for health and safety. The risk of fatigue-related accidents and injuries is a significant problem for the shift working population. This is because shiftwork places restrictions on the opportunities available for workers to obtain sleep. Shiftworkers, especially those who work night shifts, must often stay awake for long hours and sleep at times inconsistent with their body clocks, so sleep loss is common. This dissertation evaluates alternative options for arranging sleep that could potentially optimise neurobehavioural function in circumstances where long nocturnal sleep episodes are not possible. Two main approaches were used to address these aims. The first was to assess the effectiveness of split sleep-wake schedules at sustaining neurobehavioural function around the clock – with and without sleep restriction – which could have implications for work rosters in certain safety-critical industries. The second approach was to assess the effectiveness of different arrangements of daytime sleep at ameliorating the decline of night-time performance, which could have implications for the sleep strategies shiftworkers employ before and after night shifts.

It is important to ensure participants are well-rested prior to entering the laboratory. This is usually achieved with a combination of sleep diaries and actigraphy with wrist-worn accelerometers. The first two studies reported in this dissertation (Chapter 3 and Chapter 4) were conducted to validate several accelerometers for monitoring sleep/wake patterns and ensuring participant compliance with pre-study instructions.

Splitting a shiftwork schedule into multiple short work-rest cycles per day could potentially sustain performance around the clock because it would: (i) reduce the time between rest breaks, and (ii) facilitate more opportunities for nocturnal sleep than would otherwise be available to night workers on a traditional schedule. There is converging evidence that the sleep-wake system is adaptable and splitting sleep into two or more shorter episodes per day is not inherently detrimental to performance. However, a limitation of previous investigations into split sleep-wake schedules is that they usually only assess daytime performance and confound the influence of homeostatic process and circadian processes. As such, this dissertation expanded on previous research

by systematically comparing the circadian and homeostatic effects of split and consolidated sleep-wake schedules on neurobehavioural performance by means of forced desynchrony (Chapter 5). This study was then followed by an assessment of how severe sleep restriction affects simulated driving and performance on various different neurobehavioural tasks during another split sleep-wake forced desynchrony schedule (Chapter 6).

To understand whether there is an ideal arrangement of daytime sleep for performance on consecutive night shifts, this dissertation compared the effects of three broad strategies for sleep timing between simulated 12-h night shifts in the laboratory (Chapter 7). These included (i) sleeping immediately after the night shift, (ii) delaying sleep for several hours in a manner similar to day workers, and (iii) splitting sleep episodes, obtaining some in the morning and some in the afternoon. Performance during the first night shift in a roster can be impaired by sleep deprivation associated with the transition to a night-time schedule because a long preceding daytime sleep is usually impractical. As such, the final study of this dissertation assessed whether a 1-h nap prior to a simulated first 12-h night shift was sufficient to mitigate significant performance deficits compared to a subsequent shift (Chapter 8).

Several conclusions may be drawn from the results of this dissertation. First, the wrist-worn accelerometers used in the studies were suitable for monitoring sleep/wake behaviour (Chapter 3 and 4). Second, split sleep-wake schedules are not detrimental to performance and may even be beneficial for nocturnal performance (Chapter 5). The reduction of wakefulness required between sleep opportunities resulted in better performance at night during the split sleep-wake schedule than in the consolidated schedule. Third, during severe sleep restriction, tasks requiring sustained vigilance exhibit the greatest circadian variation and the worst nocturnal deficits (Chapter 6). Fourth, daytime sleep strategies (immediate, delayed, split) have no significant effects during 12-h night shifts, where the “window” in which to differentiate them is limited (Chapter 7). Finally, a prophylactic 1-h nap is likely to be sufficient to ameliorate the effects of sleep deprivation on performance during the first night shift (Chapter 8).

## Declaration of Authorship

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I certify that the work contained in this thesis has not been previously submitted either in whole or in part for a degree at any university or tertiary institution and, to the best of my knowledge and belief, the material presented in this thesis is original except where due reference is made in the text.

All substantive contributions by others to the work presented, including jointly authored publications, is clearly acknowledged.

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Signed: .....  .....

Date: ..... 04 / 05 / 2017 .....

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## List of Publications Arising from Thesis

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1. **Kosmadopoulos, A.**, Sargent, C., Zhou, X., Darwent, D., & Roach, G. D. (2012). Two for one? Validating an energy expenditure monitor against polysomnography for sleep/wake measurement. In X. Zhou & C. Sargent (Eds.). *Sleep of Different Populations* (pp. 16-20). Adelaide, Australia: Australasian Chronobiology Society.
2. **Kosmadopoulos, A.**, Sargent, C., Darwent, D., Zhou, X., Dawson, D., Muldoon, N., & Roach, G. D. (2013). Neurobehavioural performance during a split 28-h forced desynchrony schedule. In C. Sargent & X. Zhou (Eds.). *Sleep, Performance and Well-being in Adults and Adolescents* (pp. 1-6). Adelaide, Australia: Australasian Chronobiology Society.
3. **Kosmadopoulos, A.**, Sargent, C., Darwent, D., Zhou, X., & Roach, G. D. (2014). Alternatives to polysomnography (PSG): A validation of wrist actigraphy and a partial-PSG system. *Behavior Research Methods*, 46(4), 1032-1041. doi: 10.3758/s13428-013-0438-7.
4. **Kosmadopoulos, A.**, Sargent, C., Darwent, D., Zhou, X., Dawson, D. & Roach, G. D. (2014). The effects of a split sleep-wake schedule on neurobehavioral performance and predictions of performance under conditions of forced desynchrony. *Chronobiology International*, 31(10), 1209-1217. doi: 10.3109/07420528.2014.957763.
5. **Kosmadopoulos, A.**, Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2015). Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times? In G. A. Kennedy & C. Sargent (Eds.), *The Time of Your Life* (pp. 32-37). Melbourne, Australia: Australasian Chronobiology Society.
6. **Kosmadopoulos, A.**, Darwent, D., & Roach, G.D. (2016). Is it on? An algorithm for discerning wrist-accelerometer non-wear times from sleep/wake activity. *Chronobiology International*, 33(6), 599-603. doi: 10.3109/07420528.2016.1167720.
7. **Kosmadopoulos, A.**, Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2016). No first night shift effect observed following a nocturnal main sleep and a prophylactic 1-h afternoon nap. *Chronobiology International*, 33(6), 716-720. doi: 10.3109/07420528.2016.1167727.
8. **Kosmadopoulos, A.**, Sargent, C., Zhou, X., Darwent, D., Matthews, R. W., Dawson, D. & Roach, G. D. (2017). The efficacy of objective and subjective predictors of driving performance during sleep restriction and circadian misalignment. *Accident Analysis & Prevention*, 99(B), 445-451. doi: 10.1016/j.aap.2015.10.014.

## List of Publications Contributed to During Candidature

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1. Muldoon, N., Sargent, C., Zhou, X., **Kosmadopoulos, A.**, Darwent, D., & Roach, G. D. (2013). The efficacy of subjective ratings is limited during the biological night. In C. Sargent & X. Zhou (Eds.). *Sleep, Performance and Well-being in Adults and Adolescents* (pp. 7-12). Adelaide, Australia: Australasian Chronobiology Society.
2. Roach, G. D., Zhou, X., Darwent, D., **Kosmadopoulos, A.**, Dawson, D., & Sargent, C. (2017). Are two halves better than one whole? A comparison of the amount and quality of sleep obtained by healthy adult males living on split and consolidated sleep-wake schedules. *Accident Analysis & Prevention*, 99(B), 428-433. doi: 10.1016/j.aap.2015.10.012.
3. Matthews, R. W., Ferguson, S. A., Sargent, C., Zhou, X., **Kosmadopoulos, A.**, & Roach, G. D. (2017). Using interstimulus interval to maximise sensitivity of the Psychomotor Vigilance Test to fatigue. *Accident Analysis & Prevention*, 99(B), 406-410. doi: 10.1016/j.aap.2015.10.013.
4. Zhou, X., Sargent, C., **Kosmadopoulos, A.**, Darwent, D., Dawson, D., & Roach, G. D. (2017). Do split sleep/wake schedules reduce or increase sleepiness for continuous operations? *Accident Analysis & Prevention*, 99(B), 434-439. doi: 10.1016/j.aap.2015.10.027.

## Acknowledgements

---

Finally, my thesis is done. And it has left many to acknowledge in its wake.

Foremost, I would like to express my sincere thanks and heartfelt appreciation to Professor Greg Roach, my primary supervisor, and to my associate supervisors Associate Professor Charli Sargent and Dr David Darwent. You took me enthusiastically under your wings from my fledgling years as an undergraduate summer research scholar and honours student until now. I cannot think of any better combination of people to have guided me throughout this process. You believed in me when I doubted and, in your own ways, encouraged and pushed me with pragmatic advice and feedback, good humour and positivity when I needed it.



Next, I must reserve a special word of thanks to my post-doctoral support group. To Dr Xuan Zhou, who finished as I started: thank you for helping in the day-to-day management and supervision of the laboratory studies. You're a machine, and your assistance – both practical and statistical – was irreplaceable. To Dr Raymond Matthews and Dr Michele Lastella, who received their doctorates during my candidature: thank you for your invaluable counsel, insight, and moral support while navigating the 'before' and the 'after'. You showed me there was light at the end of the tunnel.

It would be remiss of me if I did not also acknowledge my fellow PhD candidates, stationed upstairs and downstairs, who accompanied me for much of my journey. In particular, I am grateful to Tom Kontou, Tessa Benveniste, and Josh Trigg. True or not, it often seems that only those *currently* undertaking a doctoral programme accurately understand the trials and tribulations involved. Without your camaraderie and generous lending of sympathetic ears, I would no doubt have lost more than a modicum of sanity. I hope that I can be similarly helpful as you also reach the end.

The list of everyone else at the Appleton Institute who supported and encouraged me is too long to recite. However, I will extend specific thanks to Professor Drew Dawson and Professor Sally Ferguson for leading by example, promoting a culture of high quality research and great collegiality.





To my patient friends, in particular: Ella, Chris, Sam and Anne. Thank you for your moral support. Your unwavering friendship the last few years is possibly more than I deserve; sorry we didn't catch up more than we did. I will make up for this. Next round of drinks are on me.



And finally, thank you to my family: my parents, Nick and Madeleine, and my twin sister, Zoë. These last several years have been a slog for all of us, not just me, full of change and transition. Through it all, Mum and Dad, you have been understanding, dependable, and supportive – above and beyond. Zoë, when I started this you were still in Adelaide and look where you are now! Miss you, but very proud.



#### *Financial Support*

I gratefully acknowledge that my doctoral candidature was financially supported by the Australian Government through the Research Training Scheme and the granting of an Australian Postgraduate Award. I also received a scholarship from the Bushfire Cooperative Research Centre, and I thank them for their support also.

Further, I acknowledge the Australian Research Council for the grants bestowed to my supervisors through the Discovery Projects scheme (DP130104843) that have supported my research.

*People say, "I'm going to sleep now," as if it were nothing. But it's really a bizarre activity. "For the next several hours, while the sun is gone, I'm going to become unconscious, temporarily losing command over everything I know and understand. When the sun returns, I will resume my life."*

*If you didn't know what sleep was, and you had only seen it in a science fiction movie, you would think it was weird and tell all your friends about the movie you'd seen.*

— George Carlin

*"Is this real? Or has this been happening inside my head?"*

*"Of course it is happening inside your head, but why on earth should that mean that it is not real?"*

— J.K. Rowling

## **Chapter 1.**

### **Introduction and Rationale**

---

## 1.1. Shiftwork and Fatigue

Shiftwork is a term that refers to schedules in which successive groups of employees work alternating periods of the day, called “shifts”, to extend the normal operating hours of an organisation anywhere up to 24 h, seven days per week (Åkerstedt, 1995; Costa, 2003). This is in contrast to traditional working hours, which typically require employees to commence work between 0730 h – 0900 h and finish between 1700 h and 1800 h, Monday to Friday. Said to be a combined product of the industrial revolution of the 19<sup>th</sup> Century and the invention of the electric light bulb, which prolonged the range of possible waking hours, the prevalence of shiftwork has proliferated in recent decades (Walsh, Dement, & Dinges, 2011). Indeed, in 2012, an estimated 16.1% of the Australian workforce regularly undertook shiftwork (with 6.9% of the workforce primarily working at night) – a substantial increase from 13.9% in 1993 (Australian Bureau of Statistics, 1994, 2013). This growth, both locally and globally, has been attributed to changing community expectations and rising customer demands for services and products, facilitated by technological advances in communication and transportation.

Many industries and occupations, in both public and private sectors, utilise shiftwork in their workforces. Government sectors which predominantly involve shiftwork typically include those that address public health and safety needs, such as emergency services (e.g., police, ambulance, and fire), healthcare, and the military. In private sectors, shiftwork is generally employed where it serves a financial interest and assists in meeting consumer demands in a competitive global environment. Industries that commonly utilise shiftwork in the private sector include retail, hospitality, mining, and transportation (e.g., aviation, rail, road, and maritime) (Australian Bureau of Statistics, 2013).

Despite the demand and need for shiftwork, these schedules have social and public health and safety costs (Costa, 2016). Shiftworkers are among the most fatigued demographic in society (Åkerstedt, 2003; Di Milia, Waage, Pallesen, & Bjorvatn, 2013; Rajaratnam et al., 2011) and fatigue is associated with higher rates of errors, accidents, injuries and fatalities (Folkard, Lombardi, & Tucker, 2005; Mitler et al.,

1988; Philip & Åkerstedt, 2006; Rajaratnam et al., 2011). There are diverse thoughts about the nature of fatigue and numerous proposed definitions (Dawson, Noy, Härmä, Åkerstedt, & Belenky, 2011; Noy et al., 2011). However, one useful definition in the literature describes fatigue as ‘a biological drive for recuperative rest’ (Williamson et al., 2011, p.499) that may present itself in various ways including sleepiness and mental exhaustion, which can affect performance.

For the purpose of risk management in an industry context, fatigue has been operationalised as a “physiological state of reduced alertness or capability to perform mental or physical tasks” caused by lack of sleep, extended wakefulness, circadian phase or workload, individually or in combination (*Civil Aviation Order 48.1 Instrument 2013* [Cth] F2017C00880, para 6.1). Any successful effort to reduce risk and mitigate fatigue in shiftworkers must address the various aspects of shiftwork schedules responsible for it – especially, circadian rhythm disruption (more details in section 1.2, p.15), sleep loss and extended wakefulness (more details in section 1.3, p.28). The following sections will review what is known about these contributors of fatigue in shiftwork, as well as potential strategies and countermeasures which could be implemented.

### 1.1.1. Types of Shift Schedules

While the purpose of shiftwork schedules is to extend the hours of operation, not all shift schedules are identical. Schedules can differ from one industry to another, and from one organisation to another, on various characteristics including: (i) the length of the shifts; (ii) the times shifts start and finish; (iii) the frequency and duration of breaks; (iv) the length of the shift cycle, (v) whether the rosters are permanent (with employees working one type of shift on a regular basis), or rotating (with employees periodically alternating shift times); and, (vi) if rotating, the speed and direction (clockwise, counterclockwise) of shift rotation, among other factors (Costa, 1997).

Historically, the most common shift schedule to facilitate 24-h coverage has been the 8-h shift system which divides the 24-h day into thirds and employs three crews of employees to work alternating 8-h shifts with 16-h breaks (Ferguson &

Dawson, 2012). The three shifts are traditionally categorised by start time and labelled as the morning shift, afternoon or evening shift, and the night shift. Another popular shift schedule is the 12-h system, in which two crews of employees work alternating 12-h (day/night) shifts with 12-h breaks (Ferguson & Dawson, 2012; Parkes, 2012; Smith, Wright, Mackey, Milsop, & Yates, 1998b). Although the longer shifts are associated with increased fatigue compared to 8-h shifts (particularly for those working at night) (Baker, Heiler, & Ferguson, 2003; Ferguson & Dawson, 2012; Kogi, 1991; Smith et al., 1998b), the benefit of 12-h shifts is that they reduce the number of consecutive days worked per week, thereby cutting the number of commutes and increasing time for recovery and social/family life (Loudoun, 2008). From an operational perspective, the 12-h shift system can be advantageous because it only requires two alternating crews of workers per 24 h rather than three; this means there are fewer handovers, which can disrupt continuity and result in errors of miscommunication (Ferguson & Dawson, 2012; Kogi, 1991).

As an alternative to the traditional 8-h and 12-h shift system, some industries – such as those involving maritime or rail operations – roster employees onto shorter, more frequent shifts to ensure around-the-clock operations (Darwent, Lamond, & Dawson, 2008; Härmä, Partinen, Repo, Sorsa, & Siivonen, 2008; Short, Agostini, Lushington, & Dorrian, 2015). Sometimes described as “watch-keeping” systems, these shift schedules differ from traditional schedules in that they entail multiple alternations of work and rest, on average, per day rather than one (Short et al., 2015). In maritime watch systems, the rosters employed on vessels variously involve work-rest cycles of “6-h on/6-h off” or “4-h on/8-h off” (Härmä et al., 2008; Van Leeuwen et al., 2013). In long distance freight rail operations, train drivers employ an alternating “relay van” system throughout the journey in cycles of “8-h on/8-h off” (Darwent et al., 2008). A potential disadvantage of split work-rest schedules is that the breaks do not facilitate long periods of uninterrupted sleep; rather, sleep is often split – obtained as a short main sleep in one break, supplemented by a nap in the other. However, limiting the duration of sustained work time with shorter shifts means that workers can rest more frequently (Short

et al., 2016). Further, the use of short work-rest cycles allows all crew on site the prospect of some night-time sleep and some daytime work.

Although it is not designed to sustain 24-h coverage, another type of shift system employed in some industries that requires employees to work multiple short shifts per day is the “split-shift”. The split-shift is usually implemented in industries where there is a predictable ebb and flow of customers across the day, such as in public transport (e.g., morning and evening rush hour), and hospitality (e.g., lunch and dinner) (Bohle, Quinlan, Kennedy, & Williamson, 2004). Employees on these schedules often work long days, arriving at work in the early morning and leaving for home late in the evening, with a break of several hours during “off-peak” times when demand for service is low (Bohle et al., 2004). Although economical for employers, split-shifts are often unpopular amongst workers because the breaks are usually too short to accomplish anything worthwhile (Hing & Breen, 2008). Further, their extended span across the daytime limits the time available for activities after work other than sleep (Bohle et al., 2004; Hing & Breen, 2008).

### 1.1.2. Fatigue and Safety in Shiftwork

Though the precise number varies from industry to industry, reports suggest that as many as 80-90% of serious accidents and fatalities in the workplace can be attributed to human error (Baron, 1988; Nagel, 1988; Salminen & Tallberg, 1996). As such, much importance has been placed on addressing behavioural, environmental and psychosocial antecedents of human error to reduce the frequency and severity of these accidents. One of the main factors responsible for human error is fatigue (Williamson et al., 2011). Fatigue in the workplace is associated with higher rates of accidents, injuries and fatalities (Folkard et al., 2005; Philip & Åkerstedt, 2006; Rajaratnam et al., 2011), which is particularly concerning for shiftworkers who are among the most fatigued demographic in society (Åkerstedt, 2003; Di Milia et al., 2013; Rajaratnam et al., 2011). There are several factors affected by shiftwork that influence the prevalence of fatigue-related accidents (Di Milia et al., 2011). However, the primary factors involved in

shiftwork-related fatigue are prior sleep/wake history (Belenky et al., 2003; Van Dongen, Maislin, Mullington, & Dinges, 2003) and time of day (Arendt, 2010).

#### *1.1.2.1. Sleep loss and extended wake in shiftwork*

Acknowledging that the optimal duration of sleep varies from individual to individual, the National Sleep Foundation recommends that adults obtain 7 h to 9 h of sleep per night (Hirshkowitz et al., 2015). However, a significant proportion of the population report obtaining much less than 7 h (Ford, Cunningham, & Croft, 2015). While there is some dispute regarding the overall direction of secular trends in sleep duration over time (Bin, Marshall, & Glozier, 2012; Bin, Marshall, & Glozier, 2011), surveys suggest about 10% of Americans and 5% of Australians regularly report sleeping <6 h per night (Bin, Marshall, & Glozier, 2013; Knutson, Van Cauter, Rathouz, DeLeire, & Lauderdale, 2010). The prevalence of short sleep (and, inversely, extended wakefulness) is greater amongst shiftworking populations and has risen over the last few decades with the increasing prevalence of shiftwork. Approximately 30% of workers in industries that have non-standard work schedules and long work-weeks report sleeping  $\leq 6$  h on average per night, an increase from 24% two decades ago (Luckhaupt, Tak, & Calvert, 2010).

Unlike permanent day workers, the body clocks (i.e., endogenous circadian pacemakers; see section 1.2.2, p.18) of shiftworkers are often misaligned with the external environment; they must work when their body clocks promote sleep and sleep when their body clocks promote activity. These constraints mean that when shiftworkers do sleep, it is frequently shorter and of poorer quality (Åkerstedt, 1987; Kogi, 1982). Indeed, in their study of locomotive engineers, Roach, Reid, and Dawson (2003) found that for breaks of similar duration, more sleep was always obtained when breaks occurred at night than when they occurred during the daytime. The disruption and reduction of sleep resulting from shiftwork has been noted in many other industries as well, including aviation, maritime, transport, and mining (Ferguson, Baker, Lamond, Kennaway, & Dawson, 2010; Gander, van den Berg, & Signal, 2008; Howard, Gaba, Rosekind, & Zarcone, 2002; Philip & Åkerstedt, 2006; Roach, Sargent, Darwent, & Dawson, 2012b). An extreme example of both sleep loss and extended wakefulness is evident in medicine, particularly for



resident physicians in training. They must often work more than 80 h per week, scheduled to on-call duty periods of 24 h – 36 h where sleep is limited and frequently interrupted (Gaba & Howard, 2002).

It is not only night workers who experience sleep loss. Workers whose shifts are scheduled during the day can experience elevated levels of fatigue if their duty start time restricts the amount of sleep they can obtain. Roach et al. (2012b), examined the effects of early start times on the sleep of short-haul aeroplane pilots. They found that pilots obtained significantly less sleep in the 12 h prior to shifts commencing between 0400 h and 0500 h than prior to shifts commencing between 0900 h and 1000 h. In the case of the pilots commencing duty early in the morning, their sleep was curtailed because of the 'Wake Maintenance Zone' (Lavie, 1986; Strogatz, Kronauer, & Czeisler, 1987), a period in the late evening where it is difficult to initiate and maintain sleep (section 1.3.3.2, p.51), which inhibited the appropriate advancement of their bedtimes.

Though its effects are often confounded by time of day, the association of sleep loss with fatigue-related errors and accidents in shiftwork is widely documented. Numerous studies in a wide variety of occupational settings have shown that workers who find it difficult to sleep or report excessive daytime sleepiness are more likely to die from injuries or make errors at work, risking the safety of others, than those who sleep well and are not excessively sleepy (Åkerstedt, Fredlund, Gillberg, & Jansson, 2002; Gaba & Howard, 2002; Howard et al., 2002).

#### *1.1.2.2. Shift time and fatigue*

Shift time is also an important factor in workplace fatigue. As a consequence of the body clock synchronising the predisposition for sleep with the night and wakefulness with the day, shifts scheduled at times usually set aside for sleep are at an increased risk of fatigue-related errors and accidents (Folkard et al., 2005; Smith, Folkard, & Poole, 1994). Many studies have analysed the frequency of work-related injuries across the day, and these reliably describe a peak in accident risk between midnight and the early hours of the morning (Folkard, Lombardi, &

Spencer, 2006; Folkard et al., 2005; Horne & Reyner, 1995; Smith et al., 1994; Violanti et al., 2012).

Integrating data from multiple published studies, Folkard et al. (2006) calculated the risk of occupational injuries and accidents across the three shifts (morning, afternoon, night) that comprise the 8-h shift system. They found that the risks increased by 15.2% on the afternoon shift and 27.9% on the night shift relative to that on the morning shift (Folkard et al., 2006). These associations between time of day and risk are consistent with what has been observed in a number of major industrial and engineering disasters in modern times. Fatigue-related human error was attributed, at least partially, to the nuclear power plant incidents of Three Mile Island in 1979 and Chernobyl in 1986 (Mitler et al., 1988). Both of these incidents occurred at night – the former began at 0400 h, and the latter at 01:23 h (Mitler et al., 1988). In the case of the Three Mile Island accident, while a mechanical problem triggered the incident, investigators concluded that it was a failure of shiftworkers to recognise and respond appropriately that caused the near meltdown to occur (Mitler et al., 1988).

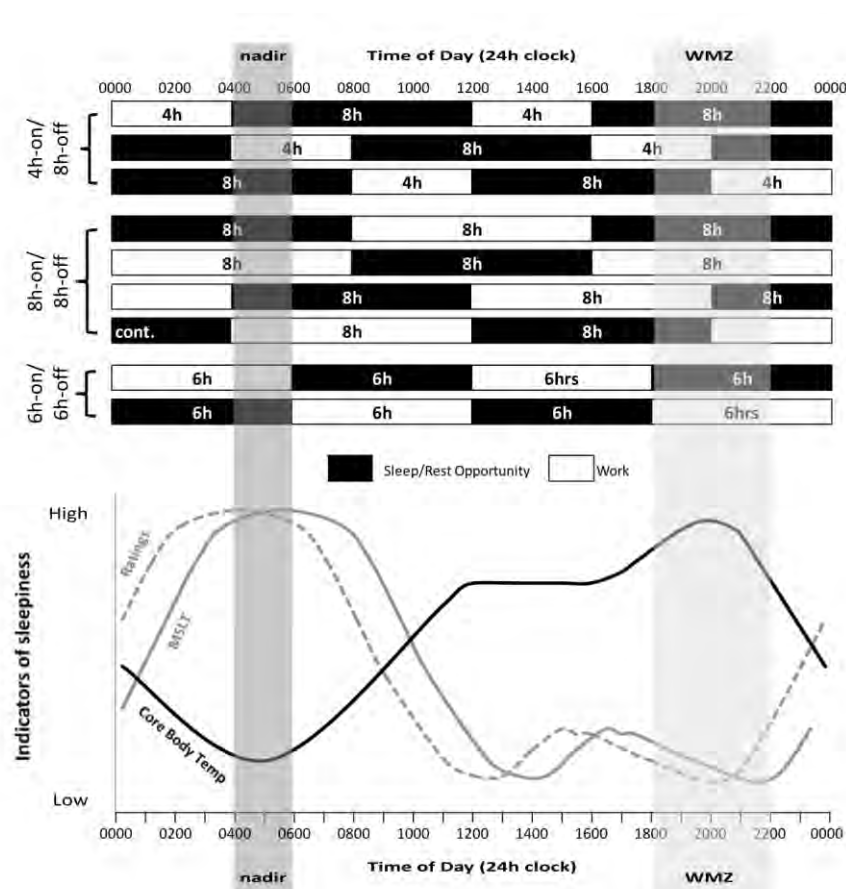
From the perspective of those who must respond to accidents, disasters, or violent crimes, the night is often the least favourable time for these events to occur. If an incident occurs at night, the first responders – whether police officers, ambulance paramedics, or firefighters – will be shiftworkers on night shift. If injuries have been caused, attending hospital staff – physicians, nurses, and technicians – will also be shiftworkers working at night. The risk of fatigue-related errors that contribute to the peak in accidents at night is also present for those who respond to them (Smith-Coggins, Rosekind, Hurd, & Buccino, 1994; Violanti et al., 2012; Waggoner, Grant, Van Dongen, Belenky, & Vila, 2012). As such, it is critical to implement countermeasures and strategies that effectively mitigate the risks of fatigue in shiftwork.

### 1.1.3. Split Work-Rest Schedules: Sleep and Sleepiness

Many industries use shiftwork schedules to meet the expectations and demands of a 24-h society, but for those industries that undertake safety-critical operations – involving emergency services, defence, health, mining and transportation, among other fields – it is even more important that performance is sustained at high standards around the clock (Short et al., 2015). As stated previously, factors that increase fatigue-related risks in traditional shiftwork schedules are sleep loss and extended wakefulness (influenced by shift and break durations), and biological circadian rhythms (influenced by shift times). Therefore, it is plausible that fatigue might be ameliorated by implementing a shift schedule that minimises circadian misalignment of sleep/wake times and optimises the duration of sleep. An approach to providing 24-h shift coverage that does not necessitate long night shifts is to divide the work-rest schedule into multiple short rotations per day (e.g., 6-h on/6-h off) as described in section 1.1.1, p.3. Dividing the roster in this way could potentially sustain performance around the clock because it would reduce the time between rest breaks and facilitate more opportunities for nocturnal sleep than would otherwise be available to night workers on a traditional schedule.

Currently, split work-rest schedules are primarily used in industries that employ workers in remote locations, such as in maritime and rail operations, and numerous studies have been conducted to investigate their effects on fatigue (Colquhoun, 1985; Darwent et al., 2008; Hansen & Holmen, 2011; Härmä et al., 2008; Lamond, Darwent, & Dawson, 2005; Lützhöft, Dahlgren, Kircher, Thorslund, & Gillberg, 2010). Recently, Short et al. (2015) reviewed the existing literature on split work-rest schedules to identify which type (i.e., 4-h on/8-h off, 8-h on/8-h off, or 6-h on/6-h off) best reduces fatigue and promotes sleep (Figure 1-1, p.10). They hypothesised that shift schedules in which (i) a greater proportion of work time coincides with the minimum of the core body temperature rhythm, i.e., the sleepest phase of the circadian pacemaker (section 1.3.2.3.2, p.43); (ii) a greater proportion of sleep opportunities occur during the wake maintenance zone (WMZ); and (iii) there is a high work-to-rest ratio, would be associated with greater sleepiness and poorer sleep (Figure 1-1, p.10). Consistent with these predictions, of the three split work-rest schedules Short et al. (2015) examined, 4-h on/8-h off

rosters were associated with better quality sleep and less sleepiness than the others. Shiftworkers on 4-h on/8-h off rosters obtained about 1 h more sleep each night than those on 6-h on/6-h off rosters and 1.3 h more sleep than those on 8-h on/8-h off rosters. However, the analyses indicated the proportion of sleep opportunities coinciding with the WMZ was not a significant contributing factor in these results. Overall, the literature regarding split work-rest schedules suggests that rosters which entail smaller proportions of work time around the body clock minimum and a lower work-to-rest ratio are preferable from a sleep and sleepiness perspective (Short et al., 2015).



**Figure 1-1** Diagram of rosters in three different split work-rest schedules, classified as 4-h on/8-h off, 8-h on/8-h off, and 6-h on/6-h off. In the upper panel, each row on the y-axis represents the roster of a separate crew member on the schedule. The x-axis depicts time of day. Black boxes indicate rest periods, and white boxes indicate work. The lower panel depicts the circadian fluctuation in subjective sleepiness ratings (Ratings), Multiple Sleep Latency Test time to fall asleep (MSLT) and core body temperature (data from Gradisar & Lack, 2004). The circadian low point (nadir) and Wake Maintenance Zone (WMZ) are overlayed across the panels in grey. [Figure and legend adapted from Short et al. (2015)].

According to Dembe, Erickson, Delbos, and Banks (2006), data from the National Longitudinal Survey of Youth, comprising over 110,000 job records, indicate nonstandard shift schedules have a higher risk for occupational injuries compared to traditional day shifts – except split-shifts, which do not present a higher risk. As such, although split work-rest schedules in non-remote operations may be more disruptive to shiftworkers' social/familial obligations than traditional schedules (Bohle et al., 2004), it is conceivable they could at least be effective for short-term emergency responses. However, there are currently no studies that directly compare split and consolidated work-rest shift schedules in terms of sleep, sleepiness, and performance at different times of day, so it is not known to what extent a split work-rest schedule might be advantageous.

#### 1.1.4. Napping and Sleep Timing Strategies

Split work-rest schedules theoretically have the capacity to reduce fatigue by permitting frequent sleep opportunities and minimising circadian misalignment. However, since most industries do not utilise these schedules, shiftworkers implement other strategies and countermeasures to sustain alertness at work. There are two primary approaches that shiftworkers employ (Bonnefond, Tassi, Roge, & Muzet, 2004; Rosekind et al., 1995). The first consists of techniques that arouse alertness – such as exposure to stimulating environmental conditions (e.g., bright light, temperature) or consuming natural (e.g., caffeine) and or pharmacological (e.g., modafinil) substances (Bonnefond et al., 2004). The second approach regards strategies that increase opportunities for sleep, rest and recovery at home or in the workplace. While the former approach can be effective at promoting alertness, it is this latter, second approach that will be the focus of this dissertation.

##### *1.1.4.1. Napping*

Naps are small portions of sleep, obtained at any time of day, variously defined as being at least 25-50% shorter than an individual's habitual night sleep (Dinges, Orne, Whitehouse, & Orne, 1987; Naitoh, 1981). When implemented by shiftworkers, the ability of napping to counter the effects of sleep loss attributed to

their work schedules have been well documented (Dinges, 1989; Rosekind et al., 1995). For some occupations that often involve long shifts – e.g., nurses (Fallis, McMillan, & Edwards, 2011; Takahashi, Arito, & Fukuda, 1999), airline pilots (Roach, Darwent, Sletten, & Dawson, 2011), and security guards (Matsumoto & Morita, 1987), napping on shift when the workload permits is very common. In these situations, napping has a compensatory function alleviating the fatigue accumulated over the course of the shift. Where naps are not possible during the shift, they are often implemented ‘prophylactically’ before work. Usually employed before night shifts, the function of these naps is to prepare for sleep loss and mitigate the extent of fatigue (Bonnetfond et al., 2004).

Although naps are often beneficial, their implementation can result in ‘sleep inertia’, described as ‘the brief period of reduced alertness and impaired cognitive performance experienced immediately after waking’ (Hilditch, Centofanti, Dorrian, & Banks, 2016; Tassi & Muzet, 2000). In the context of shiftwork this phenomenon can be problematic, especially where high levels of functioning are paramount soon after waking. However, since the main factors that influence the intensity of sleep inertia are known (i.e., sleep length, sleep quality, and sleep stage upon waking), it can be mitigated or taken into account (Bonnetfond et al., 2004; Tassi & Muzet, 2000). Sleep inertia is worst following long episodes of deep sleep, so one technique for reducing its side effects is to ensure that naps are brief, no more than 20-30 min (Hilditch et al., 2016).

#### *1.1.4.2. Sleep timing strategies*

The timing of sleep episodes is another avenue through which shiftworkers can strategically maximise sleep duration to counter the effects of fatigue (Åkerstedt, 1998; Tepas, 1982). The precise arrangement and timing of sleep in relation to surrounding shifts often depends on the time of day (Knauth et al., 1980; Roach, Dawson, Reid, Darwent, & Sargent, 2016). Most workers, regardless of shift type, obtain a single consolidated episode of sleep. In the case of conventional daytime shifts commencing in the morning, workers generally delay sleep for several hours after arriving home so that it occurs during the night (Roach et al., 2016; Tepas, 1982). This timing has the advantage of aligning the sleep-wake cycle with the

biological predisposition of the body clock, allowing workers to commence their subsequent day shift, refreshed, shortly after waking. In contrast to day workers, shiftworkers on afternoon/evening schedules tend to maximise the amount of sleep they obtain by sleeping immediately after work. As with the day workers employing the “delayed sleep strategy”, the use of the “immediate sleep strategy” by afternoon/evening workers facilitates the alignment of sleep at night (Tepas, 1982).

The best strategy for arranging sleep during the day, between night shifts is less clear. Though many night workers tend to sleep in the morning, immediately after their shift (Knauth et al., 1980; Roach et al., 2016), this approach is likely chosen for the instant relief it provides, rather than being an optimal time for sleep quality or duration. A delayed sleep strategy is not necessarily better, because sleep in the late afternoon or evening coincides with the wake maintenance zone. This ambiguity regarding the best daytime sleep strategy is exemplified in a recent field study by Roach et al. (2016), who monitored the sleep patterns of 253 locomotive engineers across 16-h breaks beginning at different times of day. They found that when the 16-h breaks from work encompassed an entire night, participants obtained a single episode of sleep on 80-93% of occasions, aligned with the night. However, when breaks occurred predominantly during the day, participants obtained more than one sleep episode on 41–50% of occasions (Roach et al., 2016). This “split sleep strategy” appears to be an attempt by some night workers to derive some of the benefits of the other sleep timing strategies – i.e., immediate relief and reduced prior wakefulness upon commencing the subsequent shift. However, it is also possible that splitting sleep during the day may reduce both its recuperative value and its ability to mitigate fatigue during the night.

#### 1.1.5. Summary

Shiftwork is a critical component of the functioning of modern global societies and yet its effects on worker fatigue have serious consequences for health and safety, especially in the case of night work. The cause of fatigue in shiftworkers can primarily be attributed to two factors – circadian rhythms and sleep disruption –

because, unlike traditional daytime schedules, shiftwork often entails working when the body clock promotes sleep and sleeping when the body clock promotes activity. These constraints mean that when shiftworkers do sleep, it is frequently too short and of poor quality (Kogi, 1982). One approach to mitigating fatigue while still providing 24-h coverage of operations is to split shiftwork rosters into multiple shorter shift per day. Such schedules minimise circadian misalignment, facilitate frequent breaks, and ensure all workers obtain at least some sleep opportunities at night. More research is required to understand how the mechanisms involved in sleep, sleepiness and performance operate during short work-rest schedules.

For shiftworkers who are not able to obtain much or any sleep during the night, alternative countermeasures and strategies are required to maintain alertness at work. Aside, from medication, light therapy and caffeinated stimulants, many shiftworkers mitigate fatigue by napping before or during work. Night workers employ various arrangements of daytime sleep in an attempt to strategically maximise sleep duration and optimise performance (Åkerstedt, 1998; Knauth & Rutenfranz, 1981). Some choose to (i) have a single sleep in the morning immediately after work, (ii) others delay sleep until several hours after work in a manner similar to day workers, and (iii) others split their sleep episodes, obtaining some sleep in the morning and some in the evening. All these sleep strategies have advantages and disadvantages, but their effectiveness at sustaining performance has yet to be systematically evaluated.



## 1.2. Circadian Rhythms

Rhythms defined as regularly occurring sequences of events or processes can be observed everywhere in the natural world, living and non-living. They are evident in the seasonal variations in weather across the year, in the lunar-dependent fluctuations of ocean tides, and the alternation of day and night. Rhythmicity is similarly prevalent in living organisms. In plant-life it is manifest in seasonal successions of dormancy and growth, in the daily opening and closing of flowers and movement of leaves, and in the process of photosynthesis (Dodd et al., 2005; McClung, 2006). In animals, rhythmicity can be observed in, among many examples, the annual migrations of numerous species responding to changes in climate and food availability (Gwinner, 1986); the lunar- and tidal-phase dependent behaviours of marine animals (Naylor, 1999; Robertson, Petersen, & Brawn, 1990); and the regular alternation of sleep and wake, rest and activity (Aschoff, 1965; Dijk & Czeisler, 1995; Freedman et al., 1999; Siegel, 2008). Perhaps the most prominent and influential rhythms in the day-to-day functioning of life on earth are those biological processes that oscillate with the 24-h day/night cycle.

Among the earliest historical accounts of biological day-night cycles were by Androstenes, an admiral serving in the 4<sup>th</sup> century campaign of Alexander the Great, who described leaf movements of the tamarind tree (Bretzl, 1903). He noted that the orientation of leaves on the tree changed across the day, rising with the sun in the morning and lowering again at night (Bretzl, 1903). For more than a millennium, rhythmic phenomena such as this were thought to be passive responses to environmental stimuli (i.e., sunlight). However, this was challenged when French scientist De Mairan (1729) observed that the opening and closing leaf cycles of the *Mimosa pudica* plant, a heliotrope (from the Greek, *helios* meaning 'sun', and *trepein* meaning 'turn' or 'bend'), persisted even when sunlight was deprived. In finding that this cyclical behaviour continued in constant darkness, de Mairan showed that the rhythms were being generated endogenously. Later experimentation revealed that the rhythms of the *Mimosa pudica* had cycles shorter than 24 h in constant lighting and that these cycles could be inverted by manipulating the order of light-dark exposure (De Candolle, 1832). The results supported the idea that the rhythms were regulated by an independent central

pacemaker or “master clock” which approximates a 24-h rhythm but can be entrained to the day-night cycle via the input of photic stimuli from the sun.

Self-sustaining biological rhythms that oscillate at periods of approximately 24 h in the absence of time cues and synchronise with the local day-night cycle are termed circadian rhythms (from the Latin *circa* meaning ‘about’, and *dies* meaning ‘day’) (Halberg, 1959). Since the early observations of circadian rhythms in plant life, hundreds more rhythms have been observed in the biological processes of all living organisms, including animals, fungi, and bacteria (Aschoff, 1965; Golden, 2003). Circadian rhythms in animals can be seen everywhere from the regulation of body temperature and sleep propensity to the secretion of hormones, heart rate, neuronal activity, and cell metabolism (Frank et al., 2013; Ishida et al., 2005; Mancia et al., 1983; Moore-Ede, Sulzman, & Fuller, 1982; Refinetti & Menaker, 1992). These rhythms are so engrained in biology processes that any disruption, such as sleeping during the day and staying awake at night, can have negative consequences for health, well-being and performance (Costa, 1996; Mistlberger, 2005; Stevens, 2016; Zhou et al., 2011).

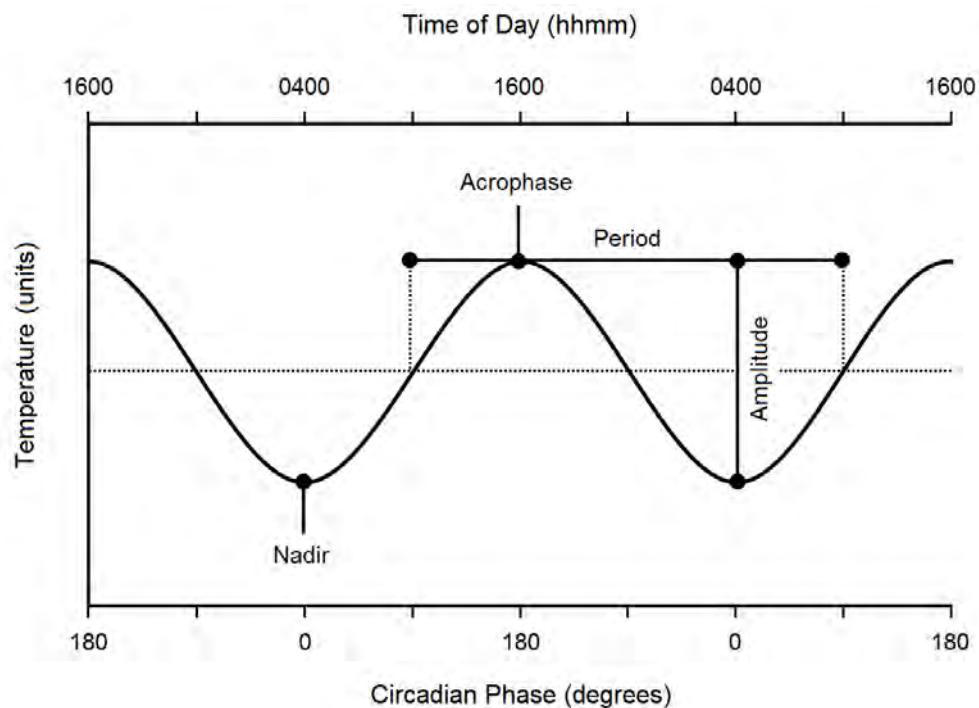
### 1.2.1. Terminology and Properties of Circadian Rhythms

#### 1.2.1.1. *Phases, periods, amplitudes*

Circadian rhythms are described in terms of their recurring variations in physiological or behavioural processes or states. Using several aforementioned rhythms as examples, such descriptions could reference rising and falling temperatures, increasing and decreasing hormone concentrations, or the times of alternating stages of sleep and wake (Darwent, Zhou, van den Heuvel, Sargent, & Roach, 2011). When describing a rhythm, a ‘phase’ refers to the time of any point of the curve in the cycle (Figure 1-2, p.17). The most frequently cited phases of a circadian rhythm are the “nadir”, which denotes the time of the minimum value on the curve, and the “acrophase”, which denotes the time of the maximum value (Figure 1-2). Circadian phases are usually mentioned in terms of the degrees on a cosine wave fitted to raw data but are sometimes referenced in terms of corresponding clock times when synchronised to the 24-h day. More broadly,

phases that are normally aligned with the environmental day are described as the 'biological day', while those normally aligned with the environmental night are described as the 'biological night'.

The 'period' of a rhythm, often denoted by the symbol  $\tau$  (tau), is the time elapsed to complete a single cycle of the wave, i.e., the time between two identical phases. For any circadian rhythm not entrained to the day/night cycle, this duration is approximately, but not precisely, 24 h (Czeisler et al., 1999). The 'amplitude' of a rhythm is the distance between the value at the acrophase and the value at the nadir (Figure 1-2, below) (Lee-Chiong, 2008).



**Figure 1-2** Cosine wave approximating the fitted circadian rhythm of core body temperature. Nadir and acrophase are defined as the minimum and maximum points of the curve, respectively. Amplitude is defined as the value from peak to trough. Period ( $\tau$ ) represents the duration between two identical phases, i.e., a single oscillation. This figure depicts two 24-h oscillations.

#### 1.2.1.2. Zeitgebers, phase shifting and entrainment

In the field of chronobiology, 'zeitgebers' (German: 'time givers') are environmental and behavioural time cues that influence the circadian pacemaker and associated rhythms (Aschoff, 1965). Specifically, a zeitgeber refers to any

stimulus or agent that is capable of: (i) inducing a 'phase shift' – i.e., displacing a rhythm such that phase markers are advanced (earlier) or delayed (later) relative to a reference time; or (ii) inducing entrainment – i.e., synchronising the period of a rhythm to the period of the zeitgeber to form a stable phase relationship (Duffy & Wright, 2005; Refinetti, 2005). Zeitgebers are primarily, but not exclusively, composed of photic stimuli and the preeminent example is light emitted during the 24-h day/night cycle (Armstrong, Cassone, Chesworth, Redman, & Short, 1986; Boivin & James, 2002; Duffy, Kronauer, & Czeisler, 1996; Klerman et al., 1998; Wever, Polášek, & Wildgruber, 1983). The effectiveness of light as a phase shifting and entraining agent depends on its intensity and duration. Dim light (<50 lux) has a significantly lower phase shifting capacity than indoor light (100 – 300 lux) or bright light (7000-12,000 lux) (Lockley, 2009). Minors, Waterhouse, and Wirz-Justice (1991) established a phase response curve (PRC) that describes the direction in which light induces a phase shift as a function of the circadian phase of exposure. According to this PRC, light in the evening, prior to the temperature nadir, delays the rhythm, while light in the morning, after the temperature nadir, advances it.

Several non-photoc zeitgebers have been observed influencing circadian rhythms, but their effects are weaker than those of light (Mistlberger & Skene, 2004). These zeitgebers include the timing of sleep and wake (Minors & Waterhouse, 1983; Wright, Hughes, Kronauer, Dijk, & Czeisler, 2001), exercise and physical activity (Baehr et al., 2003; Eastman, Hoese, Youngstedt, & Liu, 1995) and food consumption (Krauchi, Cajochen, Werth, & Wirz-Justice, 2002).

### 1.2.2. The Suprachiasmatic Nucleus is the Circadian Pacemaker

Observations of endogenous circadian rhythms allude to the existence of an underlying central pacemaker which manages and synchronises their responses to changing environmental zeitgebers. Since circadian rhythms can be entrained to the day/night cycle via photic stimuli, it was speculated that a master clock might be located in the brain, closely connected to light receptors in the retina (Hendrickson, Wagoner, & Cowan, 1972). This speculation was not without

foundation, given that the hypothalamus was known to be associated with the rhythmicity of sleep since the early 20<sup>th</sup> century (Nauta, 1993). Support for an anatomical pacemaker was reinforced with the discovery of the retinohypothalamic tract, a photic neural input pathway linking the retina to the suprachiasmatic nucleus (SCN) of the anterior hypothalamus (Hendrickson et al., 1972). Further studies with rodents experimentally confirmed that the SCN is necessary for endogenous rhythmicity and the most likely location of master circadian pacemaker (Eastman, Mistlberger, & Rechtschaffen, 1984; Moore & Eichler, 1972; Nauta, 1993; Stephan & Zucker, 1972). In these experiments, lesioning the SCN was found to severely disrupt numerous behavioural and physiological circadian rhythms, including those of drinking, sleeping, body temperature, and the production of adrenal corticosterone (Eastman et al., 1984; Moore & Eichler, 1972; Stephan & Zucker, 1972). Similarly, transplantation of healthy foetal hypothalamic tissue into rodents whose SCNs were removed was found to restore circadian rhythmicity (Drucker-Colin, Aguilar-Roblero, Garcia-Hernandez, Fernandez-Cancino, & Bermudez Rattoni, 1984). Though lesions have not been created experimentally in the human SCN, clinical case studies involving patients with a damaged hypothalamus have documented similar circadian disruptions, including the emergence of sleep disorders (Cohen & Albers, 1991). These indicate that the SCN is also the location of the master circadian pacemaker in humans.

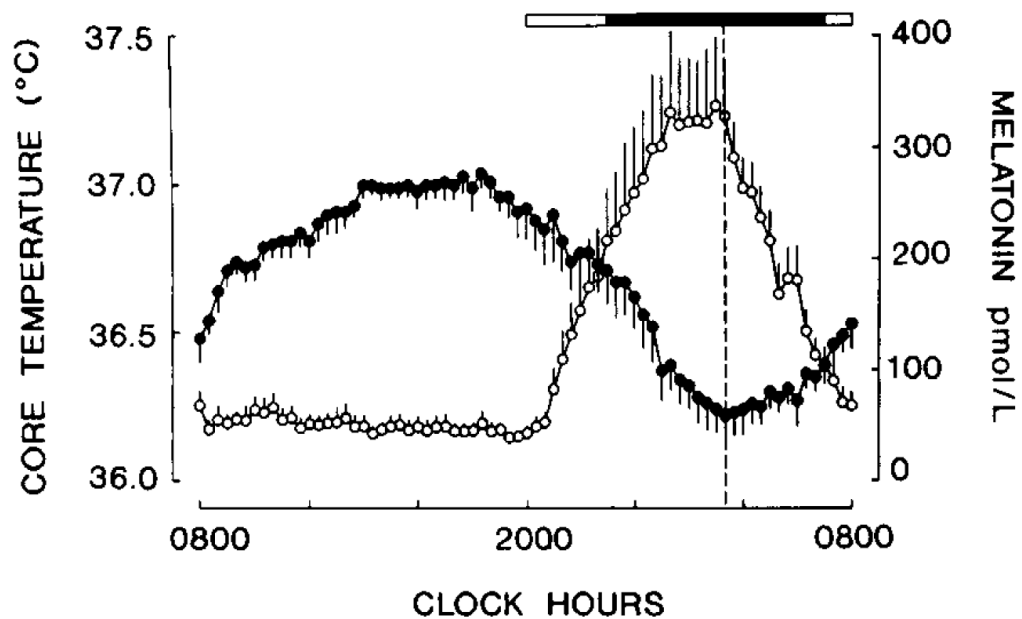
#### *1.2.2.1. Measurement of the Circadian Pacemaker*

As the endogenous pacemaker is responsible for coordinating circadian rhythms, knowing the 'circadian time' is important for determining how well it has adapted to the local environment and predicting how biological processes will progress. However, while its location within the brain is known, it is difficult to directly measure the behaviour of the circadian timing system at any given time (Hanneman, 2001; Monk, 1991). Therefore, the temporal status of the pacemaker is surmised from proxies, reliable marker rhythms which are sensitive to circadian changes and can be induced to shift and adjust accordingly (Minors, Folkard, & Waterhouse, 1996; Monk, 1991). Such rhythms include those of the hormone

melatonin, produced by the pineal gland, and core body temperature (Benloucif et al., 2005; Hanneman, 2001). Melatonin, secreted in response to sympathetic stimulation by the SCN, is thought to be the means by which the SCN regulates rhythms such as core body temperature and sleep propensity (Cajochen, Kräuchi, & Wirz-Justice, 2003; Dawson, Gibbon, & Singh, 1996; Gilbert, van den Heuvel, & Dawson, 1999; Krauchi, Cajochen, Pache, Flammer, & Wirz-Justice, 2006).

The rhythm of circulating melatonin concentrations is characterised by a predictable square-waveform (Cagnacci, Elliott, & Yen, 1992; Dawson & Encel, 1993; Lewy & Sack, 1989). Maintained at constant low concentrations during daylight, it rapidly rises in the late evening and then falls before dawn about 8-10 h later (Figure 1-3, p.21) (Cagnacci et al., 1992). The times at which melatonin concentrations increase and return to baseline levels are useful phase markers of the rhythm and are described as the hormone's respective 'onset' and 'offset'.

In contrast to melatonin, the circadian rhythm of body temperature resembles a sinusoidal wave, increasing during the day to an evening peak and falling during the night to an early morning trough around 0400 h (Cagnacci et al., 1992) (Figure 1-3). Though each of the rhythms produces a different waveform, key phases are closely related. Specifically, the onset and offset of melatonin secretion both occur contemporaneously with the respective falling and rising limbs of temperature, and the peak in melatonin coincides with the body temperature nadir (Cagnacci et al., 1992) (Figure 1-3). This inverse relationship between the rhythms of melatonin and temperature is not simply correlational, given that melatonin is known to have a role in thermoregulation (Cagnacci et al., 1992).



**Figure 1-3** Time course and 24-h patterns of mean ( $\pm$  SE) serum melatonin levels ( $\circ$ ) and body temperature values ( $\bullet$ ) in 12 early follicular phase women. Duration of nocturnal melatonin secretion ( $\square$ ); sleep time ( $\blacksquare$ ). The timing of the onset and offset of melatonin secretion and the decline and rise of body temperature are closely correlated. [Figure reproduced and legend adapted from Cagnacci et al. (1992)].

Body temperature is commonly used as the proxy of the circadian pacemaker for several reasons (Minors et al., 1996). First, compared to melatonin, it is simpler and more practical for continuous long-term measurement – usually by means of a rectal thermistor or an orally ingested monitoring capsule (Darwent et al., 2011; Minors et al., 1996). The rhythm of melatonin, in contrast, is usually derived from multiple discrete samples of blood, saliva, or urine collected at regular intervals (Benloucif et al., 2008). Second, unlike melatonin which remains flat for the majority of the circadian cycle and is suppressed by light, body temperature is sensitive to variation at every phase. Although the temperature rhythm can be masked by activity patterns, its intrinsic sinusoidal oscillation is closely associated with other circadian rhythms which dominate the field of chronobiology, such as sleep propensity, alertness, fatigue, and performance (Johnson et al., 1992; Lavie, 1986). Thus, phase shifting or adjustment of temperature in response to time cues can predict corresponding shifts on other measures.

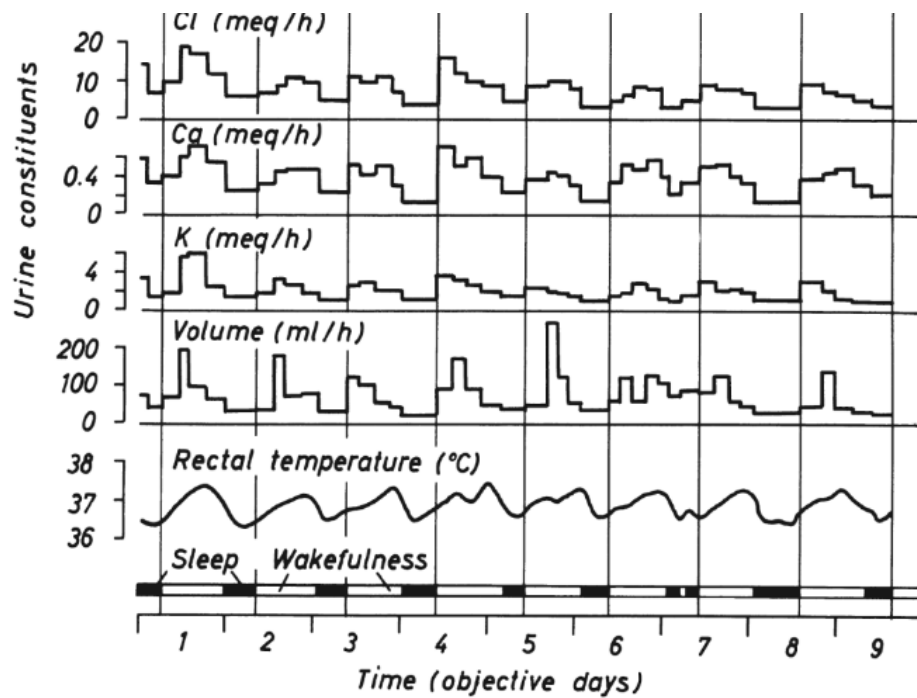
### 1.2.3. Protocols Employed in the Study of Human Circadian Rhythms

The human circadian pacemaker is usually entrained to a 24-h period such that the biological day and biological night remain in stable phase alignment with the light and dark periods of the day/night cycle. With circadian and social determinants of sleep and wake times restricting the phases at which the pacemaker is exposed to environmental and behavioural zeitgebers, this entrainment is self-reinforcing. As a result, extricating endogenous rhythms from accompanying confounding social, behavioural and environmental influences to determine intrinsic properties of the pacemaker, such as its period, is difficult. Therefore, knowledge of the human circadian pacemaker gained over the last century has been derived using various protocols that attempt to control and minimise the influence of different external factors.

#### *1.2.3.1. Free-running rhythms in time-free environments*

Following observations of 'free-running' plant and animal rhythms in constant darkness, scientists in the 20<sup>th</sup> century initially attempted to investigate human circadian rhythms in environments similarly free of zeitgebers. First conducted in a converted German World War II bunker (Aschoff & Wever, 1962) and then in caves (Siffre, 1963) and specially built laboratories (Mills, Minors, & Waterhouse, 1974), participants in free-run studies were shielded from environmental time cues – e.g., sunlight, and external sound and temperature – for several weeks or months. These studies were completed alone with no social interaction and artificial time cues such as clocks and radio were also not permitted. Participants were allowed to self-select when they slept and ate, and thus were given control over internal lighting. In these free-running conditions, experimenters observed that rhythms – such as those of body temperature, rest/activity, and urinary hormones and electrolytes – continued to oscillate but at periods significantly different from 24 h, instead averaging ~25 h (Aschoff & Wever, 1962; Siffre, 1963; Wever, 1979) (Figure 1-4, p.23).





**Figure 1-4** First experiment showing free running circadian rhythms under conditions of time isolation. Time is indicated along the x-axis in 24-h units (days), with the rest/activity cycle depicted by black ('sleep') and white ('wakefulness') boxes. From top to bottom, the figure presents the course of changes in urinary excretions of chloride, calcium, potassium and volume, followed by rectal temperature. [Figure and legend adapted from Aschoff and Wever (1962)].

Results from these early free-run protocols demonstrated conclusively that human circadian rhythms oscillate independently of zeitgebers. However, these initial assessments overestimated the true period of the circadian pacemaker later determined to have an average period closer to 24 h (Czeisler et al., 1999). This discrepancy most likely transpired because researchers were not then cognisant of the pacemaker's sensitivity to the phase-shifting properties of light, even at levels much lower than sunlight (Klerman, Dijk, Kronauer, & Czeisler, 1996; Middleton, Arendt, & Stone, 1996). In providing access to normal indoor lighting, rhythms were inadvertently made susceptible to the influence of light/dark cycles governed by participants' self-selected sleep times. Since sleep (and thus darkness) in this environment is usually initiated near the nadir of the temperature rhythm, not uniformly across the circadian cycle (Figure 1-4), exposure to light during wakefulness was generally limited to phases of the pacemaker that induce rhythms

to delay. Such delays would explain why the intrinsic oscillating period was able to extend to 25 h (Klerman et al., 1996; Middleton et al., 1996).

Though they eliminated environmental zeitgebers, free-run protocols were also limited in that they did not account for the numerous periodic extraneous behavioural factors to which circadian rhythms are also dependent (Duffy & Dijk, 2002). These factors, such as sleep, physical activity and food consumption can mask endogenous rhythms such that it is difficult to disentangle the pacemaker's precise contribution. An example of this is the body temperature rhythm. While regulated by the circadian pacemaker, body temperature is also moderated by behaviours such as sleep and physical activity (Barrett, Lack, & Morris, 1993; Gander, Connell, & Graeber, 1986; Krauchi & Wirz-Justice, 1994). Sleep and physical activity mask the endogenous rhythm by decreasing and increasing temperature, respectively (Gander et al., 1986; Krauchi & Wirz-Justice, 1994; Minors et al., 1996). Since the resultant waveform of the temperature rhythm is affected by these factors, its amplitude, period and phase markers cannot be solely attributed to the pacemaker. As such, later protocols incorporating a constant routine and/or forced desynchrony paradigm were developed to minimise the phase-shifting and masking factors associated with free-run (Minors & Waterhouse, 1984).

#### *1.2.3.2. De-masking rhythms using the constant routine protocol*

The constant routine protocol was developed to unmask the endogenous component of circadian rhythms from periodic influences both in the external environment and in behaviour (Minors & Waterhouse, 1984). Therefore, participants in this protocol are subject to consistent and unvarying environmental and behavioural conditions (Duffy & Dijk, 2002). Participants are required to remain sedentary, usually recumbent in bed in a supine position, and go without sleep for a minimum of 24 h. In this time, ambient lighting and room temperature are maintained at constant levels, and food is provided at regular intervals in identical portion-controlled sizes. Since all these factors are controlled, the waveforms of overt rhythms more closely reflect the true influence of the pacemaker (Lack & Lushington, 1996; Monk et al., 1997).

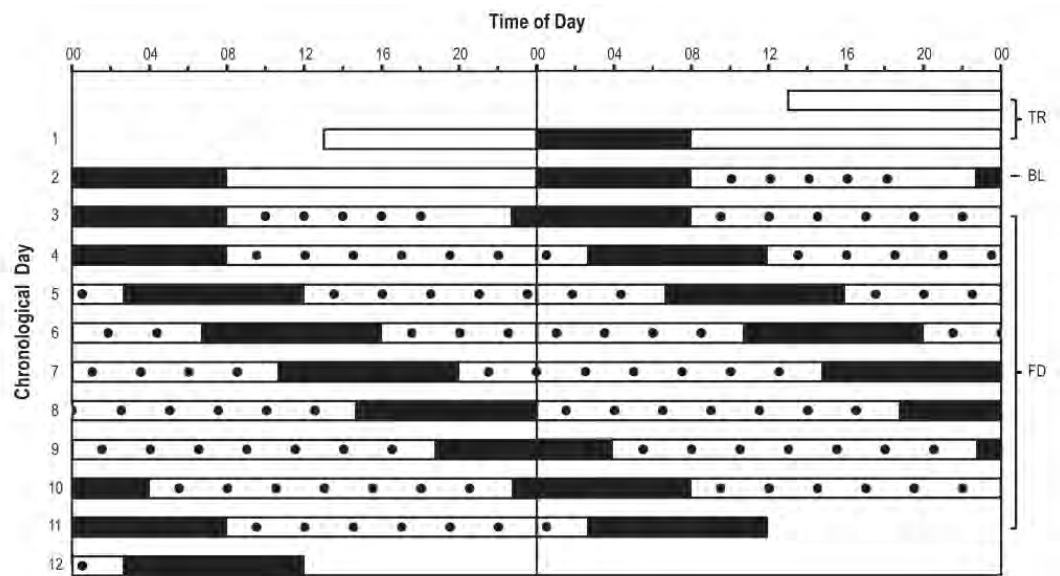
However, though this method is useful for determining the phases and amplitudes for various circadian rhythms, it is not always the most appropriate method for understanding the contribution of the pacemaker. In its strictest implementation, the constant routine involves sleep deprivation for at least 24 h, sometimes multiple days. These durations can be problematic when investigating circadian rhythms in variables which are known to be affected by time awake, such as alertness, performance, behaviour, and mood (Duffy & Dijk, 2002). In situations of prolonged wakefulness, circadian variations in these variables can be observed but are masked by monotonic decline (Brendel et al., 1990; Froberg, 1977; Johnson et al., 1992; Lack & Lushington, 1996).

#### *1.2.3.3. Controlling sleep-wake confounders by means of forced desynchrony*

Issues regarding the effect of prolonged wakefulness in the constant routine (described above) and the masking of endogenous rhythms during free-run are avoided and controlled for in the forced desynchrony (FD) protocol. Inspired by early cave studies conducted by Kleitman and Richardson (Kleitman, 1963), the FD protocol imposes a constant sleep-wake cycle (bed-to-wake ratio = 1:2) with a period outside the range of entrainment (typically,  $\tau \geq 28$  h or  $\tau \leq 20$  h) in dim light conditions, thus allowing the pacemaker to run at its intrinsic period (Czeisler et al., 1999; Dijk, Duffy, & Czeisler, 1992; Dijk, Duffy, Riel, Shanahan, & Czeisler, 1999; Wyatt, Ritz-De Cecco, Czeisler, & Dijk, 1999) (Figure 1-5, p.26). By scheduling sleep and wake in this manner, sleep need is accommodated and the pacemaker is exposed to the exogenous masking variables associated with sleep-wake behaviour evenly and systematically across the entire cycle. In this way, Czeisler et al. (1999) were able to control for masking and deduce from multiple physiological rhythms more accurately that the mean period of the circadian pacemaker is  $\sim 24.18$  h.

Since each successive 28-h (or 20-h) sleep-wake cycle in the FD protocol is offset 4 h later (or earlier) in time and initiated at different phases of the pacemaker, sleep- and circadian-dependent factors involved in any variable of interest may be uncoupled mathematically by folding data at the period of the sleep-wake cycle or at the period of the endogenous temperature rhythm (Dijk et al., 1992; Hiddinga, Beersma, & Van den Hoofdakker, 1997; Waterhouse et al., 2000). By uncoupling

sleep- and circadian-dependent factors in this way, variables of interest may be assessed at different times into the sleep-wake cycle independent of circadian phase and at different phases of the circadian pacemaker independent of sleep or wake. The use of FD in the assessment of neurobehavioural performance is discussed in section 1.4.3, p.60.



**Figure 1-5** Double raster plot of a 28-h day forced desynchrony (FD) protocol. White blocks represent scheduled wake periods, black blocks represent scheduled bed periods, and black dots represent scheduled performance testing sessions. After 2 training (TR) days and a baseline (BL) day, participants were scheduled to 7 x 28-h FD cycles comprising 9.3 h of time in bed. [Figure reproduced and legend adapted from Zhou et al. (2011)].

#### 1.2.4. Summary: The Circadian System in the Context of Shiftwork

Both transmeridian (across time zone) travel and night work are disruptive to the circadian pacemaker because they shift zeitgebers and circadian rhythms out of alignment. In the case of travel, zeitgebers at the destination are phase-shifted relative to the circadian pacemaker on departure; in the case of night work, zeitgebers exposed to at night are phase-shifted relative to the circadian pacemaker entrained for daytime activation. This desynchrony commonly manifests itself in general feelings of malaise colloquially known as “social jetlag” (Comperatore & Krueger, 1990; Wittmann, Dinich, Mellow, & Roenneberg, 2006). However, while the consequences of desynchrony following travel ameliorate with the gradual entrainment to the new time zone, consequences for night work are persistent. This is because night work by definition requires activity at times in opposition to environmental zeitgebers.

Multiple approaches to cope with circadian desynchrony and realign the pacemaker for night work may be implemented if desired (Arendt, 2010; Burgess, Sharkey, & Eastman, 2002). Since light can cause circadian rhythms to advance or delay depending on the phase of exposure (Minors et al., 1991), circadian misalignment may be minimised with a combination of strategic exposure and strategic avoidance of bright light at certain times of day (Boivin & James, 2002; Czeisler & Dijk, 1995). Indeed, Boivin and James (2002) found that shielding outdoor light in the morning with goggles and increasing exposure to bright light during the night could delay the melatonin rhythm of night workers, over several shifts, by 10 h. Other strategies for circadian adaptation to night work include oral administration of melatonin in the morning (Burgess et al., 2002) and exercise prior to habitual bedtime (Baehr et al., 2003; Eastman et al., 1995). However, these regimens may be impractical for non-permanent night workers because complete adjustment takes multiple days and requires consistent implementation to maintain. Furthermore, when employees complete stints of night work, realignment to a daytime schedule disrupts their breaks. Thus, for some workers it might be preferable to implement strategies, such as napping or caffeine consumption, that promote alertness over entrainment.

### 1.3. Sleep and Wakefulness

Many definitions of sleep have been formulated over the years. Dement and Carskadon (2011), pioneers in the field of sleep medicine, define it in the following way:

*“Sleep is a reversible behavioural state of perceptual disengagement from, and unresponsiveness to, the environment. [...] sleep is a complex amalgam of physiologic and behavioural processes. Sleep is typically (but not necessarily) accompanied by postural recumbence, behavioural quiescence, closed eyes, and all the other indicators one commonly associates with sleeping.”*  
(2011, p.16)

Similarly, The Encyclopedia of Neuroscience (2009, p.3707), describes “sleep” as “a state of rest in animals that is characterized by behavioural quiescence and decreased responsiveness to environmental stimuli”, and adds that its timing is controlled by an animal's internal biological clock such that it generally occurs at night for diurnal species and during the day for nocturnal species. Humans typically sleep for about 7 to 8 h each night (Carskadon & Dement, 2011) but this is not the same for all animals and the required amount, frequency, and timing of sleep varies from species to species (Campbell & Tobler, 1984; Siegel, 2008, 2009).

Until the advent of electroencephalography (EEG), where spontaneous electrical activity in the brain is monitored with electrodes, sleep was understood solely in terms of its behavioural characteristics (Berger, 1929; Loomis, Harvey, & Hobart, 1935, 1937). In their pioneering research, Loomis et al. (1935, 1937) were able to counter the prevailing view that sleep is a passive state. They found that neuronal activity during sleep produces waveforms in the EEG output that are different from those produced during wake. Additionally, Loomis et al. (1937) found that rhythms of activity during sleep vary systematically in accordance with its depth, indicating that sleep is not a homogenous physiological state but an active state composed of several different stages. Later findings of eye movement and changes in muscle

tone corresponding with specific patterns of neuronal activity corroborated this assessment (Aserinsky & Kleitman, 1953; Dement & Kleitman, 1957a).

Given that sleep is behaviourally characterised by a lack of volitional muscular control and diminished awareness of, and capacity to respond to, external stimuli (Carskadon & Dement, 2011; Cirelli & Tononi, 2008), it leaves animals vulnerable to attack by potential predators. In normal cases, sleep also inhibits other behaviours required for survival and evolution such as eating, drinking, and procreation. As such, according to Rechtschaffen (1971, p.88), *“if sleep does not serve an absolute vital function, then it is the biggest mistake the evolutionary process ever made”*. However, while theories regarding its evolutionary function are many, running the gamut from facilitating survival and energy conservation (Siegel, 2005, 2009) to improving brain plasticity and memory consolidation (Frank, 2006; Krueger, Frank, Wisor, & Roy, 2016), a conclusive explanation has remained elusive. Indeed, despite much research demonstrating the negative consequences of sleep deprivation for health, cognition and performance (Buxton et al., 2012; Lim & Dinges, 2010; Spiegel, Tasali, Penev, & Van Cauter, 2004; Williamson & Feyer, 2000; Zhou et al., 2011), Dement has stated that “The only reason we need to sleep that is really, really solid is because we get sleepy” (Max, 2010).

### 1.3.1. Measuring Sleep, Sleepiness and Alertness

#### 1.3.1.1. Sleep stages and sleep architecture

Sleep is comprised of multiple different stages which differ in terms of their ease of arousal, their recuperative value, and their propensity for producing dreams (Carskadon & Dement, 2011; Dement & Kleitman, 1957b; Foulkes, 1962). Gold standard sleep monitoring involves polysomnography (PSG), which involves applying electrodes to specific locations on the face and scalp to record electrophysiological activity in the brain (EEG), eye movement (electrooculography; EOG), and muscle tone (electromyography; EMG). This technique allows assessments of sleep/wake stages to be made based on their physiological rather than behavioural manifestations. Sleep/wake states and sleep

stages can be discerned from signals generated at the electrode sites with reference to standardised criteria (Iber, Ancoli-Israel, Chesson, & Quan, 2007; Rechtschaffen & Kales, 1968).

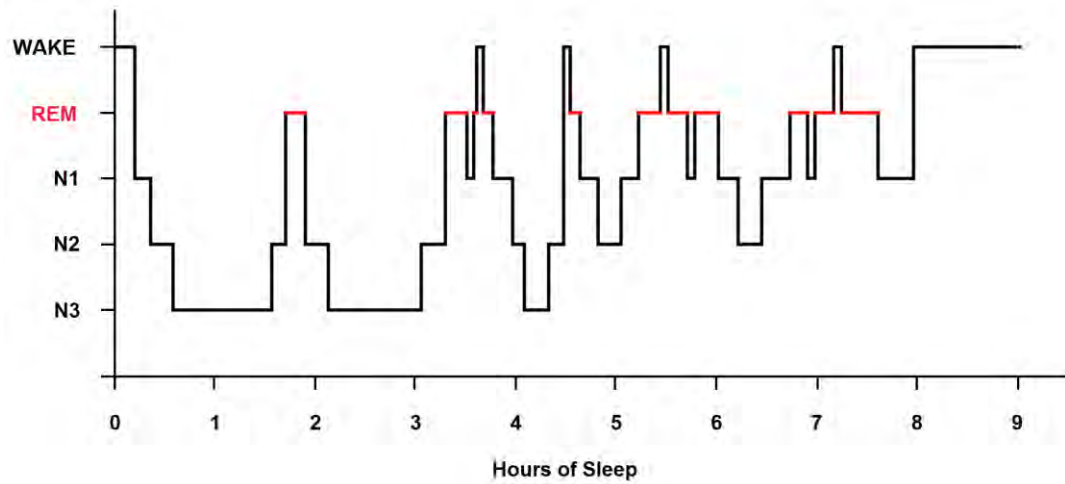
Notwithstanding recent revisions of these criteria by the American Academy of Sleep Medicine (Iber et al., 2007), sleep stages may be categorised as one of two types – that is, rapid eye movement (REM) sleep or non-rapid eye movement (non-REM) sleep (Aserinsky & Kleitman, 1953; Iber et al., 2007; Rechtschaffen & Kales, 1968). REM sleep encompasses a single distinct stage characterised by random movement of the eyes and brain activity that appears similar to wake. Non-REM sleep, in contrast, is not characterised by random eye movement. It is conventionally subdivided into three stages which span a continuum of increasing sleep depth, and are defined by the preponderance of various characteristic waveforms in the EEG (Iber et al., 2007; Siegel, 2011). These stages are named N1, N2 and N3. REM and non-REM stages rotate throughout the sleep episode in approximately 80-120 min cycles (Carskadon & Dement, 2011; Dijk, 2009). While non-REM sleep is more prevalent in the first half of sleep, Stage REM becomes more prevalent in the second half. An example of normal sleep architecture is depicted by the hypnogram in Figure 1-6 (p.32).

Stage N1 is the stage where PSG recordings first meet criteria for sleep and stop meeting criteria for wake (Carskadon & Dement, 2011). As it is the first stage through which people enter sleep, it is the lightest and most easily interrupted (Carskadon & Dement, 2011). Stage N1 sleep is thought to have little or no recuperative value (Wesensten, Balkin, & Belenky, 1999) and lasts for about 5 min if not interrupted before progressing to the deeper Stage N2 sleep (Carskadon & Dement, 2011). Stage N2 is characterised in EEG tracings by the presence of (1) sleep spindles, bursts of oscillating high frequency waves, and (2) K-complexes, short negative peaks immediately followed by a slower positive wave (Carskadon & Dement, 2011) (Figure 1-7, p.33). In the first cycle, this stage usually lasts for 10-25 min but it usually comprises 45-55% of a sleep episode overall (Carskadon & Dement, 2011) (Figure 1-6).

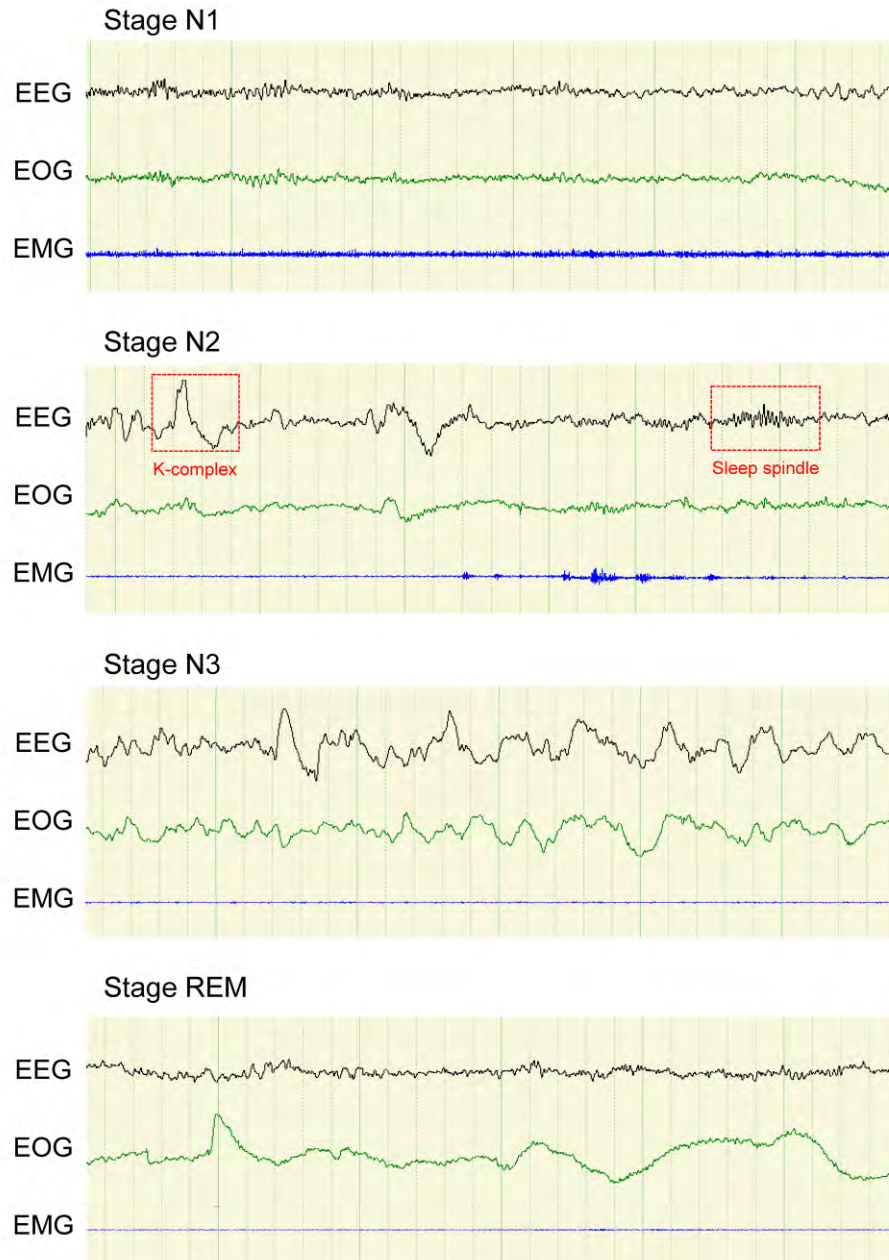


Stage N3 is the deepest stage of sleep and is commonly referred to as slow-wave sleep (SWS) after its distinctive high proportion of low-frequency EEG slow wave activity (SWA) (Blake & Gerard, 1937; Carskadon & Dement, 2011; Iber et al., 2007; Williams, Hammack, Daly, Dement, & Lubin, 1964) (Figure 1-7, p.33). N3 typically dominates the first third of a sleep episode but the precise amount of time spent in this stage is dependent on the duration of the preceding wake period (Borbély, 2001; Carskadon & Dement, 2011; Weitzman, Czeisler, Zimmerman, & Ronda, 1980). Long durations of wakefulness result in a greater proportion of deep N3 sleep during the subsequent sleep period (Dijk, Hayes, & Czeisler, 1993; Feinberg, Fein, & Floyd, 1982; Moses, Johnson, Naitoh, & Lubin, 1975; Weitzman et al., 1980). As the preponderance of N3 sleep declines across the final two-thirds of the night, N2 sleep increases, alternating with greater durations of Stage REM (Carskadon & Dement, 2011).

REM sleep is renowned for its strong association with dreaming and is characterised by sawtooth EEG waves and quick, independent eye movements (Aserinsky & Kleitman, 1953; Dement & Kleitman, 1957b; Foulkes, 1962) (Figure 1-7). Stage REM is also typically accompanied by a loss of muscle tone, resulting in paralysis, putatively to prevent the acting out of dreams (Dement & Kleitman, 1957b; Foulkes, 1962; Siegel, 2011). Unlike SWS, which is influenced by prior wake duration, REM sleep is regulated by the endogenous circadian pacemaker (Czeisler, Zimmerman, Ronda, Moore-Ede, & Weitzman, 1980b). Of the 20-25% of sleep that is REM, a majority occurs in the early morning when sleep propensity is strongest (Czeisler et al., 1980b; Dement & Kleitman, 1957b) (Figure 1-6, p.32).



**Figure 1-6** Hypnogram depicting the architecture of normal adult sleep. The x-axis represents hours into a sleep episode. Wake and sleep stages are represented on the y-axis. Sleep episodes obtained at night are generally structured such that Stage N3 (Slow Wave Sleep) dominates the first third of the episode and REM sleep dominates the final half of the episode, coinciding with the early morning.



**Figure 1-7** Sleep stages as depicted by electroencephalography (EEG), electrooculography (EOG), and electromyography (EMG) tracings. The EEG describes brain activity, the EOG describes eye movement, and the EMG describes muscle tone. Stage N2 is characterised by K-complexes and sleep spindles in the EEG. Stage N3, also known as slow-wave sleep (SWS), is characterised by low-frequency EEG waves with high amplitudes. Stage REM is characterised by sawtooth waves in the EEG, random sharp waves in the EOG, and reduced activity in the EMG.

### 1.3.1.2. Alternatives to polysomnography for sleep monitoring

Traditional PSG requires that trained personnel be on-site to operate and supervise the use of equipment overnight in a laboratory or clinic. However, ambulatory PSG systems also exist which enable sleep monitoring in the home. As these ambulatory systems can retrieve the same electrophysiological data recorded by traditional units, they can be successfully employed to provide detailed information about sleep in comfortable home environments. Despite this advantage, the use of ambulatory PSG systems is expensive and time-consuming because it still requires personnel to correctly place electrodes and manually score the recordings. As such, even ambulatory PSG can be unfeasible in field-based research where continuous direct contact with participants is costly, inappropriate or not possible. In these circumstances, actigraphy, sleep diaries, and other sleep monitoring tools are often employed as alternatives.

Sleep diaries are simple to use and inexpensive, making them suitable for use with a large number of participants. As they require participants to report times in bed and estimates of sleep onset and wake, sleep diaries can provide information about sleep patterns and be used to estimate sleep/wake measures such as sleep onset latency, total sleep time, and wake after sleep onset (Monk, Buysse, Rose, Hall, & Kupfer, 2000). Sleep diaries may also incorporate rating scales of sleep quality or fatigue, which can be interpreted in context of the sleep measures. There has been evidence to suggest that sleep diaries agree well with PSG (Rogers, Caruso, & Aldrich, 1993), but as they require self-report they are *ipso facto* only as reliable as the participant (Carney, Lajos, & Waters, 2004). To increase confidence in self-reported data, sleep diaries are often used, where possible, in conjunction with objective measures such as actigraphy (Carney et al., 2004; Paterson, Dorrian, Clarkson, Darwent, & Ferguson, 2011)

Actigraphy is a method of measuring rest/activity patterns using activity monitors. In the estimation of sleep/wake patterns, this involves the use of wrist-worn devices (Van de Water, Holmes, & Hurley, 2011). Activity monitors contain accelerometers that frequently sample and record movement. The use of actigraphy for sleep measurement is based on the association of sleep with

immobility. Various validated algorithms for sleep-monitoring activity monitors exist and these calculate sleep/wake estimates based on the amount of movement the activity monitors have recorded (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992; Sadeh, Sharkey, & Carskadon, 1994; Van de Water et al., 2011). Periods of high activity are more likely to depict wakefulness and periods of low activity are more likely to depict sleep. Given the difficulty in distinguishing between inactivity resulting from sleep and sedentary wakefulness, there is an acknowledged tendency of activity monitors to overestimate sleep duration. However, their bias has generally been deemed minimal (De Souza et al., 2003; Jean-Louis, Kripke, Mason, Elliott, & Youngstedt, 2001; Paquet, Kawinska, & Carrier, 2007; Reid & Dawson, 1999; Rupp & Balkin, 2011). As with sleep diaries, actigraphy is only able to provide summary measures of sleep/wake, not the detailed sleep-staging information of PSG. However, in addition to being comparatively more reliable than sleep diaries, the advantage of activity monitors over PSG outside the laboratory is that they can be worn for weeks at a time at minimal inconvenience to participants (Darwent, Roach, & Dawson, 2012; Roach et al., 2012b; Sargent, Halson, & Roach, 2014).

Aside from PSG and the common alternatives for measuring sleep duration and sleep patterns mentioned above, other devices exist that have their own advantages (Shambroom, Fabregas, & Johnstone, 2012; Van de Water et al., 2011). One of these devices is a waist-worn activity monitor which was developed for estimating energy expenditure but has been used and validated for monitoring sleep (Galland, Kennedy, Mitchell, & Taylor, 2012; Robillard, Lambert, & Rogers, 2012; Weiss, Johnson, Berger, & Redline, 2010). As these activity monitors are able to provide estimates of both energy expenditure and sleep, not only do they enable researchers to monitor activity patterns outside the laboratory but they also provide the flexibility to research the interaction of these behaviours with a single device (Evans et al., 2011).

Other alternatives to PSG include automated sleep-profiling systems that provide sleep stage estimates. These systems generally comprise a headband-like device that wirelessly transmits electrophysiological signals recorded in the forehead to a

small base station at the bedside for sleep stage analysis (Levendowski, Popovic, Berka, & Westbrook, 2012; Shambroom et al., 2012). Previous studies indicate that these automated wireless devices are highly concordant with PSG in terms of detecting and differentiating sleep stages (Griessenberger, Heib, Kunz, Hoedlmoser, & Schabus, 2012; Levendowski et al., 2012; Shambroom et al., 2012). However, unlike actigraphy-based monitors, these systems are limited to being worn in bed within range of the base station and do not assess sleep/wake patterns throughout the day. As such, they may not be suitable for long-term behavioural research over multiple nights. However, their simplicity and ability to estimate sleep stages make them a useful compromise for research regarding the physiological components of sleep outside a laboratory.

Depending on the research requirements, all of the aforementioned alternatives to PSG have advantages – from the type of information they provide (e.g., self-report, objective rest-wake patterns, or sleep stages), their ease of use and implementation, or even to their cost. However, despite being validated separately, the objective monitoring systems have not been assessed simultaneously with the same group of participants. This could make direct comparisons difficult for researchers trying to determine the most appropriate selection. A combined assessment of these systems against PSG would allow researchers and clinicians to make more informed choices in their practice.

#### *1.3.1.3. Sleepiness and alertness*

Sleepiness and alertness can be inferred from a variety of objective and subjective measures, ranging from physiological or biological markers to behavioural assessments and self-report. Physiological and biological indicators often report on the presence of slow wave activity in waking EEG but may also reference pupil responsiveness to light and blink duration or frequency (Åkerstedt et al., 2013; Dawson, Searle, & Paterson, 2014; Ftouni et al., 2013). In clinical settings, standardised assessments of sleepiness or wakefulness are often based on an objective behavioural outcome – that is, the time taken to fall asleep –following an instruction to sleep or stay awake. In these assessments, shorter latencies following a specific starting reference (such as a scheduled lights off time), are

thought to indicate higher levels of sleepiness and lower levels of alertness than longer latencies (Carskadon et al., 1986). These measures are most commonly employed as part of the Multiple Sleep Latency Test (MSLT) and the Maintenance of Wakefulness Test (MWT) (Carskadon & Dement, 1977; Mitler, Gujavarty, & Browman, 1982).

Self-report provides a simple and inexpensive means of obtaining and assessing feelings of sleepiness, fatigue and alertness. In spite of large individual differences, various studies have shown self-report to correlate both with physiological measures of sleepiness/alertness and performance on various neurobehavioural tasks (Åkerstedt & Gillberg, 1990; Ftouni et al., 2013; Ingre, Åkerstedt, Peters, Anund, & Kecklund, 2006). Subjective measures popularly used for rating sleepiness and alertness include Likert-type scales such as the 9-item Karolinska Sleepiness Scale (KSS), the 7-item Stanford Sleepiness Scale and the 7-item Samn-Perelli Fatigue Checklist (Åkerstedt & Gillberg, 1990; Hoddes, Zarcone, & Dement, 1972; Samn & Perelli, 1982). Visual analogue scales (VAS) are also commonly utilised for more granular assessments (Åkerstedt & Gillberg, 1990). VAS allow participants to respond to a question such as “How alert do you feel?” by placing a mark on a 100 mm horizontal line between two extreme statements (e.g., “struggling to remain awake” and “extremely alert”).

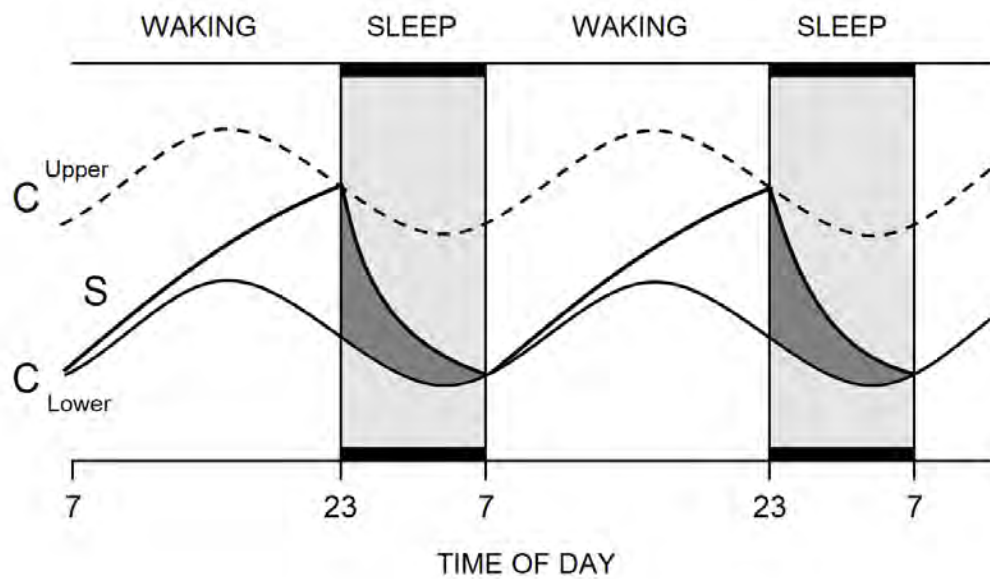
### 1.3.2. Regulation of the Sleep-Wake Cycle

#### 1.3.2.1. *The Two-Process Model*

It is broadly agreed that the cycle of sleep and wake is regulated by two separate but interacting physiological processes (Achermann & Borbély, 2003; Beersma, 1998; Dijk & Kronauer, 1999). The processes, as originally postulated by Borbély (1982) in the two-process model, include a homeostatic component, Process S, and a circadian component, Process C. Both of these theoretical constructs are considered to represent an amalgam of complex physiological systems. Together, they regulate the timing, intensity and duration of sleep, as well as the duration and composition of sleep stages (Dijk & Lockley, 2002; Dijk & von Schantz, 2005). According to the two-process model, Process S functions to maintain sleep homeostasis by reducing deviations above and below an individual's sleep duration requirements (Borbély, 1982). In turn, Process C, is thought to provide 'windows of opportunity' for sleep by influencing the propensity for sleep at certain times of day (Borbély, 1982; Campbell & Zulley, 1985; Daan, Beersma, & Borbély, 1984).

It is proposed the sleep homeostat, Process S, helps individuals meet their homeostatic sleep requirements by: (i) progressively increasing the physiological drive, or pressure, for sleep in monotonic fashion during periods of prolonged wakefulness; and (ii) exponentially reducing this drive during sleep as an individual's requirement is satiated (Figure 1-8, p.39). According to the model, sleep is initiated when Process S reaches an upper threshold of sleep pressure and ends when it reaches a lower threshold. In regulating the propensity to sleep, Process C interacts with Process S to adjust these upper and lower thresholds. Thus, it is easier to meet the sleep threshold at night and the wake threshold during the day. With these processes combined, sleep is more likely to occur after an extended period of wakefulness at night than it is to occur after a short duration of wakefulness during the day (Borbély, 1982; Dijk & Czeisler, 1994) (Figure 1-8).





**Figure 1-8** Time course of the homeostatic Process S and circadian Process C. Process S increases the pressure for sleep during periods of wake and reduces during sleep. Process C produces an alerting signal during the day which peaks and declines in the late evening. These processes interact to maintain the timing and consolidation of sleep-wake behaviour. Homeostatic upper (sleep) and lower (wake) thresholds fluctuate with circadian phase. [Figure adapted from “A two process model of sleep regulation” by A. A. Borbely, 1982, *Human Neurobiology*, 1: 195-204].

### 1.3.2.2. Homeostatic sleep regulation

#### 1.3.2.2.1. Physiological basis of Process S.

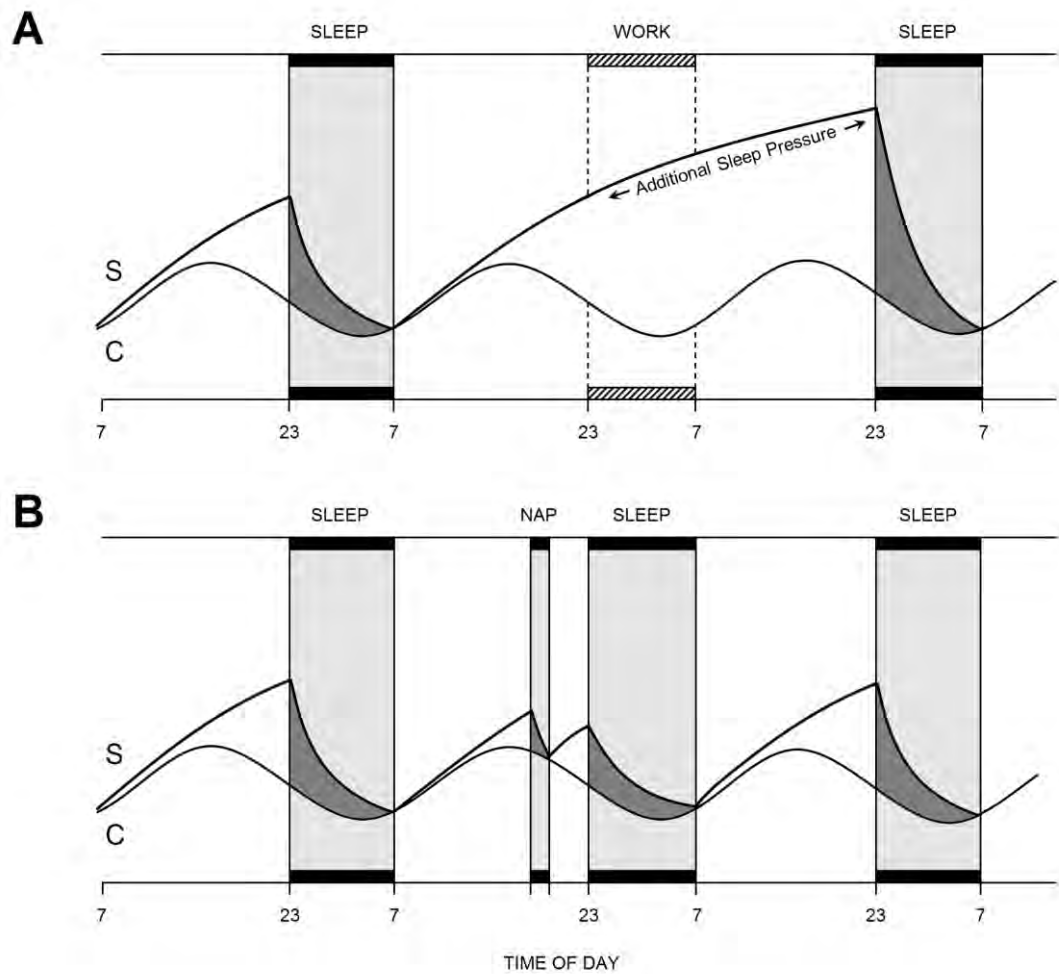
Unlike Process C, which is located in the suprachiasmatic nucleus (SCN) of the hypothalamus, an anatomical residence of the sleep homeostat has not been identified. However, hypotheses have been proposed for a neurochemical basis of sleep homeostasis (Basheer, Strecker, Thakkar, & McCarley, 2004). These posit that the physiological drive to sleep mirrors the accumulation and dissipation of sleep-promoting substances in the brain. In particular, significant evidence exists for a role of adenosine in the mediation of sleep pressure (Basheer, Porkka-Heiskanen, Strecker, Thakkar, & McCarley, 2000; Roehrs, Carskadon, Dement, & Roth, 2011). Adenosine is a nucleoside produced naturally in the brain as a by-product of energy metabolism. Not only does the endogenous production of adenosine increase with prolonged wakefulness and decrease during sleep, but

experimental administration to the brain has been found to induce sleepiness (Basheer et al., 2000; Huang, Urade, & Hayaishi, 2011). Adenosine and other sleep-promoting substances are proposed to have this soporific effect by inhibiting the expression of wake-promoting neurons (Huang et al., 2011).

#### 1.3.2.2.2. *Physiological markers of Process S.*

Notwithstanding continued research into the role of adenosine and other substances in the regulation of sleep homeostasis, EEG slow-wave activity (SWA), predominant in SWS (stage N3) but also present in other non-REM stages, remains the classic marker of the homeostatic process (Daan et al., 1984; Rusterholz, Dürri, & Achermann, 2010; Webb & Agnew, 1971). Deep sleep comprising SWA is the most restorative and it occurs in greatest proportions at sleep onset when the homeostatic drive to sleep is strongest. SWA is believed to be a marker of Process S because, consistent with predictions of the two-process model, its intensity at sleep onset and its subsequent rate of decline is independent of the effects of circadian phase and is determined by sleep/wake history (Daan et al., 1984; Rusterholz et al., 2010; Tobler, Borbély, & Groos, 1983; Webb & Agnew, 1971) (Figure 1-9, p.41).

During sleep episodes following total sleep deprivation and partial sleep restriction, the intensity of SWA is increased relative to baseline sleep episodes, reflective of an increased drive at sleep onset (Borbély, Tobler, & Hanagasioglu, 1984; Brunner, Dijk, & Borbély, 1993; Dijk et al., 1993) (Figure 1-9A). Moreover, gains in SWA are proportionate to the amount of sleep lost. Aeschbach et al. (1996) found more SWA in long sleepers following total sleep deprivation than in those who typically require shorter sleep. Reinforcing its position as a marker of Process S, there is evidence from napping studies that scheduling several naps across the day interrupts and diminishes the increase in low-frequency waking EEG (Cajochen, Knoblauch, Krauchi, Renz, & Wirz-Justice, 2001). Furthermore, SWA during night-time sleep is reduced when preceded by a daytime nap in the afternoon or early evening (Werth, Dijk, Achermann, & Borbély, 1996) (Figure 1-9B).



**Figure 1-9** Schematic of the time course of the interaction between Process S and Process C during sleep deprivation (panel A) and following a nap (panel B). The x-axis depicts time of day. [Figure adapted from "A two process model of sleep regulation" by A. A. Borbely, 1982, *Human Neurobiology*, 1: 195-204, and "Mathematical models of sleep regulation" by P. Achermann & A. A. Borbely, 2003, *Frontiers in Bioscience*, 8: s683-693].

### *1.3.2.3. Circadian regulation of sleep*

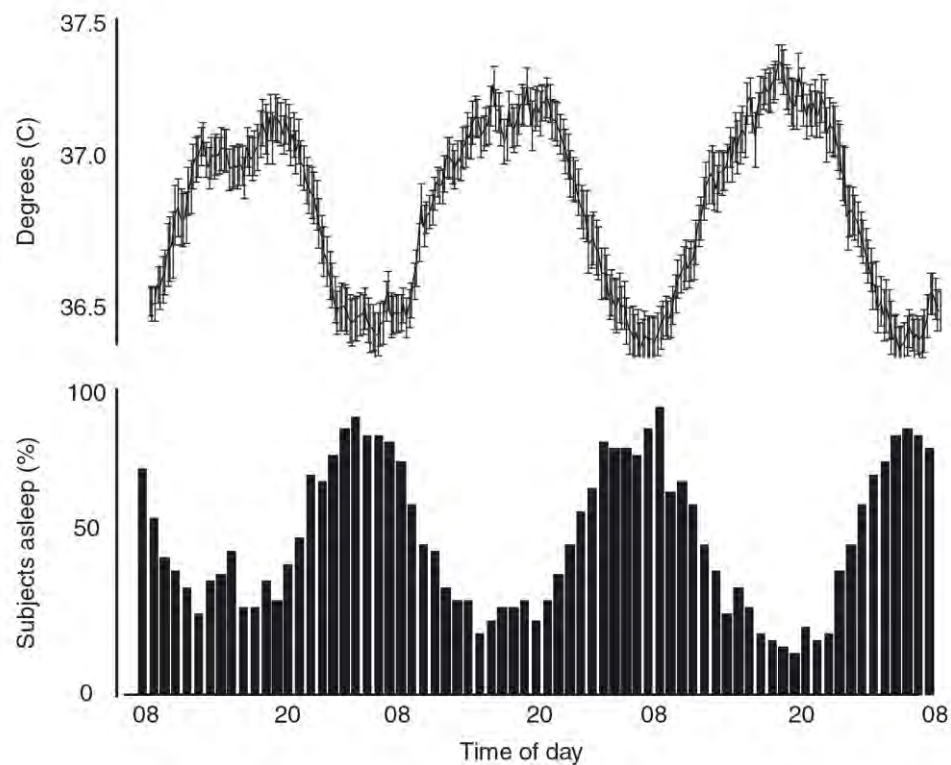
#### *1.3.2.3.1. Physiological basis of Process C.*

The synchronicity of the sleep-wake cycle with the 24-h day was once viewed as a simple response to environmental stimuli but is now understood to be regulated endogenously by a central endogenous pacemaker (Dijk & Czeisler, 1994, 1995). Entrained to the light-dark cycle, this 'master clock' generates wake-promoting signals that oppose the sleep-promoting homeostat during the day and dissipate during the night. As described earlier (section 1.2.1.2, p.18), it is well-established both by animal studies and clinical case studies that this pacemaker of physiological and behavioural rhythms is located in the SCN (Cohen & Albers, 1991; Dijk & Lockley, 2002; Eastman et al., 1984; Johnson et al., 1992; Tobler et al., 1983; Wright, Hull, & Czeisler, 2002). With regard to sleep-wake activity, Eastman et al. (1984) found that rats with lesions in the SCN did not exhibit any circadian rhythms in dim light, and rats with partial lesions produced only weak rhythms when exposed to a light-dark cycle. In humans, Cohen and Albers (1991) reported results of a clinical patient with a damaged hypothalamus which severely disrupted the sleep-wake cycle and body temperature rhythm. With this evidence, the SCN is considered to be the biological manifestation of Process C in the two-process model.

In mammals, melatonin secreted by the pineal gland exhibits a rhythm synchronised to the 24-h day by the light/dark cycle (Lewy & Sack, 1989). It remains at low concentrations during daylight hours and increases, peaks, and declines during the night. Increases in circulating melatonin concentration are associated with greater sleep propensity and experimental administration of the hormone supports a role of melatonin in the promotion of sleep (Gilbert et al., 1999; Reid, van den Heuvel, & Dawson, 1996; Sack, Hughes, Edgar, & Lewy, 1997). Indeed, there is evidence from several studies that melatonin is involved in the regulation of core body temperature and that it is this relationship that may be responsible for the soporific effects of melatonin (Cajochen et al., 2003; Dawson et al., 1996; Gilbert et al., 1999; Krauchi et al., 2006).

#### 1.3.2.3.2. *Circadian rhythms of sleep timing, sleep duration and sleep propensity.*

The human sleep-wake cycle is usually characterised by a single period of wake followed by a major sleep episode every 24-h. This alternation of sleep and wake normally coincides with the daily light-dark cycle, such that sleep occurs at night and wake occurs during the day. That sleep-wake states usually alternate in this manner has been recognised for as long as humans have set aside periods of time to sleep. However, only over the last century has it been recognised that this rhythmicity is influenced by endogenously-generated mechanisms rather than culturally-engendered habit. The first human studies to indicate this involved time-isolation protocols conducted over several weeks in controlled environments where ambient lighting was not dictated by the Earth's axial rotation (section 1.2.3.1, p.22) (Aschoff, 1965; Aschoff, Gerecht, & Wever, 1967; Czeisler, Weitzman, Moore-Ede, Zimmerman, & Knauer, 1980a; Mills et al., 1974; Zulley, Wever, & Aschoff, 1981). In these conditions, endogenous circadian rhythms were able to run at their intrinsic period. These observational studies showed that the rhythmicity of sleep propensity roughly mirrors the circadian course of core body temperature (e.g., Figure 1-10, p.44). For the majority of participants experiencing time-isolation, self-selected sleep episodes had periodicities comparable to that of their free-running temperature rhythms and were consistently initiated near the nadir of each temperature cycle. In a shorter 3-day time isolation protocol, Campbell and Murphy (2007) showed that middle-aged and older adults obtained shorter durations of night-time sleep than young adults but the spontaneous timing of sleep during disentrainment remained consistent.



**Figure 1-10** Relationship between sleep recorded throughout 72 h of time isolation and the circadian rhythm of core body temperature. Time of day is depicted across the x-axis in hours. The top panel describes the group average temperature curve (in degrees Celsius) of 50 participants aged 18 to 81 years. The bottom panel is a histogram of the percentage of participants asleep during any part of any given hour during the protocol. [Figure reproduced and legend adapted from Campbell and Murphy (2007)].

Most participants maintained monophasic sleep-wake patterns similar to those observed under entrained conditions. However, in some longer free-run studies, about a third of participants exhibited ‘spontaneous internal desynchronisation’ of the sleep-wake and temperature rhythms (Aschoff et al., 1967; Czeisler et al., 1980a; Strogatz et al., 1986; Wever, 1979; Zulley & Campbell, 1985). For these free-running participants, sleep and wake oscillated at periods ranging from 30 h to 50 h, decoupled from the intrinsic near-24-h rhythm of body temperature (Aschoff, 1965; Czeisler et al., 1980a). Nonetheless, sleep duration was found to be strongly dependent on circadian phase, as it was correlated with the phase of the temperature rhythm at bedtime (Czeisler et al., 1980a; Strogatz et al., 1986). Sleep

episodes initiated after the circadian acrophase, approaching the temperature minimum, were longer than those initiated on the rising limb of temperature.

Early constant routine studies that measured self-reported sleepiness and alertness across multiple days of sleep deprivation provide further evidence of the circadian rhythmicity of sleep and sleepiness (section 1.2.3.2, p.24). Although masked by cumulative declines due to the homeostatic influence of prolonged wakefulness, circadian variation in self-reported sleepiness and alertness coincided with the peaks and troughs in body temperature (Dijk et al., 1992; Froberg, 1977; Johnson et al., 1992; Monk et al., 1997).

Perhaps the most sophisticated evidence that sleep is modulated by circadian factors is from studies where the sleep-wake and temperature rhythms are forcibly desynchronised. Since the sleep-wake cycles imposed under forced desynchrony (FD) protocols are well outside the range of entrainment (Czeisler et al., 1999; Wever et al., 1983; Zulley et al., 1981), sleep can be systematically assessed at different combinations of circadian phase and prior sleep/wake duration. This enables circadian-dependent effects to be isolated from influences of the sleep homeostat. Consistent with the findings of free-run protocols, rhythms of sleep duration and sleep latency (i.e., the time to fall asleep; a marker of sleepiness) in sleep-wake schedules with periods of 20 h and 28 h reflected the phase-course of body temperature (Dijk & Czeisler, 1995; Wyatt et al., 1999). With the sleep homeostat controlled, time until sleep onset was demonstrably shorter around the temperature nadir and longer at the acrophase (Dijk & Czeisler, 1995; Wyatt et al., 1999). This pattern was reversed for sleep duration. That is, sleep persisted for longest when centred on the temperature nadir and was shortest when centred on the temperature acrophase. A similar phase-course of sleep propensity has been observed in more recent research by Sargent, Darwent, Ferguson, Kennaway, and Roach (2012a). In their FD study, participants were assigned to a schedule that either minimised the homeostatic sleep drive with a high sleep-to-wake ratio (i.e., 1:2) or increased it with a low ratio (i.e., 1:5) involving wake extension and sleep restriction. Results from this study confirm that the propensity to sleep is highest around the circadian nadir of the

temperature rhythm following habitual levels of homeostatic sleep pressure. Under an increased homeostatic load, this effect was found to be masked, the propensity to sleep high at all circadian phases (Sargent et al., 2012a).

#### 1.3.2.3.3. *Circadian rhythms in sleep architecture.*

Circadian rhythms are exhibited in the composition of sleep as well as its duration and propensity (Czeisler et al., 1980b; Endo et al., 1981; Zulley, 1980). In an early study, Webb and Agnew (1971) scheduled participants' sleep episodes during the day. They found that inverting the sleep-wake cycle reduced the arousal threshold so that wake-time during sleep increased. In the same study, Webb and Agnew (1971) found that sleep periods initiated at 2300 h comprised more stage REM sleep than periods initiated during the day at either 0700 h or 1500 h. Later, Zulley (1980) reported on the sleep of participants living for a month in underground units isolated from external time cues. In this study, it was found that the amount of REM present in a given sleep episode was largely dependent on its timing in relation to the free-running temperature rhythm. REM sleep was inversely associated with temperature cycles such that the greatest amounts were obtained in sleep episodes near the temperature minimum (Zulley, 1980). This pattern has been confirmed in multiple other experiments, with and without time isolation in underground bunkers (Czeisler et al., 1980b; Endo et al., 1981; Webb & Agnew, 1971). In normally entrained conditions, the amount of REM sleep progressively increases until the end of the sleep episode, coinciding with the early morning temperature minimum. This is in contrast to surges of REM sleep during time isolation, which tends to remain constant across the entire sleep episode. This difference is explained by variations in the phase relationship between the sleep-wake cycle and temperature rhythm in these two environments (Zulley et al., 1981). Sleep episodes during time isolation are usually initiated at later phases of the temperature cycle than those obtained when entrained. The regulation of REM sleep in this manner is in contrast to the homeostatic regulation of SWS, as previously described.



### 1.3.3. Monophasic and biphasic sleep

Unless work/social obligations demand otherwise, sleep in Western societies such as Australia and the US is generally obtained in a single episode every night. This has led to a common perception that the human sleep-wake system is naturally monophasic and that this arrangement is biologically optimal. However, human behaviour does not necessarily reflect biological needs and the notion that the human sleep-wake system operates best when sleep is consolidated into a single episode is disputed (Campbell & Zulley, 1989; Ekirch, 2001; Yetish et al., 2015). There is evidence that napping can fulfil a biological propensity for sleep during the day (Campbell & Zulley, 1989; Lack & Lushington, 1996), and it is argued in some quarters that that it may be natural – and thus preferable – for sleep to be segmented at night (Ekirch, 2001; Wehr, 1992). Though nocturnal sleep is ubiquitous the world-over, one only has to look to siesta-based societies and student populations to see that alternative approaches to sleep, such as napping, can also be popular (Campbell & Murphy, 2007; Lan, Lan, Wen, Lin, & Chuang, 2007; Lund, Reider, Whiting, & Prichard, 2010; Naska, Oikonomou, Trichopoulou, Psaltopoulou, & Trichopoulos, 2007; Yang, Wu, Hsieh, Liu, & Lu, 2003). That the normal arrangement of sleep each day can differ across cultures clearly indicates human sleep is not the strictly monophasic phenomenon it is oft assumed to be. However, this does not mean *ipso facto* that human sleep is intrinsically biphasic, nor that napping or segmented sleep is necessary or beneficial.

#### 1.3.3.1. Sleep trends in pre-industrial societies

Historical and present-day pre-industrial societies have often been studied for the insight they can provide into human behaviour and biological functions undisturbed by modern technology and social obligations (Ekirch, 2001; Yetish et al., 2015). Assuming that sleep patterns observed in pre-industrial societies align with evolutionary requirements more closely than those of post-industrial societies, these communities provide important avenues of enquiry in the study of human sleep. Over the past decade, a review of pre-industrial sleep patterns in the British Isles by historian Roger Ekirch (2001) has dominated the debate over whether sleep is polyphasic. He argues that the modern consolidation of night-time

sleep is unnatural and contradicts our “primeval” sleep patterns. Drawing on an array of historical sources, from diary accounts to classical literature mentioning sleep, Ekirch (2001) concludes that sleep in pre-industrial Britain, and Western Europe more broadly, was often interrupted midway during the night by an hour of quiet wakefulness. In the time between what he terms “first sleep” and “second sleep”, people would pray, reflect, evacuate their bowels, engage in sexual relations or visit neighbours (Ekirch, 2001). Ekirch proposes that engagement in this ostensibly natural segmentation of sleep dwindled by the time of Industrial Revolution, as a consequence of delayed bedtimes with the advent of electric lighting.

Assuming that sleep patterns in Britain and mainland Europe were segmented as Ekirch describes, it would be a leap to conclude that sleeping in this way is ideal – or that consolidated sleeps are unnatural and pathological – from this research alone. Indeed, a recent study by Yetish et al. (2015) investigating the sleep of contemporary equatorial African and South American hunter-gatherer communities found nothing to corroborate Ekirch’s assertions. Depending on the season, Yetish et al (2015) found that members of these isolated communities typically slept 2 h to 4 h after sunset and woke up around sunrise. Sleep was predominantly monophasic; there was no evidence for regular extended nocturnal awakenings, and napping in the afternoon was documented on approximately only 22% of days. These findings are significant because they were observed in multiple isolated hunter-gatherer populations at latitudes where early humans evolved.

Rather than emerging as a biological requirement of human evolution, it is possible nocturnal sleep became segmented in Europe sometime after humans migrated out of Africa (Yetish et al., 2015). This hypothesis is supported by Wehr (1992), who scheduled participants to long photoperiods (periods of sunlight) of 16 h (8 h darkness at night) for a couple of weeks, followed by short photoperiods of 10 h (14 h darkness at night) for a month. With sleep encouraged during darkness and no stimulating activities permitted, Wehr (1992) observed that sleep was consolidated when exposed to long photoperiods but gradually bifurcated into two nocturnal episodes when exposed to short photoperiods. Since Europe is situated

further from the equator, daylight comprises a significantly shorter period of the day during winter. Thus, segmented sleep may have developed ‘naturally’ as a consequence of migration to higher latitudes.

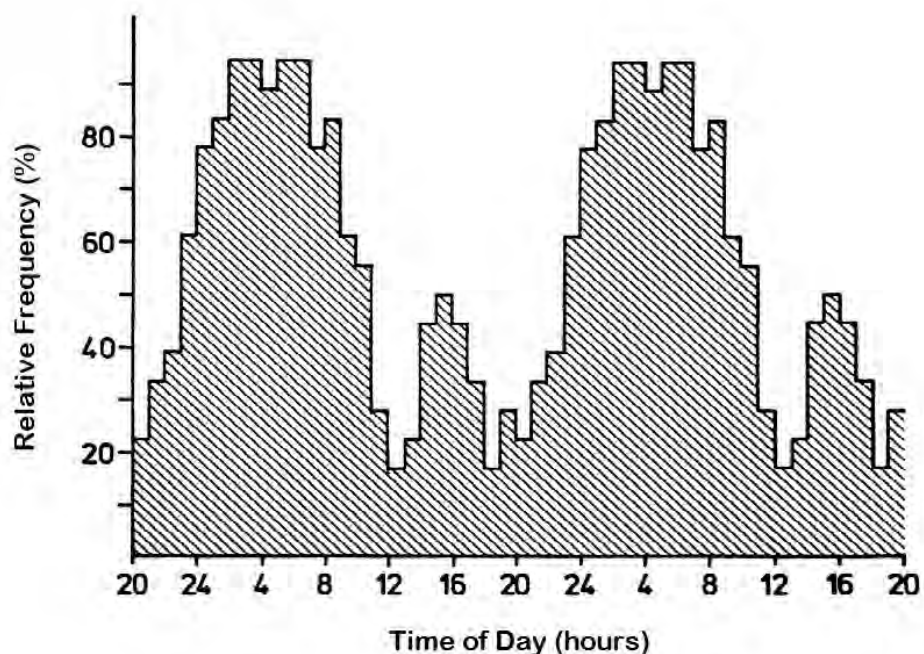
Combined, these historical and anthropological studies suggest that humans can accommodate different arrangements of sleep depending on the environment. However, it is difficult to conclude from these that the human sleep-system is polyphasic. Segmented nocturnal sleep patterns in pre-industrial Europe may simply have transpired in response to longer nights compared to regions near the equator where day/night lengths are similar. Furthermore, although Yetish et al. (2015) observed daytime napping in contemporary pre-industrial societies, it was not frequent. Since any predisposition to nap may have been confounded by obligations to the community (e.g., hunting and gathering food), the question of whether sleep is biphasic or monophasic is better addressed in controlled laboratory conditions.

#### *1.3.3.2. Napping in time-free environments*

Since free-running protocols are careful to eliminate exogenous zeitgebers and do not impose a sleep-wake schedule, they are arguably able to evince patterns of sleep that reflect an intrinsic need. Early studies employing time-free environments appeared to support the proposal that sleep is monophasic (Aschoff, 1965), showing a clear preference for a single night-time sleep episode. However, this conclusion has been disputed on the basis that instructions to participants on how to behave during the protocol assumed monophasic sleep as the norm (Campbell & Murphy, 2007; Campbell & Zulley, 1989). Participants in these studies were instructed to maintain a regular schedule of waking behaviour (e.g. three meals per day) and sleep when they believed a major sleep period was approaching. Had napping been permitted or encouraged, a different arrangement of sleep may have emerged (Campbell & Zulley, 1989).

Free-running protocols may not be able to elucidate a biological predisposition for biphasic sleep even when napping is permitted because it is not a behavior habitually engaged in by many people. As such, disentrainment protocols have

been designed to encourage the expression of napping (Campbell, 1984; Campbell & Zulley, 1985; Nakagawa, 1980). A variation of the free-run design, disentrainment protocols increase the likelihood of napping by minimising behavioural alternatives to sleep – e.g., reading, writing, social interaction, music, physical activity – in addition to removing zeitgebers (Campbell & Zulley, 1985, 1989). Over a 72-h period of disentrainment, Campbell and Zulley (1985) observed that sleep episodes exhibited a bimodal distribution (Figure 1-11, below). A primary peak in sleep propensity occurred at night, around the temperature minimum, and a secondary peak occurred in the afternoon between successive minima. With an average duration of about 8.8 h, sleep episodes spontaneously initiated after 2000 h, composing the primary peak in sleep frequency, were termed “anchor sleeps” or “major sleep episodes” (Figure 1-11). Sleep episodes initiated between major sleep episodes, labelled naps, averaged 1.7 h and formed the secondary peak in sleep frequency. With a phase position corresponding to clock times of 1400 h – 1600 h under entrained conditions, this secondary peak correlates with napping times in siesta-based cultures (Campbell & Zulley, 1985)



**Figure 1-11** Double-plotted distribution of sleep episodes in time-free environments when napping is permitted. The x-axis represents time of day in hours. The y-axis represents the relative frequency of sleep episodes, as a percentage of total possible sleep episodes, comprising all or part of any given hour of the day [Figure reproduced from Campbell and Zulley (1985)].

Although most participants demonstrate a monophasic sleep pattern in free-run studies, there is support for a biphasic sleep propensity in cases where participants exhibit ‘spontaneous internal desynchronisation’ of the sleep-wake cycle and temperature rhythm (see p.44). When naps were included in the analyses of these cases, a bimodal distribution of sleep again emerged (Strogatz et al., 1987; Zulley & Campbell, 1985). Sleep onset tended to cluster around two temperature phases: a primary peak occurred around the temperature minimum and a smaller peak occurred mid-way between successive minima, corresponding to a clock time of 1500 h (Czeisler et al., 1980a; Zulley et al., 1981). In addition to these findings, Strogatz et al (1987) identified phases between the bimodal peaks of sleep onset at which sleep episodes are rarely initiated and sleep is difficult to maintain. These periods, termed ‘Wake Maintenance Zones’, lasted a couple of hours and occurred approximately 8 h before and 5 h after the temperature nadir (Strogatz et al., 1987). For those going to bed between 2300 h and 0700 h under entrained conditions, the phases at which it was difficult to fall asleep corresponded to clock times of 1900 h – 2200 h and 1000 h – 1100 h (Lavie, 1986; Shekleton et al., 2013; Strogatz et al., 1987).

#### *1.3.3.3. Experimental manipulation of sleep-wake timing*

Findings from free-run and disentrainment protocols in which participants are allowed to choose their own sleep-wake schedules suggest a biphasic propensity for sleep. However, the nature of the human sleep-system can also be elucidated by evaluating sleep during imposed sleep-wake schedules. For instance, Lack and Lushington (1996) conducted an ‘ultradian routine’ protocol which required participants to remain supine in environmental conditions similar to those of the constant routine (section 1.2.3.2, p.24). However, unlike the constant routine, participants completing this protocol were permitted to sleep in cycles of 10 min every half hour – equating to a total sleep opportunity of 8 h in 24 h. With brain activity monitored continuously with electrodes, Lack and Lushington (1996) observed a minor mid-afternoon peak in the propensity to sleep, followed by an evening dip, in addition to the major peak at night for a majority of participants. Although this minor afternoon peak in sleep propensity was not evident for all

participants and was subject to large individual differences, it further validates the 'post-lunch dip' in alertness as an endogenous physiological phenomenon.

A more recent laboratory study suggests that splitting sleep opportunities into main "anchor sleep" episodes at night and daytime naps is not detrimental to overall sleep duration and quality (Mollicone, Van Dongen, & Dinges, 2007). Mollicone et al. (2007) assigned participants to sleep schedules which restricted night-time main sleeps to different durations, with or without a supplementary daytime nap. Following multiple days in these schedules, the researchers were able to conclude that sleep duration and the amount of deep SWS obtained by participants were functions of the total sleep opportunity provided per 24 h rather than how sleep times were arranged. Those participants assigned shorter night-time sleeps supplemented by daytime naps did not fare worse in terms of their sleep duration than participants who were assigned a similar total sleep opportunity consolidated into a single night-time episode. Thus, whether or not humans are naturally biphasic sleepers, such patterns can be satisfactorily accommodated. It should be noted, however, that it remains to be seen whether these findings may be generalised to night workers whose major sleeps occur during the daytime. It is possible segmenting sleep is only beneficial when the majority of sleep occurs at night. Thus, more research is needed to determine how biphasic sleep schedules affect sleep duration and quality at different times of day.

#### 1.3.4. Summary

Sleep is a complex phenomenon that is an integral component of every day. Several techniques exist to measure sleep, and stages of sleep, in addition to the gold standard technique of PSG. These devices have been validated to differing extents, but have not all been compared with each other. The regulation of sleep and wake is thought to involve physiological circadian and homeostatic mechanisms which operate in synchrony. The homeostatic process influences sleep depth and duration based on prior sleep/wake history, and the circadian process helps to regulate the timing of sleep. Human physiology promotes the circadian propensity for sleep at night and wake during the day. Sleep episodes obtained at contrasting

times have a lower arousal threshold, meaning they are more easily disrupted and less beneficial for recuperation. Though people typically obtain a single sleep episode each night, research from various protocols suggests the human sleep system accommodates biphasic sleep schedules; indeed, napping in the afternoon is common in many countries.

#### *1.3.4.1. Sleep, circadian rhythms and shiftwork*

From the information presented in this and previous sections regarding sleep and circadian rhythms, it is clear to see that shiftwork may be problematic for the health and safety of workers. Humans, and indeed all mammals, are geared for wakefulness and sleep at certain times. When the work schedule does not align with the circadian pacemaker, shiftworkers are required to work at times conducive to sleep and sleep at times conducive to wakefulness. For night workers, the periods allowed for sleep or wake are completely reversed such that on-shift alertness must be sustained in the absence of a circadian arousal signal and daytime sleep must be maintained despite one. Thus, misalignment of work-rest schedules with internal circadian rhythms has the potential to form a negative feedback loop, compounding the fatigue during shifts and reducing the capacity to fully recover between them. This conflict may in large part explain the prevalence of fatigue-related incidents in shift work. However, given what is known about sleep propensity, daytime napping, and the accumulation of sleep pressure, it may be possible for sleep to be strategically arranged to benefit shiftworkers.

## 1.4. Neurobehavioural Performance

Although Borbely's (1982) two-process model was developed to understand sleep regulation, it has provided the field of sleep and fatigue research a framework for considering individuals' alertness and ability to function while awake (Åkerstedt & Folkard, 1997). Sleep and wake represent two physiological states on opposing ends of a continuum of consciousness. As such, propensities for wake and alertness are inversely associated with propensities for sleep and sleepiness. Given that wakefulness is a prerequisite to fulfil day-to-day obligations, its relationship with sleep has important implications for neurocognitive function and performance. The two-process model reinforces the fact that wakefulness and waking functions are not simply affected by sleep and circadian processes in isolation but by their interaction. As such, the following sections will evaluate the individual and combined effects of sleep and circadian factors on constructs such as vigilance (or sustained attention), which underlie performance on more complex neurobehavioural tasks (Baulk, Biggs, Reid, van den Heuvel, & Dawson, 2008; Jackson, Croft, Kennedy, Owens, & Howard, 2013; Wright, Lowry, & LeBourgeois, 2012).

### 1.4.1. Measures of Neurobehavioural Performance

#### *1.4.1.1. The Psychomotor Vigilance Test – A measure of state instability*

In the realm of sleep and fatigue-related performance research, a number of measures are employed to assess vigilance and neurobehavioural function. The most widely-used of these is the Psychomotor Vigilance Test (PVT), usually completed on a computer or hand-held device (Dinges & Powell, 1985; Dorrian, Rogers, & Dinges, 2005). This test assesses the ability to sustain attention by measuring reaction times to stimuli presented at random intervals over a set period. Here, faster mean response times over the course of the test indicate improvements in neurobehavioural function. With participants asked to respond as quickly as possible, reaction times greater than 500 ms are deemed lapses of attention and represent "brief moments of low arousal during which subjects [are] unable to respond to the task at hand" (Doran, Van Dongen, & Dinges, 2001, p.254).



Indeed, this is supported by neuroimaging studies which show that fast responses correspond with activation of sustained-attention networks in the brain, while lapses correspond with regions associated with inattention and disengagement – particularly during sleep deprivation (Drummond et al., 2005).

The popularity of the PVT may be attributed to (i) its ease of use and administration; (ii) its resistance to learning effects over time; and (iii) its sensitivity to changes in sleep and wake duration (Dorrian et al., 2005). Of interest to sleep and fatigue research is that while lapses become more frequent with prolonged wakefulness and following sleep loss, they remain interspersed between response times at near-baseline levels (Doran et al., 2001). It is hypothesised this moment-to-moment variability in performance captures a state of instability whereby the ability to sustain attention is affected by the competing pressures of the homeostat and compensatory effort (Drummond et al., 2005). Thus, although the PVT does not measure ‘real world’ performance directly, it is believed to capture the underlying effects of sleep loss on cognitive processes often critical to them – i.e., the ability to attend and respond promptly to a salient signal (Doran et al., 2001; Drummond et al., 2005; Howard et al., 2007; Jackson et al., 2013). In this respect, the PVT is considered by some to have high ecological validity (Dorrian et al., 2005).

#### *1.4.1.2. Other measures of performance*

Other tasks are employed in sleep and fatigue research to measure specific facets of cognitive function or performance. For example, cognitive tasks such as the Digit Symbol Substitution Test (DSST), Serial Addition / Subtraction Test (SAST), and the Stroop inhibition task tap into constructs of processing speed and executive function (Burke, Scheer, Ronda, Czeisler, & Wright, 2015; DeStefano & LeFevre, 2004; Proust-Lima, Amieva, Dartigues, & Jacqmin-Gadda, 2007; Wechsler, 1981). In contrast, simulator-based tests can measure various dimensions of “real-world” performance – such as steering control and crash risk for driving (Jongen, Perrier, Vuurman, Ramaekers, & Vermeeren, 2015; Philip et al., 2005; Ranney, Simmons, Boulos, & Macchi, 1999). Although sleep deprivation does not affect all cognitive domains equally (Burke et al., 2015; Cain, Silva, Chang, Ronda, & Duffy, 2011; Chee

et al., 2008) and not all measures of performance are as sensitive as the PVT to sleep-dose, these tests can provide insight into the spectrum of influence of the sleep and circadian systems (Balkin et al., 2004; Burke et al., 2015; Drummond, Brown, Salamat, & Gillin, 2004; Lo et al., 2012).

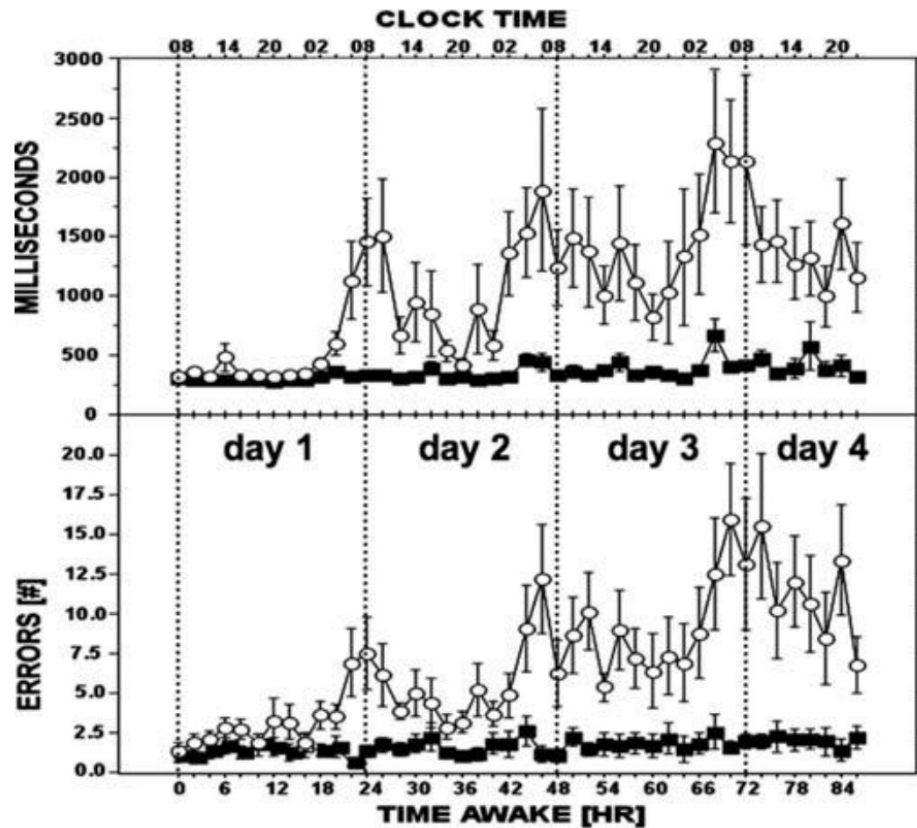
## 1.4.2. Total Sleep Deprivation and Sleep Restriction

### *1.4.2.1. Total sleep deprivation*

The homeostatic-circadian regulation of neurobehavioural performance is most often investigated with total sleep deprivation (TSD) protocols requiring anywhere from 24 h to 90 h of sustained wakefulness (Doran et al., 2001; Pilcher, Band, Odle-Dusseau, & Muth, 2007). These protocols are usually conducted under constant routine conditions (section 1.2.3.2, p.24) to avoid or control for the potential masking of performance rhythms by environmental and behavioural stimuli (Graw, Krauchi, Knoblauch, Wirz-Justice, & Cajochen, 2004). During the period of sustained wakefulness, neurobehavioural performance is measured at regular intervals to capture both the accumulation of homeostatic sleep pressure and variations in circadian phase. In this way, TSD protocols facilitate understanding about the regulation of performance in terms of prior wake and circadian phase.

A feature of the homeostatic system, neurobehavioural performance during TSD declines and becomes more variable with increasing prior wakefulness (Doran et al., 2001). This decline tends to worsen at an accelerated rate following 17 h of wakefulness, which usually coincides with habitual bedtime (Dawson & Reid, 1997; Doran et al., 2001). Indeed, in their seminal study Dawson and Reid (1997) equated cognitive performance at this duration of wakefulness with performance at a blood alcohol concentration of 0.05%. Since TSD protocols do not isolate the influence of the circadian pacemaker from the sleep homeostat, cumulative declines in performance across hours of wake are masked by a circadian rhythm. This rhythm parallels that of core body temperature such that best and worst performance occurs near the local maxima and minimum of each circadian cycle, respectively (Dijk et al., 1992; Doran et al., 2001; Monk et al., 1997). This interaction can be observed in the results of Doran et al. (2001): lapses and false

starts on the PVT became increasingly more frequent and variable with prior wake, but improved around the subjective day (Figure 1-12, below).



**Figure 1-12** The contributions of the circadian pacemaker and sleep homeostat to reaction time and errors on the PVT over 88 h of total sleep deprivation. The sleep homeostat is responsible for the overall increase in reaction time and errors, while the circadian pacemaker is responsible for the rhythmic variations each day [Figure reproduced and legend adapted from Doran et al. (2001)].

#### *1.4.2.2. Chronic and acute sleep restriction*

While the TSD paradigm can reveal how circadian phase and prior wake operate in concert to regulate performance, it cannot provide any information about the effects of sleep dose. This is an important limitation because, while few people typically go without any sleep for more than 24 h, a significant number obtain less than they would like or need to function optimally (Anderson & Horne, 2008; Wilsmore et al., 2013). Sleep restriction protocols address this gap by allowing neurobehavioural performance to be assessed at regular intervals following a fixed duration of time in bed (TIB) on one or more consecutive days. It was known quite early in experimental sleep research that severe restriction to 4 h of TIB or less produced significant performance deficits after a single night and cumulative declines across multiple nights (Gillberg & Åkerstedt, 1994; Tilley & Wilkinson, 1984; Wilkinson, Edwards, & Haines, 1966). In other studies, comparatively moderate restriction to between 4 h and 7 h of TIB per night was also shown to also produce acute and chronic performance deficits, though less pronounced (Dinges et al., 1997; Herscovitch & Broughton, 1981).

Two systematic investigations into the acute and chronic effects of sleep dose on neurobehavioural function were published by Van Dongen et al. (2003) and Belenky et al. (2003). Participants in their studies were subjected to one of several sleep doses across multiple consecutive nights. Van Dongen et al. (2003), assigned sleep doses of 8 h, 6 h, or 4 h for 14 days or TSD (0 h) for three days, while Belenky et al. (2003) assigned sleep doses of 9 h, 7 h, 5 h or 3 h over a period of 7 days. Consistent with previous research, these studies revealed significant impairments – i.e., longer and more variable reaction times on the PVT – following a single night of sleep restriction when the sleep dose was below 6 h but not when it was greater than 6 h. However, restriction to 7 h or less sleep was sufficient to impair performance over multiple days, with the rate of cumulative decline shown to be dose dependent. Indeed, restricting sleep to 6 h per night for two weeks produced deficits equivalent to 1 night of TSD, while restricting sleep to 4 h produced deficits equivalent to 2 nights of TSD (Van Dongen et al., 2003).

Interestingly, Van Dongen et al. (2003) were able to demonstrate that the cumulative declines they observed in their experiment were a consequence of extended wakefulness rather than the reduction of sleep per se. If sleep loss itself was responsible for the declines in performance across days of sleep restriction, performance deficits would be expected to correlate with the amount of sleep lost. However, performance deficits following 14 days of sleep restriction were less severe than following 3 days of TSD, despite more sleep being lost over the course of the protocol. This inconsistency does not exist if the primary contributor to these deficits is considered to be wakefulness in excess of a critical ceiling for stable function. Here, the total additional wakefulness sustained each night during sleep restriction was less than the amount of wakefulness sustained during 3 days of TSD.

Although the TSD and sleep restriction protocols provide valuable insight into the homeostatic-circadian regulation of neurobehavioural performance and the effects of sleep dose and wake extension, they do have some limitations. For both protocols, the interaction of homeostatic and circadian processes cannot be adequately examined because they occur in synchrony and are usually assessed at fixed combinations. For example, performance deficits attributed to a level of prior wake might also be influenced by a circadian phase because both typically co-occur when measured. The only way to evaluate the independent and interactive contributions of the circadian pacemaker and sleep homeostat to performance is to uncouple them. This separation can be achieved with a forced desynchrony protocol (See section 1.2.3.3, p.25, for a description of the protocol; for its effect on performance, see section 1.4.3 on p.60).

#### *1.4.2.3. Sleep loss on different cognitive domains and driving performance*

Findings from numerous sleep restriction and total sleep deprivation protocols demonstrate that cognitive domains and performance tasks are not equally sensitive to the effects of sleep loss and prolonged wakefulness (Balkin et al., 2004; Lim & Dinges, 2010; Lo et al., 2012). Balkin et al. (2004) demonstrated these differential effects of sleep restriction in a protocol which limited participants to 3 h, 5 h, 7 h, or 9 h time in bed across seven days. In this study, they showed that

although performance on a variety of different tasks deteriorated with sleep restriction in a dose-responsive manner, measures of sustained attention, such as the PVT, were the most sensitive to the reduction of sleep. In a meta-analysis of the effects of total sleep deprivation, Lim and Dinges (2010) arrived at similar conclusions. They observed no effects of sleep deprivation on measures of reasoning and crystallised intelligence, which are believed to be extremely stable. However, they reported large declines in the ability to sustain attention and moderate declines in processing speed and working memory.

Recently, Jackson et al. (2013) compared the effects of sleep loss on various cognitive tasks and simulated driving performance. They reported that measures of sustained attention and driving both deteriorated across a night of sleep deprivation. However, consistent with the aforementioned studies above, a night without sleep did not significantly impair processing speed or executive function. These findings were interpreted as highlighting the importance of attention as a factor in drowsy driving. Jongen et al. (2015) extended upon these findings by comparing the effects of 24 h of sleep deprivation on cognitive performance and on-the-road driving in a real car. Here, they observed large effect size declines in the standard deviation of lane position (a measure of road tracking error), and overall instructor ratings of driving quality. As with Jackson et al. (2013), the deterioration of driving performance with sleep deprivation was associated with similarly large declines for attention-based psychometric tasks, including the PVT, performed just prior to the drive. In contrast, some cognitive tasks, such as the DSST, demonstrated moderate declines while others, such as a psychomotor tracking task, demonstrated no significant declines.

#### 1.4.3. Forced Desynchrony

As described in section 1.2.3.3, p.25, the forced desynchrony (FD) paradigm desynchronises homeostatic and circadian processes by extending or shortening the subjective day – typically, to 28 h or longer (e.g., Cohen et al., 2010; Dijk et al., 1992; Zhou et al., 2011) or 20 h or shorter (e.g., Carskadon & Dement, 1975; Wyatt et al., 1999) – outside the range of entrainment (Duffy & Wright, 2005; Zulley et al.,

1981), over multiple consecutive days. The consequence of this is that the circadian pacemaker continues to oscillate at its near-24-h intrinsic rhythm while the sleep and wake alternate at the period of the subjective day (Czeisler et al., 1999). During FD, sleep and wake are restricted to fixed proportions of each cycle. For most studies, this ratio of sleep-to-wake is set to 1:2, equivalent to 8 h TIB per 24 h (Czeisler et al., 1999; Matthews et al., 2012a; Wyatt et al., 1999). When FD protocols are employed to investigate the regulation of neurobehavioural performance, test bouts are administered at frequent intervals to capture changes with prior wake and circadian phase. Since wake episodes are phase-shifted with every sleep-wake cycle, performance measured over the course of successive episodes encapsulates the whole range of circadian phases over several consecutive days.

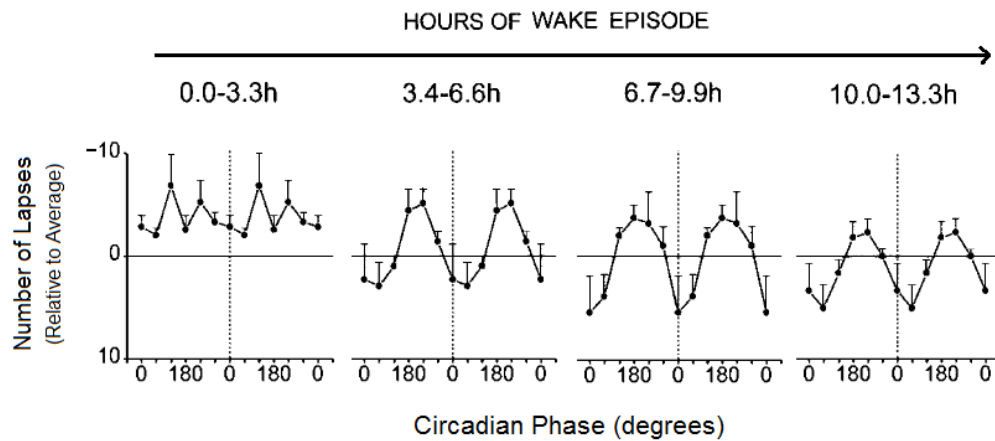
This capacity to systematically measure performance at every combination of prior wake and circadian phase makes the FD paradigm a powerful tool for revealing the independent contributions of the sleep homeostat and circadian pacemaker. When performance is folded at the period of the circadian cycle, the influence of the homeostat across levels of prior wake is revealed (Dijk et al., 1992). Likewise, when performance is folded at the period of the sleep-wake cycle, the contribution of the circadian pacemaker is revealed. In this way, early FD studies were able confirm inferences drawn from TSD studies. Controlling for prior wake, these studies revealed that the impact of circadian phase on performance follows the rhythm of core body temperature; it becomes worse and more variable around the temperature nadir and faster near the temperature acrophase (Dijk et al., 1992; Wyatt et al., 1999). Similarly, they showed that the effects of wakefulness on neurobehavioural performance are consistent with its effects on sleep pressure; that is, increased prior wake results in worse and more variable neurobehavioural performance (Dijk et al., 1992; Wyatt et al., 1999).

In contrast to observations during TSD that performance remains relatively stable for the first 16 h of wakefulness before rapidly declining, FD data reveal that performance steadily deteriorates within as little as 7 h of wakefulness (Dijk et al., 1992). This discrepancy between the TSD and FD protocols is evidence of the

moderating influence of the circadian pacemaker in the former. The first 16-h of TSD usually comprises the entirety of a habitual wake period, coinciding with the rising limb of core body temperature rhythm. As such, the apparent stability of performance with prior wake can be explained by the neutralising influence of the pacemaker (Dijk et al., 1992). Following 16 h of prior wake, the influence of the homeostat during TSD is similarly moderated because it coincides with the falling limb of the temperature rhythm. No longer “propped up” by an alerting signal, performance declines with increased wakefulness comparatively unfettered. In revealing the main effects of prior wake and circadian phase independent of each other as it does, the FD paradigm emphasises the significance of the circadian-homeostatic phase relationship.

As well as revealing their main effects on performance, the FD paradigm uniquely permits investigations into the interaction of the circadian and homeostatic systems. This can be achieved by evaluating changes in performance across circadian phase at each level of prior wake and vice versa. Assessing performance in this manner, early FD studies demonstrated that the contributions of circadian phase and prior wake interact in a non-linear manner such that their effects are dependent on each other (Dijk et al., 1992; Silva, Wang, Ronda, Wyatt, & Duffy, 2010; Wyatt et al., 1999). The rate of performance decline with increasing prior wakefulness was observed to be more severe around the circadian nadir than it was around the circadian acrophase. Alternatively, it could be interpreted that the contribution of circadian phase was dependent on the duration of elapsed wakefulness. These interactions are evident in the results of Wyatt et al. (1999), which show that the effect of circadian phase on lapsing is small when prior wake is low but large when prior wake is high (Figure 1-13, p.63). Overall, performance is best around the peak of the temperature rhythm, within a few hours of waking, and is worst around the trough of the temperature rhythm after many hours of wakefulness.





**Figure 1-13** Depiction of the interaction of prior wake and circadian phase the total number of lapses obtained during the PVT. Levels of prior wake are represented by each panel, in order of increasing duration from left to right. Circadian phase is depicted on the x-axis, with 0 representing the nadir of core body temperature. The y-axis describes performance relative to the average of the protocol. Negative values indicate fewer lapses and positive values indicating more lapses [Figure and legend adapted from Wyatt et al. (1999)].

#### 1.4.3.1. Cognitive domain-dependent influences of prior wake and circadian phase during forced desynchrony

It is known that the homeostatic and circadian systems affect some cognitive domains more so than others (Lo et al., 2012). Most studies which have investigated the independent and combined effects of these systems by means of forced desynchrony have only assessed performance on simple attentional tasks (Darwent et al., 2010; Zhou et al., 2011). However, two forced desynchrony studies conducted by Wright et al. (2002) and Burke et al. (2015) have specifically assessed higher order cognitive tasks requiring working memory and executive control. Consistent with previous findings, they observed that performance on these tasks tended to decline as a function of prior wakefulness and was poorest near the minimum of the temperature rhythm (Wright et al., 2002). However, there were differences in how circadian and homeostatic process interacted, as well as the extent to which different tasks were affected. For example, Burke et al. (2015) found that for tasks requiring inhibitory control, performance varied with circadian phase but changed little in circadian amplitude with increasing homeostatic sleep pressure (Burke et al., 2015). In contrast, for tasks requiring

selective visual attention and goal-directed behaviour, they found cognitive throughput was sensitive to changes in homeostatic sleep pressure and circadian phase separately, as well as their interaction. Together, these results show that higher-order cognitive domains are differentially susceptible to the interaction of processes involved in sleep-wake regulation. This has implications for understanding the mechanisms that affect performance on various 'real-world' tasks under different conditions (Jackson et al., 2013; Matthews et al., 2012a).

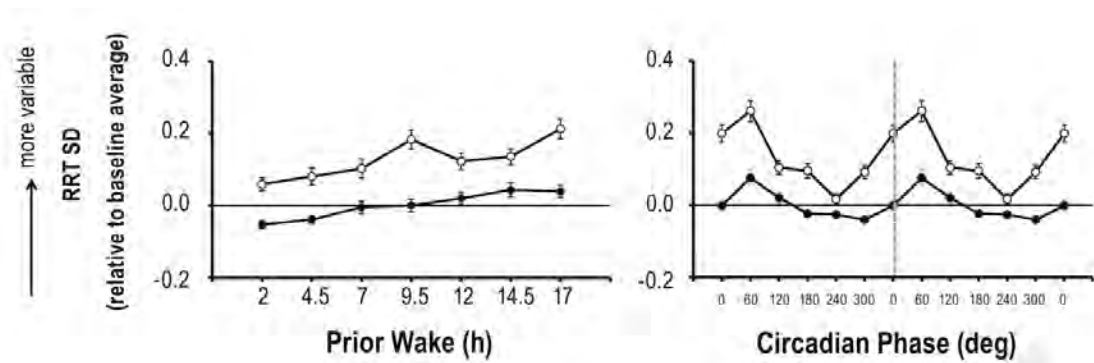
#### *1.4.3.2. Sleep dose and sleep restriction during forced desynchrony*

Until recently, FD protocols investigating the regulation of neurobehavioural performance have maintained the duration of sleep/wake opportunities consistent with proportions recommended for a 24-h day (Belenky et al., 2003; Van Dongen et al., 2003). For protocols with 20-h and 28-h sleep-wake cycles, this has resulted in scheduled sleep opportunities of 6.67 h and 9.33 h and scheduled wake periods of 13.33 h and 18.67 h, respectively (Dijk et al., 1992; Wright et al., 2002; Wyatt et al., 1999). While satisfactory for most purposes, keeping sleep at this dosage limited the capacity to understand the circadian-homeostatic regulation of performance under conditions of high sleep pressure. Cohen et al. (2010), Zhou et al. (2010, 2011), Matthews et al. (2012a, 2012b), and others have addressed these issues in the last few years by incorporating wake extension and/or sleep restriction into their protocols as an additional factor. In addition to the traditional 1:2 ratio, these studies have included protocols with sleep-to-wake ratios ranging from 1:3 for moderate sleep restriction (equivalent to 6 h TIB per 24 h), to 1:5 for severe sleep restriction (equivalent to 4 h TIB per 24 h) (Matthews et al., 2012b; Zhou et al., 2011).

One of the first studies to depart from a traditional 1:2 allocation of sleep and wake during force desynchrony was conducted by Cohen et al (2010), for the purpose of investigating both the chronic and acute effects of sleep loss on neurobehavioural function. In their study, the sleep:wake ratio was manipulated across 42.85-h cycles over three weeks in two different FD protocols. While sleep and wake were maintained at 1:2 in a control protocol, the ratio in the sleep restriction protocol was reduced to 1:3.3 (equivalent to 5.6-h of time in bed per 24 h). As such,

participants recurrently experienced acute sleep loss during 32.85 h of sustained wakefulness per 42.85-h cycle, and chronic sleep loss in the form of a reduced sleep-to-wake ratio over three weeks. Cohen et al (2010) observed that with each successive week, sleep restriction accelerated the rate of decline in performance over time awake except for the first few hours after waking. The lack of impairment early in each wake period suggests the 10-h sleep opportunities were able to dissipate homeostatic sleep pressure accumulated due to acute sleep loss in the preceding 32.4 h wake period. However, the increased rate of performance decline observed across the remaining portions of wake in this study indicates that apparent recovery from acute sleep loss can mask the cumulative chronic impact of long-term sleep loss.

Of all the FD studies to investigate the influence of multiple different sleep doses on performance at different combinations of prior wake and circadian phase, the first published and most widely cited is that of Zhou et al. (2011). In their study, Zhou and colleagues compared a standard sleep dose of 9.33 h TIB per 28 h with a severely restricted sleep dose of 4.67 h TIB per 28 h. Included as measures of neurobehavioural function were response time, lapses, and response time variability (i.e., the SD of response times), all derived from the PVT. Zhou et al. (2011) found that all measures exhibited main effects of, and interactions between, circadian phase and prior wake consistent with the earlier studies of Dijk et al. (1992) and Wyatt et al. (1999). While they did not observe any main effects of sleep dose (9.33 h v 4.67 h), Zhou and colleagues (2011) did observe significant 2-way interactions of sleep dose  $\times$  prior wake and sleep dose  $\times$  circadian phase. The first of these interactions demonstrated that sleep restriction produces significantly worse (i.e., slower) and more variable performance than a standard sleep dose at 9.5 h and 17.5 h of prior wake (Figure 1-14, below). The second interaction demonstrated that sleep restriction produces significantly worse and more variable performance than a standard sleep dose, predominantly around the temperature nadir (Figure 1-14). As there were no 3-way interactions, prior wake did not modulate the impact of sleep restriction around the circadian nadir. That is, sleep restriction results in significantly poor night-time performance, even following short durations of wakefulness.



**Figure 1-14** Depictions of the 2-way interactions of sleep dose with prior wake and circadian phase on response time variability. Prior wake and circadian phase are depicted on the x-axis. Response time variability relative to baseline is depicted on the y-axis. Open circles depict values during restricted sleep and black circles depict values during standard sleep [Figure and legend adapted from Zhou et al. (2011)].

#### 1.4.3.2.1. Investigating task-dependent effects of sleep dose, circadian phase, and prior wake by means of forced desynchrony.

As previously discussed in section 1.4.2.3 (p.59), it has long been recognised that sleep loss does not affect performance on all tasks in all cognitive domains the same way (Drummond et al., 2004; Harrison & Horne, 1998; Harrison, Jones, & Waterhouse, 2007). However, while there has been research into the differential effects of sleep-wake regulatory processes on various cognitive domains during forced desynchrony (Burke et al., 2015; Wright et al., 2002), there has been comparatively little which has also incorporated sleep dose as a factor. This is an important area to expand research because sleep restriction, circadian phase and prior wake all have significant effects on their own and understanding how they interact for complex tasks could inform strategies to counter adverse effects (Matthews et al., 2012a, 2012b).

#### 1.4.4. Split-Sleep Studies

The sum of research into the homeostatic-circadian regulation of neurobehavioural performance indicates that sleep dose, prior wake, and circadian phase are all contributing factors that interact and are dependent on each other. Where one factor is not ideal for performance, deficits may be mitigated by the other two. For example, deficits attributed to being awake at an adverse circadian phase may be mitigated by ensuring sufficient sleep has been obtained during the day and wakefulness is not prolonged beyond the habitual duration (Bonnet, 1991). Similarly, a deficit attributed to insufficient sleep may be moderated by ensuring wakefulness coincides with the circadian acrophase and does not extended beyond the habitual duration (Belenky et al., 2003). While adjusting sleep duration or sleep timing may be satisfactory for sustaining performance in most circumstances, in many situations – such as shiftwork – obtaining an adequate amount of sleep can be difficult both during the day and the night. In such cases, “split sleep” strategies are often employed as non-pharmacological, non-photic alternatives to maintain performance by reducing the duration of wakefulness between sleep episodes (Bonnefond et al., 2004; Bonnet, 1991; Ficca, Axelsson, Mollicone, Muto, & Vitiello, 2010; Roach et al., 2011; Ruggiero & Redeker, 2014). Typically, “split sleep” schedules refer to arrangements that allow for two or more sleep episodes per 24-h period, rather than one (Jackson, Banks, & Belenky, 2014). As defined by Jackson et al. (2014), this includes arrangements where a main sleep is supplemented by one or more naps; where sleep is divided into two main periods of similar duration; or where multiple naps are scheduled with no main sleep. The following sub-sections will summarise findings regarding the effects that different napping and split sleep-wake schedules have on neurobehavioural performance and alertness.

##### *1.4.4.1. Napping protocols*

A significant amount of research has been conducted into the effectiveness of naps at counteracting sleep loss and sustaining neurobehavioural function by alleviating sleep pressure (Dinges et al., 1987; Ficca et al., 2010; Rosekind et al., 1995). Much of this has focused on night-time function because, where performance is

concerned, naps are often obtained in relation to the night shift (Rosa, 1993; Sallinen et al., 2003). The usefulness of naps is generally supported by research, but the extent of their benefits is often dependent on factors related to their duration and timing relative to the night shift – i.e., whether naps are obtained during the shift or taken prophylactically prior to work (Bonnefond et al., 2004; Bonnet, Gomez, Wirth, & Arand, 1995; Centofanti, Hilditch, Dorrian, & Banks, 2016; Ficca et al., 2010; Hilditch et al., 2016; Howard, Radford, Jackson, Swann, & Kennedy, 2010; Lovato, Lack, Ferguson, & Tremaine, 2009).

#### 1.4.4.1.1. *Compensatory naps.*

Compensatory naps obtained during the night, ranging from 30 min to 4 h long, have been shown to alleviate accumulated fatigue and improve night-time performance (Ficca et al., 2010; Ruggiero & Redeker, 2014). Sallinen, Härmä, Åkerstedt, Rosa, and Lillqvist (1998) showed that naps of either 30- or 50-min duration taken at 0100 h or 0400 h were sufficient to improve performance at the end of the night shift compared to no naps. In the field, Bonnefond et al. (2001) observed that industrial workers provided with a 1-h nap opportunity between 2330 h and 0330 h reported progressive improvements in alertness and satisfaction. Similarly, Takahashi et al. (1999) found that a 2-h nap opportunity was sufficient to improve alertness in nurses on 16-h night shifts.

It is not convenient in all workplaces to accommodate long naps during the night shift, but the effectiveness of shorter compensatory naps is mixed and dependent on the time of night obtained (Ruggiero & Redeker, 2014). For instance, Centofanti et al. (2016) found that a 30-min nap opportunity ending at 0400 h was not long enough to improve overall performance during the night, but it was long enough to induce temporary deficits due to sleep inertia (Hilditch et al., 2016). In contrast, Purnell et al. (2002) found that a 20-min nap obtained on shift earlier in the night, between 0100 h and 0300 h, was sufficient to improve performance. Similarly, Lovato et al. (2009) were able to demonstrate the usefulness of a 30-min nap opportunity scheduled at 0230 h – 0300 h, when obtained in conjunction with a 2-h prophylactic daytime nap (1500 h – 1700 h). Although the nap resulted in some temporary declines due to sleep inertia, consistent with Hilditch et al. (2016),

napping earlier during the night facilitated better performance from 0400 h to 0700 h overall (Lovato et al., 2009).

#### 1.4.4.1.2. *Prophylactic naps.*

Prophylactic naps have also been shown to be helpful. Macchi et al. (2002) and Ranney et al. (1999) showed that 3-h nap opportunities in the early afternoon (1400 h to 1700 h) to supplement prior partial sleep restriction extended benefits to night-time function. Professional long-haul drivers who napped demonstrated significant improvements in alertness, neurobehavioural performance and simulated driving from 2400 h to 0730 h compared to when they did not (Macchi et al., 2002; Ranney et al., 1999). Bonnet (1991) and Bonnet et al. (1995) published dose-response studies on the various effects of prophylactic naps on subsequent performance and alertness across two nights of sustained wakefulness. Well-rested participants were randomly assigned to either a condition of total sleep deprivation (0 h of time in bed) or an afternoon nap condition comprising 2 h, 4 h, or 8 h of time in bed, staggered to end at 2000 h. In both studies it was found that performance and alertness across the first 24 h improved significantly for all nap conditions compared to total sleep deprivation in a dose-responsive manner: a long nap was better than a short nap, and a short nap was better than no nap. The benefits of the different naps did not extend beyond 30 h of sustained wakefulness. Bonnet et al. (1995) also compared the effects of the prophylactic naps with those of caffeine administered during the night. Caffeine was better than placebo and of similar value as short naps. However, it was not as effective, nor its benefits as long-lasting, as an 8-h nap (Bonnet et al., 1995).

#### 1.4.4.1.3. *Napping to counteract the first night shift effect.*

Sleepiness and neurobehavioural impairment are often reported to be particularly poor on the first night shift in a roster (Folkard, 1992; Hansen, Geving, & Reinertsen, 2010; Purnell, Feyer, & Herbison, 2002; Santhi, Horowitz, Duffy, & Czeisler, 2007). This is because, in addition to requiring wakefulness at an adverse circadian phase, the transition from daytime to night-time work is frequently associated with extended wakefulness and sleep deprivation (Åkerstedt, 2003; Knauth et al., 1980; Lamond et al., 2003; Santhi et al., 2007; Tepas, Walsh, &

Armstrong, 1981). Strategic napping has been investigated as a means of ameliorating performance decline on the first night shift to ease the transition to a night roster (Ruggiero & Redeker, 2014). Purnell et al. (2002) implemented a field-based study in which workers were permitted a single 20-min nap (between 0100 h and 0300 h) during two consecutive night shifts in one condition, and no nap in a control condition. Testing the workers before and after each shift, Purnell and colleagues found that a single 20-min nap was long enough to significantly improve performance measured at the end of the first shift but not on the second shift. This may be due to an overall reduction of sleep pressure by the end of the second night shift compared to the first, since participants had slept during the day.

While Purnell et al. (2002) found that a 20-min compensatory nap opportunity during the night can mitigate performance decline associated with the first shift, it is not clear to what extent a short prophylactic nap could also mitigate decline on this shift. Several studies regarding the efficacy of napping before night work show that it can improve performance across various periods of extended wakefulness (Bonnet, Gomez, Wirth, & Arand, 1995; Schweitzer et al., 2006). However, these studies have not compared improvements on the first night shift with performance on subsequent shifts. Conversely, studies that *have* evaluated performance across multiple night shifts and have identified the first night to be particularly poor, have not evaluated the efficacy of a prophylactic nap (Hansen et al., 2010; Lamond et al., 2004; Santhi et al., 2007). Understanding the extent of benefits associated with napping would help workers employ strategies that improve worktime function.

#### *1.4.4.2. Split sleep-wake protocols*

Several split sleep-wake protocols have been employed over the last several decades to elucidate the effects that non-monophasic arrangements of sleep have on performance and alertness at different times of day. Various, these protocols have been conducted in the laboratory to either: (i) simulate split work-rest schedules that permit multiple sleep opportunities per day, such as the rapidly rotating, short work-rest watch-keeping rosters employed in maritime operations (see section 1.1.1, p.3); or (ii) advance the theoretical understanding of the sleep-wake system and the effects of dividing sleep episodes on waking function.

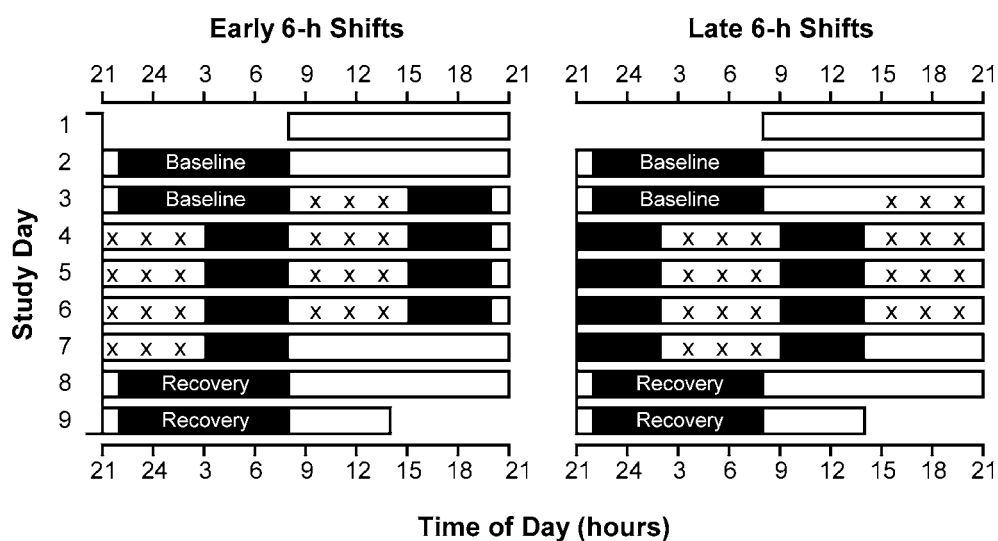


#### 1.4.4.2.1. *Effects of simulated split work-rest rosters.*

Regarding the first of these aims, Eriksen, Gillberg, and Vestergren (2006) monitored changes in sleepiness during a 66-h laboratory simulation of a rapidly rotating “6-h on/6-h off” watch-keeping schedule. This was because, of the few previously published investigations of fatigue in ship watch-keeping systems, most primarily described changes in physiological and behavioural rhythms across sea voyages that were not able to control for confounding factors, such as “actual” rather than “rostered” work durations (Colquhoun, 1985; Colquhoun, Blake, & Edwards, 1968; Colquhoun et al., 1988). Further, the previous studies monitored “4-h on/8-h off” schedules, while the “6-h on/6-h off” schedule, which requires the employment of only two alternating crews rather than three, has become increasingly popular (Eriksen et al., 2006). Under experimental conditions, Eriksen et al. (2006) were able to control for the sequence of watches participants undertook, as well as the duration of the “journey”. The results of their study showed participants were significantly sleepier during the two simulated 6-h watches from 2400 h to 1200 h, adjacent to the circadian nadir of body temperature, than they were during the afternoon and evening watches. The results also revealed sleepiness significantly increased across all watches, except for the 0600 h – 1200 h watch, evidence of a homeostatic influence (Eriksen et al., 2006).

More recently, Short et al. (2016) conducted a similar laboratory protocol with the aim of addressing limitations in the Eriksen et al. (2006) study. In addition to simulating a 4-day “6-h on/6-h off” watch-keeping schedule, their protocol also included objective measures of sleep and performance, as well as an initial baseline day of consolidated night-time sleep and daytime wakefulness for comparison. Participants were permitted 10 h of time in bed during the baseline night, and 5 h of time in bed during each of the two 6-h rest breaks per day in the simulated roster. Two “crews” of participants completed separate complementary conditions to achieve 24-h coverage for the four alternating 6-h watches in the schedule (Figure 1-15, p.72). Short et al. (2016) observed no overall differences between the baseline day and the rest of the protocol in terms of sustained attention on the PVT. However, consistent with the findings by Eriksen et al.

(2006), performance did exhibit circadian fluctuations, such that response times were slower during the simulated night shifts. Although participants reported feeling sleepier during the 4-day simulated roster than the baseline day, sleepiness did not get progressively worse across the protocol. The absence of cumulative deficits during this study indicates that split work-rest rosters lasting several days are not inherently detrimental to neurobehavioural function, though precautions are still be necessary to address nocturnal deficits.



**Figure 1-15** Diagram of the two complementary 6-h on/6-h off “early” and “late” shift schedules simulated by Short et al. (2016). Time of day is described across the x-axis, and study day is listed along the y-axis. Black boxes indicate scheduled time in bed, and crosses indicate test sessions. [Figure based on the description in Short et al. (2016)].

#### 1.4.4.2.2. Comparisons of consolidated and split-sleep schedules.

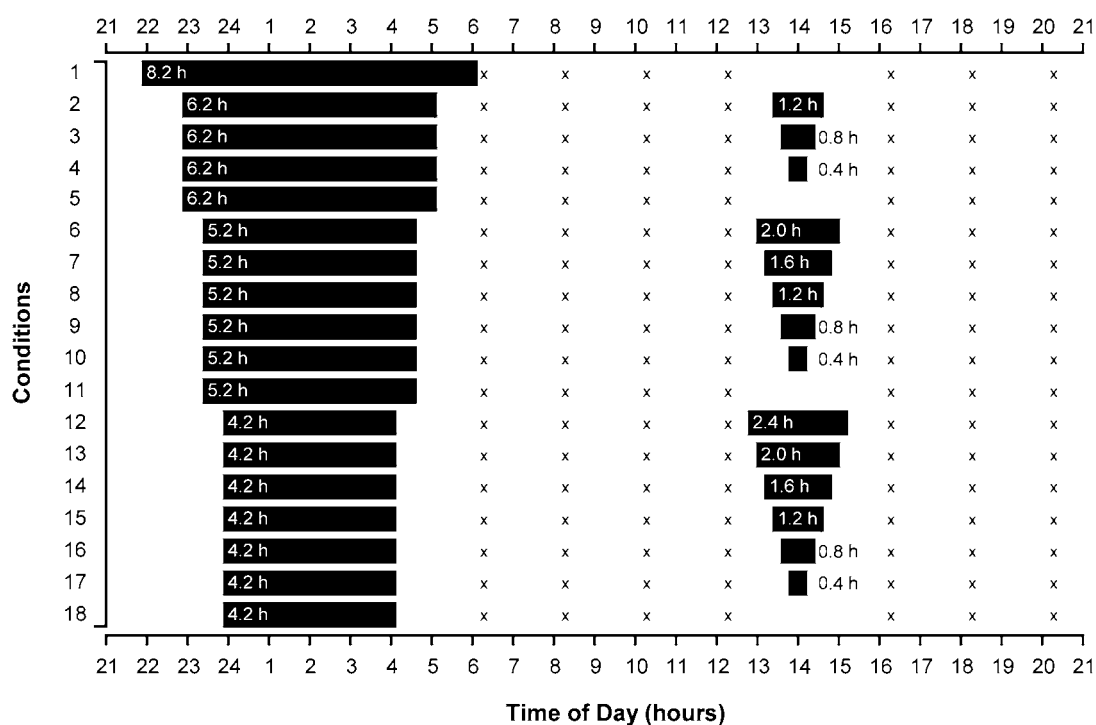
The first experiment to directly compare the effects of consolidated- and split-sleep schedules was conducted by Nicholson et al. in 1985. In this study, daytime performance was assessed following 8 h of time in bed in two counterbalanced conditions. In one condition, the entirety of time in bed comprised a single 8-h episode at night (2300 h – 0700 h). In the other condition, time in bed was obtained in two 4-h episodes, one in the evening (1800 h – 2200 h) and one in the morning (0800 h – 1200 h), separated by 10 h of wakefulness during the night (Nicholson et al., 1985). The overall finding of this experiment was that there were

no differences in performance between the conditions on various neurobehavioural tasks. However, since performance was assessed during the daytime, the authors were not able to make conclusions regarding the effects of splitting sleep on night time function. Further, the protocol only permitted comparisons of performance following a single night of split- or consolidated sleep, and was designed such that it could not disentangle the interaction between circadian and homeostatic processes or comment on the effects of total sleep duration (Nicholson et al., 1985).

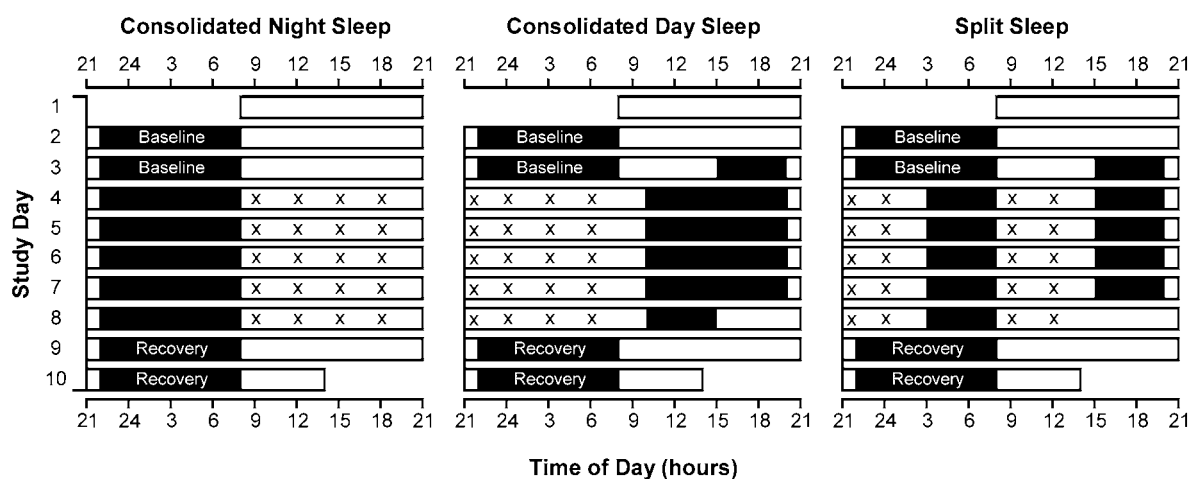
Several of these limitations in Nicholson et al. (1985) were addressed by Mollicone, Van Dongen, Rogers, and Dinges (2008), who sought to determine whether split sleep schedules are feasible for safety-critical operations, specifically space flight, when opportunities for night-time sleep are restricted. Participants in their study were assigned to one of 18 conditions maintained for 10 days, comprising different combinations of major “anchor sleep” opportunities at night (ranging from 4.2 h to 8.2 h) and daytime naps of varying length (ranging from 0 h to 2.4 h) (See Figure 1-16, p.75). Neurobehavioural performance was measured in each of these conditions at regular intervals during the day. In doing this, Mollicone et al. (2008) could make conclusions about the benefits (or not) of obtaining a long night-time anchor sleep episode over a short anchor sleep supplemented by a daytime nap. Their overall results were consistent with those of the dose-response sleep restriction studies previously described (section 1.4.2.2, p.58); performance was primarily dependent on total time in bed per day, with less time in bed resulting in greater impairment, both immediately and across successive days (Mollicone et al., 2008). These findings suggest that, provided the same total opportunity for sleep, split sleep-wake schedules are not inherently worse than consolidated schedules, at least for daytime performance.

Since the majority of research that has supported splitting sleep as a feasible option for sustaining performance has neither accounted for major sleep opportunities during the day nor performance at night, these issues were targeted by Jackson et al. (2014). Similar to the protocol by Short et al. (2016), Jackson et al. (2014) developed three laboratory protocols that allocated participants 10 h of

total time in bed per day, either consolidated at night, consolidated during the day, or split into two short 5-h opportunities, for 5 consecutive experimental days (Figure 1-17, p.75). Overall, performance measured during the day and the night of the split schedule was not significantly different from either daytime performance following consolidated night-time sleep opportunities or night-time performance following consolidated daytime sleep opportunities. Participants scheduled to the



**Figure 1-16** Representation of a single day of each condition in the dose-response split-sleep experiment conducted by Mollicone et al. (2008). Time of day is described across the x-axis, and conditions 1 to 18 are listed along the y-axis. Black boxes indicate scheduled time in bed, and crosses indicate performance testing sessions common to all conditions. The regimens depicted for each condition were maintained for 10 days. [Figure based on the description in Mollicone et al. (2008)].



**Figure 1-17** Schematics of the consolidated and split sleep schedules conducted by Jackson et al. (2014). Time of day is described across the x-axis, and study day is listed along the y-axis. Black boxes indicate scheduled time in bed, and crosses indicate test sessions. [Diagram adapted from Jackson et al. (2014)].

daytime sleep condition did, however, obtain significantly less sleep while in bed and felt sleepier than participants in the other two conditions. These results reinforce the conclusions of Mollicone et al. (2008) that splitting sleep does not impair function overall and support the proposition that split schedules may reasonably be employed where it is not practicable to obtain a single consolidated sleep at night. However, given Jackson et al (2014) only conducted one of the two possible complementary split sleep-wake schedules, they were still not able to indicate how the schedule affected performance at all times of day. Further, it remains to be seen whether homeostatic and circadian processes have different independent and interactive effects on performance during split sleep-wake schedules compared to consolidated sleep-wake schedules.

#### 1.4.5. Summary: Known Unknowns about the Effects of Split-Sleep Schedules and Daytime Sleep Strategies

In summary, the aforementioned studies of neurobehavioural performance show that sleep restriction and sleep deprivation can have both acute and chronic consequences for performance deterioration; that, performance worsens with increasing prior wakefulness, due to accumulating homeostatic sleep pressure, and declines around the daily body temperature minimum, due to the dissipating alerting signal of the circadian pacemaker; and that the interaction of circadian and homeostatic processes can mitigate and exacerbate the response to sleep loss. Research with napping protocols indicates that naps can be successfully employed in the afternoon, evening and during the night to ameliorate declines in nocturnal function. More recent research suggests that it is not necessary for sleep to be obtained in a single episode to sustain waking function, that the total amount of sleep is most important.

While the evidence indicates that short work-rest schedules that permit napping and split-sleep episodes may be viable alternatives to traditional shift schedules, the research to date could be extended. For instance, the studies of Nicholson et al. (1985), Jackson et al. (2014), and Short et al. (2016) did not investigate split sleep-wake schedules at all times of day and only did so at fixed pairings of prior

wakefulness (homeostatic sleep pressure). Confounding homeostatic and circadian processes in this way means it is not clear how a split work-rest schedule affects neurobehavioral performance and sleepiness at a given time of day, following a given amount of prior wakefulness, compared to a consolidated schedule. Further, it is not known how these split schedules affect performance on different neurobehavioural tasks, which utilise various cognitive processes, when sleep is restricted. These are questions that may only be addressed through the use of a forced desynchrony protocol.

## **1.5. Thesis Research Aims**

### **1.5.1. Chapter 3 and Chapter 4**

It is important to ensure participants in laboratory studies are well-rested prior to entering the laboratory so that findings can be attributed to the manipulation of sleep schedules after arrival. Rather than use PSG, this is usually achieved with a combination of sleep diaries and actigraphy with wrist-worn activity monitors or other devices that estimate sleep (Section 1.3.1.2, p.36). The aims of the first two studies in this dissertation were to validate the ability of several wrist-worn activity monitors and a wireless sleep-staging system at estimating sleep and wake (Chapter 3); and to develop a simple objective method of ensuring participants comply with pre-study instructions to wear the activity monitors (Chapter 4).

### **1.5.2. Chapter 5**

Split work-rest schedules may be useful for providing 24-h coverage of shifts and sustaining performance around the clock in safety-critical industries (section 1.1.3 p.9). However, previous investigations into the utility of split sleep-wake schedules on performance have usually only assessed it during the daytime and/or confounded the influence of the homeostatic and circadian processes (section 1.4.4.2, p.70). In Chapter 5, the aim of this dissertation was to expand on previous research by systematically comparing the effects of these processes on neurobehavioural performance during split and consolidated sleep-wake schedules by means of forced desynchrony.

### **1.5.3. Chapter 6**

Simple neurobehavioural tasks are often used as proxies for more complex real world tasks. However, the effects of sleep loss on performance vary for tasks that require different skills or utilise different cognitive processes – and these effects can change across different circadian phases (Section 1.4.3.2.1, p.66). The primary aim of Chapter 6 was to assess the effects of severe sleep restriction on simulated driving, performance on different neurobehavioural tasks, and subjective



measures of alertness, during a split sleep-wake forced desynchrony schedule. The secondary aim of this chapter was to determine which measures best predicted impairments in simulated driving due to sleep restriction at different circadian phases.

#### 1.5.4. Chapter 7

Night workers approach daytime sleep between consecutive shifts with different strategies, according to personal preference, that can be broadly categorised into three main types. These strategies include sleeping immediately following the night shift, delaying sleep to reduce time awake before the subsequent night shift, and splitting sleep – obtaining some immediately and delaying the remainder (section 1.1.4, p.11). The evidence to support any one of these approaches as optimal for sustaining night-time function is limited, particularly for long night shifts (section 1.4.5, p.76). Therefore, the aim of Chapter 7 was to determine whether there is an ideal arrangement of daytime sleep between consecutive night shifts by comparing their effect on performance during simulated 12-h night shifts.

#### 1.5.5. Chapter 8

Performance during the first night shift in a roster is prone to impairment by sleep deprivation often associated with the transition to a night-time schedule. Prophylactic napping before night shifts is often done to mitigate the deterioration of performance and is likely to be particularly beneficial for the first shift (section 1.4.4.1.3, p.69). As such, the final study of this dissertation assessed whether a 1-h nap prior to a simulated first 12-h night shift was sufficient to mitigate significant performance deficits compared to a subsequent shift.

## **Chapter 2.**

### **General Methods**

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## 2.1. Ethics

The studies included in this thesis received ethics approval from the Central Queensland University Human Research Ethics Committee and the University of South Australia Human Research Ethics Committee, following guidelines established by the National Health and Medical Research Council of Australia. Participants were informed about the procedures involved in their respective studies. Participation in these studies was voluntary, and participants were advised that they could withdraw from the research at any time. Participants provided informed consent, in writing, prior to commencement.

## 2.2. Participants

### 2.2.1. Recruitment

Interest in participation was sought from the general public. Recruitment Flyers were pinned to notice-boards in South Australian-based university campuses and metropolitan Adelaide backpackers' hostels (Appendix A). Advertisements were also placed on the popular classifieds website 'Gumtree.com.au' and sent to subscribers of South Australian universities' job seekers mailing lists. Information Sheets (Appendix B) and General Health Questionnaires (Appendix C) were emailed in response to expressions of interest. Volunteers who returned a completed questionnaire, met the inclusion criteria, and did not meet exclusion criteria were invited to the laboratory for an interview about the protocol requirements and a guided tour. In Protocol 2 and Protocol 3, participant selection was also based on volunteers' regular sleep-wake patterns as determined by a week of wrist actigraphy with a Sleep Diary (Appendix D). After being fully informed about the protocols, selected participants were provided Consent Forms to complete on arrival to laboratory (Appendix E).

#### 2.2.1.1. *Inclusion and exclusion criteria*

For inclusion in the studies, participants had to be 18-35 years old, have a body mass index (BMI) of 18.5 – 25 kg/m<sup>2</sup>, and maintain regular sleep durations of at

least 7 h per night. Volunteers were excluded if they identified as smokers, reported any current medical or psychiatric disorders, or used recreational or prescription drugs. As per guidelines for participation in experimental chronobiology research (Portaluppi, Smolensky, & Touitou, 2010), volunteers were excluded if they had undertaken shiftwork or reported transmeridian (across more than two zones) travel in the previous two months. Volunteers were excluded if they had an Epworth Sleepiness Scale score >10, a Pittsburgh Sleep Quality Index >5, or regularly consumed high quantities of caffeine or alcohol.

#### 2.2.1.2. Participant demographics

A total of 82 volunteers were recruited to participate in one of the three laboratory studies. Three withdrew before completing the forced desynchrony (FD) study for personal reasons. The demographics of the remaining 79 participants are detailed in Table 2-1.

The 45 volunteers participating in the FD study were divided into three between-groups conditions. Thirteen volunteers participated in a FD protocol with a consolidated sleep-wake schedule, 16 participated in a protocol with a split sleep-wake schedule, and 16 participated in a protocol with a sleep-restricted (SR) split sleep-wake schedule. One-way ANOVAs revealed that the three groups did not significantly differ in terms of age, BMI, or self-reported usual bedtime, get-up time, and sleep duration (Table 2-2).

**Table 2-1** Participant characteristics in each study.

Characteristic	Study 1 Single Night Sleep (n=22)		Study 2 Forced Desynchrony (n=45)		Study 3 Night Shifts (n=12)	
	M	SD	M	SD	M	SD
Age (y)	23.85	3.83	22.73	2.73	22.92	5.23
BMI (kg/m <sup>2</sup> )	22.37	2.08	22.30	2.11	22.89	1.38
Bed time (h)	23.49	0.70	23.31	1.13	23.50	1.33
Get up time (h)	8.05	1.05	8.17	1.14	7.88	1.57
Sleep Duration (h)	7.94	1.14	8.06	0.82	7.58	0.70

**Table 2-2** Comparison of participants in forced desynchrony schedules.

Characteristic	Consolidated (n=13)		Split (n=16)		SR Split (n=16)		F(2,42)	p
	M	SD	M	SD	M	SD		
Age (y)	22.46	2.22	22.56	2.87	23.13	3.07	0.25	0.779
BMI (kg/m <sup>2</sup> )	22.25	2.14	22.03	1.88	22.63	2.44	0.31	0.738
Bed time (h)	23.40	0.80	23.02	1.56	23.52	0.82	0.85	0.433
Get up time (h)	8.18	0.92	8.23	1.30	8.09	1.21	0.06	0.941
Sleep Duration (h)	8.13	0.82	8.31	0.66	7.74	0.90	2.16	0.129

SR, Sleep-Restricted

## 2.3. Procedures and Protocols

The laboratory studies reported in this thesis differ in duration, laboratory environment, timing of allocated sleep-wake opportunities, and testing procedures. In common between all studies, however, was that participants were required to maintain regular sleep-wake patterns, with at least 7 h time in bed (TIB) each night, for the week before the commencement of the protocol. Activity monitors (section 2.4.3) and sleep diaries were used to verify compliance on arrival to the laboratory.

### 2.3.1. Study 1 – Single Night Sleep

The single night sleep study was involved in the study reported in Chapter 3. Participants attended the sleep laboratory at the Appleton Institute, Central Queensland University, on two occasions at least one week apart. On each occasion, participants were provided a single 9.5-h sleep opportunity (2200 h–0730 h) in individual bedrooms. During this sleep period, participants wore two activity monitors on their non-dominant wrist and a wireless, dry electrode sleep monitoring system on their forehead. Electrodes were also attached to the face and scalp for polysomnographic sleep monitoring.

### 2.3.2. Study 2 – Forced Desynchrony

Results from the FD protocols are included in Chapters 4, 5 and 6. The FD protocol with the consolidated sleep-wake schedule was conducted in a sleep laboratory at the Centre for Sleep Research, University of South Australia. The FD protocols with split and SR split sleep-wake schedules were conducted in a sleep laboratory at the Appleton Institute, Central Queensland University. Both laboratories are windowless, sound attenuated, and free of external time cues. Lighting in each was maintained at 10-15 lux at the angle of gaze during wake periods and extinguished (<.03 lux) during sleep periods. The target ambient temperature throughout the laboratories during the protocols was 21-23 °C. Participants resided in the laboratories in groups of three or four. Participants were assigned their own separate bedrooms, living rooms, workstations for testing, and bathroom facilities. A communal dining area was available for meal times. In both laboratories, closed circuit television cameras were installed to monitor participant behaviour in all rooms except bathrooms.

#### 2.3.2.1. Consolidated schedule

The consolidated schedule was involved in Chapter 5. This schedule was conducted over 12 chronological days, and is depicted in Figure 2-1A (p.86). The consolidated sleep-wake schedule began with two training days and a baseline day separated by two periods of TIB (2400 h – 0800 h). During training days, participants were habituated to laboratory conditions and introduced to a 1-h test battery of neurobehavioural tasks and subjective scales, which were practised to minimise learning effects. On the baseline day, participants completed five 1-h test batteries beginning 1.5 h after waking, with 2-h intervals, to establish a starting reference level for each participant on each task. Following the baseline day, the FD phase of the protocol began. This FD phase comprised 7 × 28-h sleep-wake cycles of 9.33 h TIB and 18.67 h of wake (equivalent to 8 h TIB / 24 h). Test batteries during the wake periods began 1.5 h after lights were turned on, with subsequent testing conducted every 2.5 h thereafter.

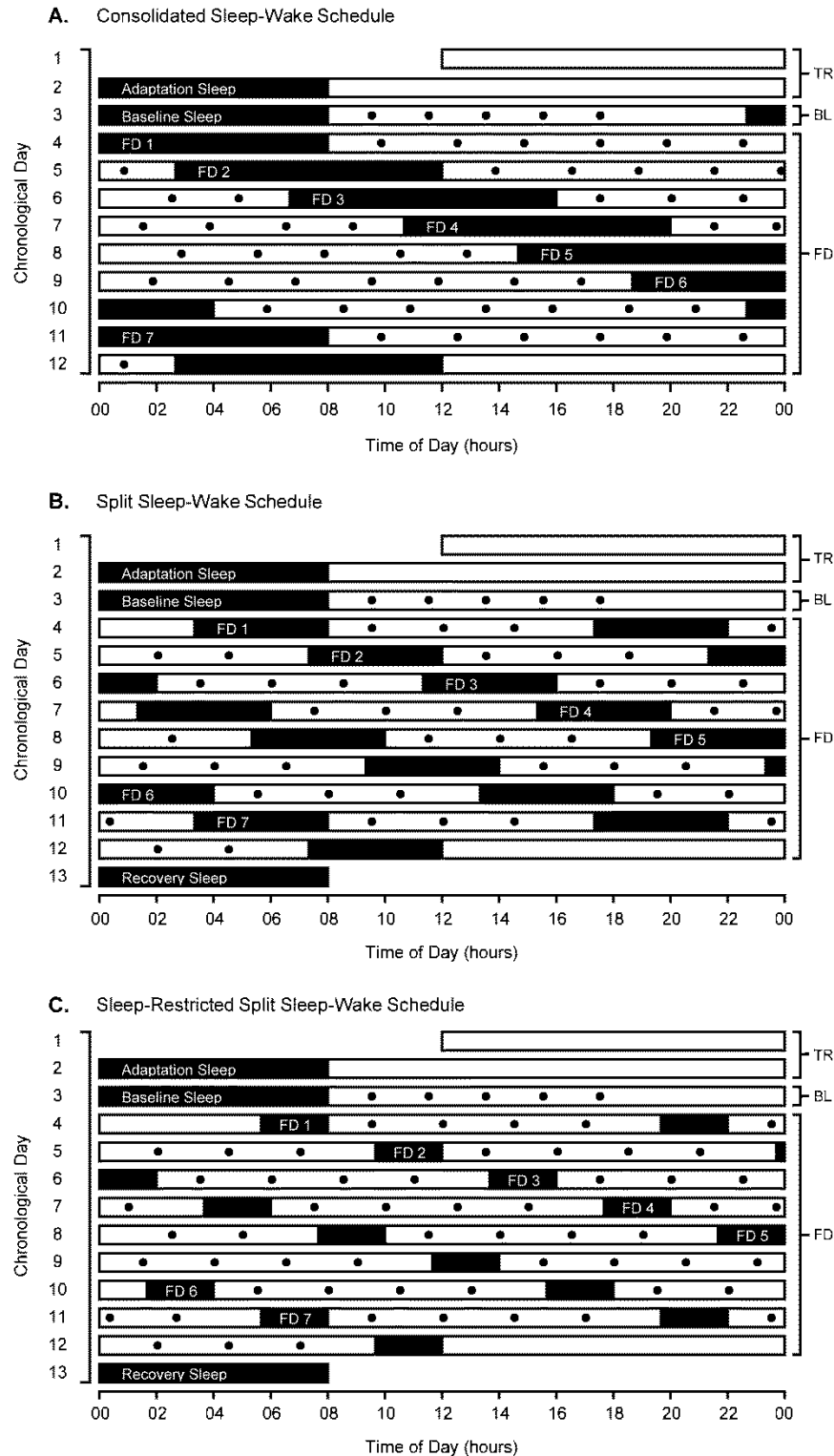
Between bouts of testing, participants were permitted to read, write, watch DVDs, and listen to music in their own living rooms, but were not permitted to undertake any strenuous activities or sleep outside designated periods. Interaction between participants was minimal – limited to meal times occurring 0.5 h ('breakfast'), 7.5 h ('lunch'), and 15 h ('dinner') into each wake period. Research staff monitored the participants' compliance with these instructions in person and via a closed-circuit television system. A montage of electrodes for polysomnography was applied to each participant approximately an hour before schedule sleep periods.

#### *2.3.2.2. Split schedule*

The split schedule was involved in Chapter 4, Chapter 5 and Chapter 6. Training and baseline days in this protocol are identical to that of the consolidated schedule detailed above. During the FD phase, participants obtained the same total sleep opportunity every 28 h as those participating in the consolidated schedule (i.e., 9.33 h TIB). However, the split schedule differs in that each 28-h FD period was divided into two 14-h cycles comprising 4.67 h of TIB and 9.33 h of wake (Figure 2-1B, p.86). As with the consolidated schedule, test batteries began 1.5 h into each wake period and were conducted at 2.5-h intervals. Meal times occurred 0.5 h and 7.5 h after lights were turned on and consisted of 'breakfast' and 'lunch' in the first 14-h cycle, and 'light breakfast' and 'dinner' in the second cycle. Following the FD phase, participants in the split schedule obtained remained in the laboratory for a recovery sleep (2400 h – 0800 h) before departing.

#### *2.3.2.3. Sleep-restricted split schedule*

The SR split schedule was involved in Chapter 4 and Chapter 6. As with the split schedule described above, each 28-h FD period was divided into two 14-h cycles of sleep and wake. The only aspect in which the SR split schedule differs from the split schedule is that TIB was halved during the FD phase to 4.67 h every 28 h (Figure 2-1C, p.86).



**Figure 2-1** Diagrams of the three 28-h forced desynchrony protocols used within this dissertation. Panel A depicts the consolidated schedule, panel B depicts the split schedule, and panel C depicts the SR split schedule. The x-axis indicates clock time across a 24-h period and the y-axis plots successive 24-h periods in the study. Training (TR) days and a baseline (BL) day were followed by a forced desynchrony (FD) phase. Black rectangles represent time in bed. Black circles represent testing sessions.



### 2.3.2.4. Forced desynchrony test battery

The 1-h test battery conducted during the FD protocols included several neurobehavioural tasks and subjective scales, listed in Table 2-3, below. Not all of the tasks from the FD test battery are reported in this thesis. Chapter 5 reports results from the Psychomotor Vigilance Test (PVT), the Karolinska Sleepiness Scale (KSS) and a visual analogue scale (VAS) of pre-test self-assessed ability to perform. As well as these tasks, Chapter 6 reports results from the Digit Symbol Substitution Test (DSST), the Simulated Driving Task, the Serial Addition / Subtraction Test (SAST), and a VAS of alertness. Further information about tasks used in FD protocols is detailed in section 2.4.1., p.90.

**Table 2-3** Tasks included in the 1-h forced desynchrony test battery.

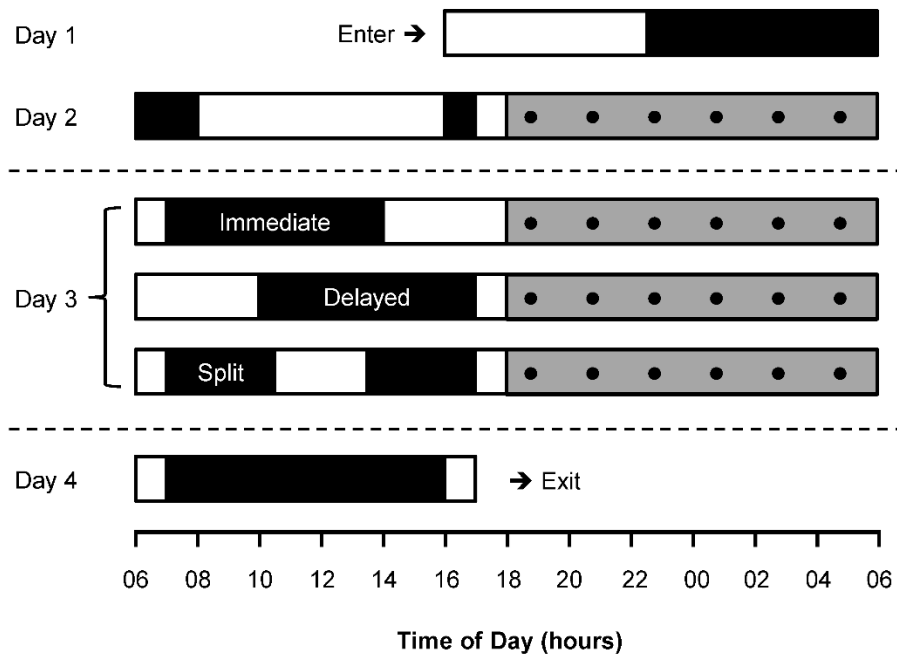
Task	Duration
Profile of Mood States (POMS)	Approx. 10 min
Visual Analogue Scales (VAS)	Approx. 30 s
<ul style="list-style-type: none"> <li>Alertness scale</li> <li>Pre-test performance rating</li> </ul>	
Karolinska Sleepiness Scale (KSS)	Approx. 30 s
Digit Symbol Substitution Test (DSST)	1.5 min
Simulated Driving Task	10 min
Serial Addition and Subtraction Test (SAST)	5 min
Stroop Task	5 min
Psychomotor Vigilance Test (PVT)	10 min
Visual Analogue Scales (VAS)	Approx. 1 min
<ul style="list-style-type: none"> <li>Post-test performance rating</li> <li>Appetite scales</li> <li>Hunger scales</li> </ul>	

### 2.3.3. Study 3 – Simulated Night Shifts

Results from the simulated night shift study are reported in Chapter 7 and Chapter 8. This protocol was conducted at the Appleton Institute and the laboratory was configured to accommodate six participants at a time. Participants had their own bedrooms, living rooms, workstations and bathroom facilities. Participants had access to the time, but were isolated from external environmental cues. Room temperature was maintained at 21-23°C. During wake periods, ambient light was maintained at normal indoor levels (~300 lux). Lights were extinguished (i.e., <.03 lux) during sleep periods.

#### 2.3.3.1. *Schedule*

Participants attended the laboratory on three separate occasions, each covering a 4-day period, exactly one week apart. Each visit consisted of an adaptation night, two 12-h simulated night shifts separated by a daytime sleep opportunity, and a final daytime recovery sleep (Figure 2-2, p.89). The first evening and subsequent morning were used to train participants on the performance tasks. Participants were given 9.5 h TIB (2230 h – 0800 h) on the adaptation night to familiarise them with the sleep monitoring equipment and to eliminate any prior sleep debt. On the following afternoon, participants were scheduled a 1-h nap (1600 h – 1700 h) to prepare for the first night shift. After completing their first simulated night shift (1800 h – 0600 h), participants were provided a 7-h sleep opportunity. On each occasion participants attended the laboratory, the timing of this daytime sleep changed to reflect one of three different types of sleep pattern commonly exhibited by night workers – i.e., an immediate sleep (0700 h – 1400 h), a delayed sleep (1000 h – 1700 h), or a split sleep (0700 h – 1030 h and 1330 h – 1700 h). The order in which the different daytime sleeps were obtained by participants was randomised and counterbalanced between participants. Daytime sleeps were followed by a second night shift (1800 h – 0600 h) and then a 9-h recovery sleep (0700 h – 1600 h). Participants exited the laboratory on the final day at 1700 h. During the simulated night shifts, participants completed a 30-min test battery every two hours (i.e., 6 in total), with the first test battery beginning 30 min after the start of the night shift.



**Figure 2-2** Diagram of the simulated consecutive night shift protocol used within this dissertation. X-axis represents time of day (hours) and y-axis represents days in the protocol. Black rectangles represent time in bed (TIB), and shaded rectangles represent simulated night shifts. Black circles represent 30-min testing sessions. The temporal placement of TIB on Day 3 was dependent on whether participants were undergoing the Immediate, Delayed, or Split sleep condition.

### 2.3.3.2. Night shift test battery

The 30-min test battery conducted during the night shift study included the neurobehavioural tasks and subjective scales listed in Table 2-4. Chapter 7 and Chapter 8 report results from the PVT, the SAST, the KSS, and VAS of alertness and pre-test self-assessed ability. Information about these tasks is detailed in section 2.4.1., p.90.

**Table 2-4** Tasks included in the 30-min test battery during simulated night shifts.

Task	Duration
Profile of Mood States (POMS)	Approx. 10 min
Visual Analogue Scale (VAS)	Approx. 30 s
<ul style="list-style-type: none"> <li>• Alertness scale</li> <li>• Pre-test performance rating</li> </ul>	
Karolinska Sleepiness Scale (KSS)	Approx. 30 s
Samn-Perelli Fatigue Checklist (SPFC)	Approx. 30 s
Digit Symbol Substitution Test (DSST)	1.5 min
Serial Addition and Subtraction Test (SAST)	5 min
Psychomotor Vigilance Test (PVT)	10 min
Visual Analogue Scale (VAS)	Approx. 30 s
<ul style="list-style-type: none"> <li>• Post-test performance rating</li> </ul>	

## 2.4. Materials and Equipment

### 2.4.1. Test Battery

#### 2.4.1.1. Psychomotor Vigilance Test (PVT)

The PVT was used in the studies reported in Chapter 5 to Chapter 8. The PVT is a simple response time task used to measure sustained attention (Dinges & Powell, 1985; Wilkinson & Houghton, 1982). It is performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA) comprising a four-digit LED display and two push-button response

keys on its upper surface (Dorrian et al., 2005). The task requires participants to remain vigilant to the LED display for 10 min, responding to stimuli presented on the display at random at 2- to 10-s intervals, as quickly as possible, by pressing the response key with the thumb of their dominant hand. Response times in milliseconds (ms) appear on the LED display for one second. Increased mean response times (RT) over the 10-min period indicate poorer vigilance and a reduced ability to sustain attention. Four metrics were derived from the 10-min task. These were: the number of lapses (response times  $\geq 500$  ms), the mean reciprocal response time (RRT;  $\text{ms}^{-1} \times 10^{-3}$ ), the mean slowest 10% of RRT ( $\text{ms}^{-1} \times 10^{-3}$ ), and the mean fastest 10% RT (ms). Reciprocals were used for mean and slowest speeds to reduce the contribution of long responses to the overall distribution of response times (Basner & Dinges, 2011; Jewett, Dijk, Kronauer, & Dinges, 1999a). The instructions for the PVT were as follows:

*This task measures your reaction time. As soon as you see the red numbers appear in the top window, press and release the button using your thumb. You must use the button which corresponds to your dominant hand. The numbers in the display show how fast you responded (in milliseconds), with smaller numbers representing faster response times. The aim is to pay close attention to the stimulus window for the full 10 minutes of the task and respond by pressing the button as quickly as possible when you see the red numbers appear. However, do not try to guess or anticipate the stimulus by hitting the button too soon, or an error message (FS) will appear. Also, don't press the other button, or another error message (ERR) will appear. Try your best to get the lowest number you can, whilst avoiding error messages. If you forget to release your finger, the text screen will remind you after a short time.*

#### 2.4.1.2. Simulated Driving Task

The simulated driving task was used in the study reported in Chapter 6. This task was conducted using the York Driving Simulator (YDS; DriveSim 3.0; York Computer Technologies, Kingston, Canada) on a desktop computer, with a wheel

mounted to the desk and acceleration and brake pedals fixed to the floor. This simulation lasts 10 min in duration and emulates a night-time/twilight rural drive on a single carriageway, two-lane road with target speeds of 100 km/h on straight sections and 80 km/h on winding sections. Participants are required to overtake a single car appearing 7 min into the task. Participants are instructed to keep as close to the speed limit as possible, using the pedals as necessary, and to stay within the left lane (standard within Australian). Driving performance was expressed as a function of the variability of the vehicle's position within the lane, i.e., the standard deviation of lateral position (SDLAT). Lane position, sampled in 40-ms epochs, was calculated as the distance in metres from the centre point of the car to the centre of the road. SDLAT was selected to represent driving performance as it is consistently found to be the most fatigue-sensitive continuous driving measure (Åkerstedt et al., 2010; Matthews et al., 2012a; Philip et al., 2003). The instructions for the simulated driving task were as follows:

*This test will assess your performance during a 10 minute simulated drive. At the end of 10 minutes, the test will stop – but you won't actually arrive anywhere. The simulator is configured as a vehicle with automatic transmission. The aim of the test is to drive normally – this means you should drive on the left hand side of the road and steer the wheel with both hands, staying within your lane and within the speed limit. The speed is indicated on the speedometer at the bottom of the screen. The red shape that you see in the middle of your screen is the bonnet of your car – use this to keep within your lane. There are two different speed limits on the track – 110 km/hr on the straight parts of the track and 80 km/hr around corners. The 110 km/h signs are in red and white; the 80 km/h signs are in black and white. The drive simulates a “country drive” at night – there are no intersections or traffic lights. Also, there won't be any other cars travelling in the opposite direction to you. If you come up to a car that is in front of you, just overtake it and drive past it. There is no need to use your indicators during this test. If you crash, press the toggle behind the left side of the wheel to start driving again.*

#### 2.4.1.3. Serial Addition / Subtraction Test (SAST)

The SAST was used in the studies reported in Chapter 6 to Chapter 8. Conducted on a desktop computer, this 5-min task is a measure of cognitive throughput, capturing changes in both sustained attention and declarative working memory (Darwent et al., 2010; DeStefano & LeFevre, 2004; Gunzelmann, Gluck, Moore, & Dinges, 2012; Imbo & Vandierendonck, 2007). Participants were presented a series of single-digit addition and subtraction sums (e.g.,  $9 + 4 = \square$ ,  $3 - 7 = \square$ ) on a computer monitor, one at a time, in white text on a black background. Participants were required to answer as many sums as possible within the timeframe by entering the appropriate positive or negative operator and digit/s on a keypad. New sums were presented 2 to 4 s after the previous response. Performance on this task is determined by the total count of correct responses. The instructions for the SAST were as follows:

*On the computer screen, you will be presented with a series of simple addition and subtraction sums. The format of the sums will be consistent and will be as follows: (1) positive plus positive, (2) positive minus positive, (3) negative plus positive, and (4) negative minus positive. You will need to provide your answer by pressing the correct symbol (either + or -) and digit(s) on the keyboard. You will then need to press enter and this will determine the speed of your response. You must only use the number pad on the right-hand side of the keyboard to enter your answers. There will be a 2 to 4 second pause before the next sum is presented. You will only be able to enter your answers using your dominant hand. The aim of the test is to respond to each sum as accurately and quickly as possible. The test will go for 5 minutes.*

#### 2.4.1.4. Digit Symbol Substitution Test (DSST)

The DSST is included in Chapter 6. The DSST is a measure of cognitive throughput, affected by processing speed, working memory, and visuomotor coordination (Joy, Kaplan, & Fein, 2004; Salthouse, 1978; Wechsler, 1981). In this task, participants are presented a key of ten digits (0 to 9) matched to ten symbols at the top of a sheet of paper. Below this key are rows of blank squares,

each paired with a randomly assigned digit. Using a ballpoint pen, participants are required to create as many digit-symbol pairs as possible in 90 s by drawing the corresponding symbol below each digit. The number of digit-symbol pairs correctly completed in this time served as the performance metric. Although the DSST is susceptible to learning effects (Beres & Baron, 1981), these were minimised by requiring participants to practise the task multiple times during training days. Learning effects were further minimized by presenting participants a new key each testing session, with different digit-symbol combinations. Further, the blank squares in each row were assigned different digits in each testing session. The instructions to participants for the DSST were as follows:

*On the top of the page, you will see a list of symbols with a corresponding list of numbers. The aim of this test is to substitute as many symbols for numbers as possible in the allocated time of 90 secs. You must move from left to right, filling in each box, without leaving any blanks. If you leave a blank box, your score will only be calculated up to that blank box. You must be as accurate and as quick as possible. The symbols must be legible and closely resemble the symbol you are attempting to draw. Symbols will be marked incorrect if they are allocated to an incorrect number OR if they are not legible. If the symbol you have drawn resembles two or more symbols, it will also be marked incorrect.*

#### 2.4.1.5. Visual Analogue Scales (VAS)

Self-assessed ability (Chapter 5 to Chapter 8) and subjective alertness (Chapter 6 to Chapter 8) were both assessed using non-numeric visual analogue scales (VAS). These VAS required participants to answer questions by placing a vertical mark on a 100 mm continuous horizontal line between two diametrically opposed statements. The question ‘how well do you think you will perform?’ (VAS Performance) was anchored by the statements ‘extremely poorly’ on one end and ‘extremely well’ on the other end. Similarly, the question ‘How alert do you feel?’ (VAS Alert) was anchored by the statements ‘struggling to remain awake’ and ‘extremely alert and wide awake’. Participants were told:



*These questions are asking you to rate how well you think you will perform during this test battery and how alert you feel. For each scale, you are required to rate how you feel right now by placing a vertical mark along the horizontal line between the two statements.*

#### *2.4.1.6. Karolinska Sleepiness Scale (KSS)*

In Chapter 5 to Chapter 8, the KSS was used as a measure of subjective sleepiness (Åkerstedt & Gillberg, 1990). On this 9-point scale participants were required to rate their sleepiness by circling the number (1-9) which corresponded to the statement that best described how they were feeling. The instructions to participants were:

*This scale is used to assess how sleepy you feel right now. Please read each statement from 1 to 9, below, and circle the one that best describes how you feel:*

- 1 = Extremely alert,*
- 2 = Very alert,*
- 3 = Alert,*
- 4 = Rather alert*
- 5 = Neither alert nor sleepy*
- 6 = Some signs of sleepiness*
- 7 = Sleepy, but no effort to keep awake*
- 8 = Sleepy, some effort to keep awake*
- 9 = very sleepy, great effort to keep awake, fighting sleep*

### 2.4.2. Polysomnography

In all of the studies reported in this thesis, sleep in the laboratory was assessed using standard polysomnography (PSG) (Keenan & Hirshkowitz, 2011). This comprised electroencephalographic (EEG), electrooculographic (EOG), and electromyographic (EMG) recordings of brain activity, eye movement, and muscle tone, respectively (Keenan & Hirshkowitz, 2011). Recordings were derived using a montage of gold-cup electrodes (Grass™, Astro-Med, Inc., West Warwick, Rhode Island, USA) placed on the face and scalp following the International 10-20 system; two channels for the EEG (C3-M2, C4-M1), two channels for EOG (left and right outer canthi), and three channels of chin EMG (Iber et al., 2007). Prior to application, the placement site of each electrode was scrubbed with NuPrep® Skin Prep Gel (Weaver and Co., Aurora, Colorado, USA) and gauze. Electrodes placed on the scalp (C3, C4, M2, M2) were filled with Elefix™ EEG paste (Nihon Kohden, Tokyo, Japan) and affixed with gauze. Electrodes placed elsewhere were filled with conductive gel (Electro-gel, Electro-Cap International, Inc., Eaton, Ohio, USA) and affixed with Micropore™ (3M™, Neuss, Germany) or Hypafix® (BSN Medical, Hamburg, Germany) tape.

The PSG data were recorded directly to the Graef and E-Series EEG/PSG data acquisition and storage systems (Compumedics Pty Ltd, Melbourne, Victoria, Australia). Sleep records were manually scored by a trained technician, in accordance with established criteria, in 30-s epochs (Iber et al., 2007). Each epoch was classified as a stage of sleep (N1, N2, N3, R) or wake. Sleep measures derived from the scored PSG outputs included total sleep time during time in bed (TIB), and time spent in each stage of sleep during TIB.

### 2.4.3. Wrist Activity Monitors

Activity monitors were used in all studies reported in this thesis. These devices contain omnidirectional piezoelectric accelerometers that sample and convert movement to digital activity counts at 32 Hz (Van de Water et al., 2011) and are worn by participants on the wrist of their non-dominant hand. Two activity monitors were employed – the Actiwatch and the Actical (Phillips Respironics,

Inc., Bend, Oregon, USA). The specifications of each device are described in Table 2-5, adapted from technical information sheets provided by Philips Respironics. The Actiwatch is designed to generate estimates of sleep/wake from patterns of activity (Kushida et al., 2001) and the Actical is designed to generate estimates of energy expenditure (Heil, 2006). However, there is some evidence to suggest that the Actical can also be used for sleep/wake monitoring (Evans et al., 2011; Galland et al., 2012; Robillard et al., 2012; Weiss et al., 2010). The Actiwatch was used in Chapter 3 and Chapter 5, and the Actical was used in Chapters 3 to 8.

**Table 2-5** Actiwatch and Actical activity monitor specifications.

Specifications	Actiwatch	Actical
Weight	16 g	16 g
Dimensions	28 x 27 x 10 mm	29 x 37 x 11 mm
Frequency Range	0 – 7.2 Hz	0.5 – 3.2 Hz
G-force range	0.05 – 10 G	0.05 – 2 G
Sampling rate	32 Hz	32 Hz
Activity count	Peak count per 1-s interval	Mean count per 1-s interval
Activity score	Sum of 1-s counts within an epoch	Sum of 1-s counts within an epoch

In conjunction with sleep diaries, activity monitors were used to assess the sleep-wake patterns of participants for the purpose of participant selection (Chapter 4 to Chapter 8) and to ensure selected participants maintained regular sleep patterns of ~7 h duration per day prior to arrival in the laboratory (Chapter 3 to Chapter 8).

For the FD studies reported in Chapter 5 and Chapter 6, activity counts from activity monitors worn in the laboratory were used to de-mask the effects of physical activity when generating circadian phase estimates (section 2.5, p.99).

#### 2.4.3.1. Actiware sleep software

Actiware-Sleep software version 3.4 (Philips Respironics, Inc., Bend, Oregon, USA) was used to derive sleep and wake estimates from actigraphic data recorded within self-reported bedtimes. This software employs a validated algorithm to generate weighted scores for each 1-min epoch based on its recorded activity count and the activity counts in the surrounding 2-min (Kushida et al., 2001; Oakley, 1997). The equation applied to each epoch is as follows:

$$A = 0.04E_{-2} + 0.2E_{-1} + 2E_0 + 0.2E_{+1} + 0.04E_{+2}$$

Where  $A$  = weighted activity score derived from counts of the current and surrounding epochs;  $E_0$  = activity counts recorded during current epoch;  $E_{-n}$  = activity counts recorded during preceding epochs;  $E_{+n}$  = activity counts recorded during following epochs. Epochs during sleep periods are classified as wake if their weighted scores fall above the specified sleep/wake threshold (default threshold = 40).

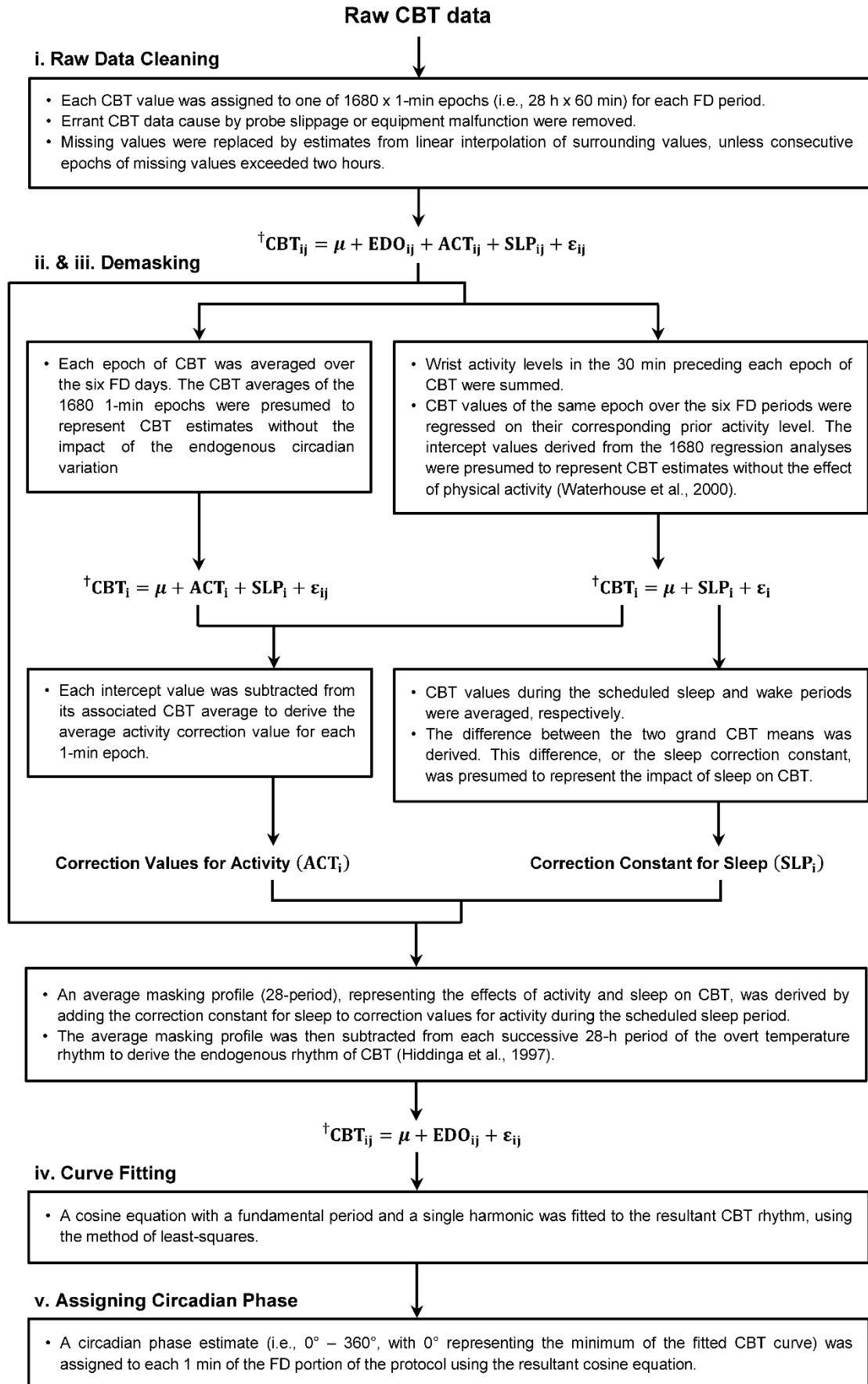
#### 2.4.4. Measurement of Core Body Temperature

Core body temperature was used in the FD studies reported in Chapter 5 and Chapter 6 to estimate circadian phase (section 2.5, p.99). Core body temperature was continuously recorded in 1-min intervals using a rectal thermistor (Steriprobe 491B; Cincinatti Sub-Zero Products, Cincinnati, Ohio, USA) connected to an ambulatory recording device (Mini-logger series 2000, Mini-Mitter, Bend, Oregon, USA). The thermistors were self-inserted 10 cm beyond the anal sphincter and were only removed for bowel movements and whole-body ablutions. While the thermistors were inserted, the ambulatory recording devices were kept in a pouch worn around participants' waists.

## 2.5. Circadian Phase Estimation

Circadian phase estimates in the FD studies reported in Chapter 5 (5.2.4.1) and Chapter 6 (6.2.4.5), were generated for each participant from core body temperature recorded during six 28-h periods (FD 2 to FD 7). These estimates were produced by means of a five-step de-masking process to account for the effects of sleep and physical activity on core body temperature rhythms (Darwent et al., 2010). The method is described in detail in Figure 2-3. Briefly, the first step involved cleaning the raw temperature data to remove erroneous or missing values due to slippage of the thermistor or malfunction of the equipment. The second step involved de-masking physical activity, measured with wrist activity monitors, using a purification of intercepts approach (Hiddinga et al., 1997; Waterhouse et al., 2000). The third step involved de-masking for sleep-wake differences using a sleep-state correction factor (Hiddinga et al., 1997). The fourth step involved fitting a cosine equation with a fundamental period and a single harmonic to the de-masked CBT data using the method of least squares. The final step involved assigning a circadian phase estimate (i.e., 0°–360°, with 0° representing the minimum of the fitted core body temperature curve) to each 1 min of the FD portion of the protocol using the resultant cosine equation.

**Figure 2-3** Flowchart showing the steps involved in estimating circadian phase from core body temperature (CBT). <sup>†</sup>Each epoch of CBT within each FD day is assumed to be a linear combination of the grand mean, the effects of the endogenous circadian system, physical activity level and sleep-wake state; i.e.,  $CBT_{ij} = \mu + EDO_i + ACT_{ij} + SLP_{ij} + \epsilon_{ij}$ , where  $i$  = epoch,  $j$  = FD period, CBT = core body temperature,  $\mu$  = the grand mean of CBT, EDO = the effect of the endogenous circadian system, ACT = the effect of activity level, SLP = the impact of sleep state, and  $\epsilon$  = error term.



## **Chapter 3.**

### **Validation of Alternatives to Polysomnography**

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Wrist Accelerometers and a Wireless Sleep-Staging System

**Peer-reviewed publication associated with this chapter (Appendix F):**

**Kosmadopoulos, A.**, Sargent, C., Darwent, D., Zhou, X., & Roach, G. D. (2014). Alternatives to polysomnography (PSG): A validation of wrist actigraphy and a partial-PSG system. *Behavior Research Methods*, 46(4), 1032-1041.  
<http://dx.doi.org/10.3758/s13428-013-0438-7>.

### 3.1. Introduction

In laboratory-based sleep research, polysomnography (PSG) is the gold standard for measuring sleep. PSG provides detailed information about sleep architecture, sleep duration and sleep quality. However, in field-based settings, this technique is expensive, time-consuming, and impractical because it requires the attendance of a sleep technologist to set up equipment and apply electrodes to multiple sites on the face and scalp (Van de Water et al., 2011). Therefore, a variety of alternative options for objective sleep measurement have been developed. The most frequently employed alternative in the field involves wrist actigraphy (Van de Water et al., 2011). Other alternatives derive sleep stage estimates by approximating PSG and simplifying the means of recording electrophysiological brain signals (Shambroom et al., 2012).

Wrist actigraphy is a method of recording rest and activity patterns using wristwatch-like devices known as activity monitors. The advantage of wrist actigraphy over PSG in the field is that it is simple, non-invasive, unobtrusive, and can be measured for weeks with less inconvenience to participants. Activity monitors contain accelerometers that sample and record movement at regular intervals (Van de Water et al., 2011). Validated algorithms can then be used to calculate sleep/wake estimates based on the amount of activity recorded (low activity being associated with sleep, and high activity being associated with wakefulness) (Cole et al., 1992; Sadeh et al., 1994; Van de Water et al., 2011). Threshold-based algorithms estimate sleep and wakefulness based on whether activity scores, calculated for each epoch (usually 30- or 60-s) during the monitoring period, fall above or below an activity threshold which is set post hoc. Epochs with scores above this threshold during sleep periods are classified as wake (Kushida et al., 2001; Paquet et al., 2007). Lowering the threshold increases their ability to detect wakefulness, but compromises the ability to detect sleep (Hyde et al., 2007; Kushida et al., 2001; Signal, Gale, & Gander, 2005). Although there is an acknowledged tendency of activity monitors to overestimate sleep by misidentifying quiescent wakefulness as sleep, it has not inhibited their use in many studies with different populations (Darwent et al., 2012; Paterson, Dorrian, Pincombe, Grech, & Dawson, 2010; Roach, Petrilli,



Dawson, & Lamond, 2012a; Roach et al., 2012b; Sargent et al., 2014; Tremaine et al., 2013) and the bias has generally been deemed minimal, particularly when used in conjunction with sleep diaries (Carney et al., 2004; De Souza et al., 2003; Jean-Louis et al., 2001; Kanady, Drummond, & Mednick, 2011; Kushida et al., 2001; Paquet et al., 2007; Reid & Dawson, 1999; Rupp & Balkin, 2011; Signal et al., 2005).

Activity monitors are not solely developed for measuring sleep. For example, some devices are designed to produce estimates of energy expenditure from waist actigraphy, using different algorithms (Heil, 2006). Nonetheless, the component technology (i.e., accelerometers) and theoretical basis of these devices (i.e., that movement is positively associated with energy expenditure) are similar to those of activity monitors developed for sleep (Evans et al., 2011). The potential for these devices to produce concurrent estimates of both energy expenditure and sleep/wake patterns has recently been recognised (Evans et al., 2011; Weiss et al., 2010). Recent validation studies support the use of energy expenditure monitors to also measure sleep and wake (Evans et al., 2011; Galland et al., 2012; Kosmadopoulos, Sargent, Zhou, Darwent, & Roach, 2012; Robillard et al., 2012; Weiss et al., 2010). However, for those studies that estimated sleep and wake with energy expenditure monitors using threshold-based algorithms designed for sleep/wake monitors, recommendations have been conditional on selecting a threshold lower than the default for sleep/wake monitors (Kosmadopoulos et al., 2012; Weiss et al., 2010). Increased wake detection and better overall performance at a low threshold, relative to the default medium threshold, has led to speculation that an additional threshold reduction may improve performance further (Kosmadopoulos et al., 2012). However, the extent to which this may inhibit sleep detection is not clear, given the increased wake detection is at the expense of sleep detection.

As movement is only an indirect gauge of sleep and wakefulness, actigraphy is limited to calculating summary measures, such as 'total sleep time' and 'wake after sleep onset'. Therefore, other alternatives to PSG derive sleep-stage information from physiological data obtained using less expensive and time-

consuming methods (Shambroom et al., 2012; Van de Water et al., 2011). Included among these are simplified approximations of PSG which calculate sleep/wake estimates from an amalgamation of electrophysiological signals in the forehead, and take the form of headbands. So far, this form of wireless sleep-staging has been found to agree well with PSG in terms of detecting sleep and differentiating sleep stages (Griessenberger et al., 2012; Shambroom et al., 2012). When compared to results derived from sleep/wake monitors, this method seems better able to identify sleep and wake and its estimations of sleep and wake are more frequently confirmed by PSG (Shambroom et al., 2012). However, selecting sleep-monitoring devices and associated activity thresholds requires knowledge of how well these systems compare against PSG under the same conditions. There has been no systematic evaluation of sleep/wake monitors and energy expenditure monitors, at different sleep/wake thresholds, together in a single study. Similarly, the self-administered wireless sleep-staging system has only been compared with sleep/wake monitors at their default threshold, and not with the energy expenditure monitor. Therefore, the aim of this study was to address these gaps by concurrently evaluating their capacities to distinguish sleep from wake, epoch-by-epoch, and in terms of total sleep time (TST), sleep efficiency, wake after sleep onset (WASO) and sleep onset latency (SOL).

## **3.2. Methods and Materials**

### **3.2.1. Participants**

Participants were 22 young adults (18 male, 4 female) who responded to advertisements placed online and on public noticeboards in Adelaide, South Australia. They were aged  $23.85 \pm 3.83$  years (mean  $\pm$  SD; range = 19 – 30 years) and had a body mass index (BMI) of  $22.37 \pm 2.08$  kg/m<sup>2</sup> (range = 19.05 – 25.10 kg/m<sup>2</sup>). Participants were screened by interview and general health questionnaire. Criteria for inclusion were habitual bedtimes between 2200 h and 2400 h, sleep durations of 7 – 9 h per night, and a body mass index of 18.5 – 25 kg/m<sup>2</sup>. Volunteers were excluded if they reported medical problems, sleep

difficulties, smoking, regular excessive consumption of alcohol or caffeine, or transmeridian travel / shiftwork in the previous two months.

#### *3.2.1.1. Ethics*

This study was approved by the Central Queensland University Human Research Ethics Committee following the guidelines of the National Health and Medical Research Council of Australia. Participants provided written informed consent and were given an honorarium for their involvement.

### **3.2.2. Procedure**

Participants attended the sleep laboratory on 2 occasions, at least one week apart. On each occasion, participants were provided a 9.5-h sleep opportunity (2200 h – 0730 h) in individual bedrooms. During this sleep period, each participant wore both activity monitors on their wrist, a wireless sleep monitoring system on their forehead, and had electrodes attached to their face and scalp for PSG. All sleep-monitoring devices, including the PSG system, stored data in 30-s epochs and were time-synchronised to the same computer clock prior to each sleep period so that corresponding epochs could be aligned (Kushida et al., 2001). Twenty participants attended the laboratory for two non-consecutive night sleeps, and two participants attended for a single night sleep. Forty-two sleep periods were assessed.

### **3.2.3. Sleep Monitoring Systems**

#### *3.2.3.1. Polysomnography*

The gold standard measure of sleep was PSG, conducted using the Siesta Portable EEG system (Compumedics, Melbourne, Victoria, Australia) and Grass<sup>TM</sup> gold-cup electrode leads (Astro-Med, Inc., West Warwick, Rhode Island, USA). Brain activity was monitored with two channels of EEG (C3-A2, C4-A1); eye movement was monitored with right and left EOG, and muscle tone was measured with two channels of chin EMG. Sleep/wake stages were manually

scored from PSG recordings by an experienced sleep technician, in 30-s epochs, following Rechtschaffen and Kales (R&K) criteria (Rechtschaffen & Kales, 1968).

### 3.2.3.2. Activity monitors

The sleep/wake monitor used in this study was the Actiwatch-64 (Mini-Mitter Philips Respironics, Bend, Oregon, USA) and the energy expenditure monitor was the Actical Z-series (Mini-Mitter Philips Respironics, Inc.). Devices were worn on the non-dominant wrist, with the Actiwatch placed closer to the hand. The activity monitors contain an omnidirectional piezoelectric accelerometer and sample movement at 32 Hz. The number of activity counts recorded each second reflects the intensity of movement at that time, with larger counts indicative of increased movement. The total activity count for each user-defined epoch duration is calculated by summing the counts recorded during that epoch. Activity counts for the Actical are consistently lower than for the Actiwatch as it records the mean count per second whereas the latter records the peak.

#### 3.2.3.2.1. Sleep/wake estimation

The sleep/wake monitor's accompanying software (Actiware version 3.4; Mini-Mitter Philips Respironics, Inc.) was used to derive sleep and wake estimates for all epochs recorded using both activity monitors. This software employs a validated algorithm to generate weighted scores for each 30-s epoch based on its activity count and the counts in the surrounding 2-min (Kushida et al., 2001; Oakley, 1997). The equation applied to each epoch is as follows:

$$A = 0.04E_{-4} + 0.04E_{-3} + 0.2E_{-2} + 0.2E_{-1} + 2E_0 + 0.2E_{+1} + 0.2E_{+2} + 0.04E_{+3} + 0.04E_{+4}$$

Where A = weighted activity score derived from counts of the current and surrounding epochs;  $E_0$  = activity counts recorded during current epoch;  $E_{-n}$  = activity counts recorded during preceding epochs;  $E_{+n}$  = activity counts recorded during following epochs. Epochs during sleep periods are classified as wake if their weighted scores fall above the specified sleep/wake threshold. Thresholds for this study include three pre-set thresholds (low = 20, medium = 40, high = 80) and a customised threshold (very low = 10).

### 3.2.3.3. Wireless sleep-staging system

The wireless sleep-staging system used in this study was the Zeo (Newton, Massachusetts, USA). The Zeo is a portable, automatic sleep-staging tool that includes: a headband containing three dry electrodes, which record and transmit electrophysiological signals from the forehead; and a base station that wirelessly receives these signals for analysis (Shambroom et al., 2012). The signals recorded via the headband approximate an amalgamation of the brain activity, eye movement and muscle tone recorded with PSG; the Zeo automatically scores these signals into sleep and wake stages using proprietary algorithms based on R&K criteria (Shambroom et al., 2012). The sleep stages reported by the Zeo system are condensed, such that stages 1 and 2 sleep are reported together as ‘light sleep’, and stages 3 and 4 sleep are reported together as ‘deep sleep’. Wake and REM sleep are reported separately according to the standard definitions. Staff placed the wireless sleep-staging system on participants’ foreheads prior to the start of the sleep period.

### 3.2.4. Epoch-By-Epoch Comparisons

After being aligned with PSG, corresponding epochs from all devices at all thresholds were classified into one of four categories, True Sleep (TS), False Sleep (FS), True Wake (TW), and False Wake (FW), based on their agreement with PSG (see Table 3-1).

**Table 3-1** Sleep/wake agreement matrix.

Device	Polysomnography	
	Sleep	Wake
Sleep	True Sleep (TS)	False Sleep (FS)
Wake	False Wake (FW)	True Wake (TW)

For all of the three devices, five statistical measures of epoch-by-epoch concordance were then calculated from the number of epochs in each category:

*Agreement* =  $[(TS+TW)/(TS+FW+TW+FS)]*100$  = percentage of all sleep and wake epochs correctly detected by the device;

*Sensitivity* =  $[TS/(TS+FW)]*100$  = percentage of sleep epochs correctly detected by the device;

*Specificity* =  $[TW/(TW+FS)]*100$  = percentage of wake epochs correctly detected by the device;

*Positive Predictive Value (PPV)* =  $[TS/(TS+FS)]*100$  = percentage of epochs correctly estimated by the device to be sleep; and,

*Negative Predictive Value (NPV)* =  $[TW/(TW+FW)]*100$  = percentage of epochs correctly estimated by the device to be wake.

Agreement, sensitivity, and specificity indicate the proportion of true sleep and wake epochs (as determined by PSG) with which a device agrees. In contrast, PPV and NPV indicate the likelihood that an estimation of sleep or wake using an alternative to PSG is true.

#### 3.2.4.1. Cohen's Kappa.

Cohen's Kappa ( $\kappa$ ) were calculated based on the epoch-by-epoch device comparisons, to evaluate agreement with PSG beyond what could be expected by chance alone (Sim & Wright, 2005). Agreement was interpreted against guidelines of Landis and Koch (1977), where 0-.20 indicates slight agreement, 0.21-0.40 is fair, 0.41-0.60 is moderate, 0.61-0.80 is substantial and 0.81-1.0 is almost perfect.

### 3.2.4.2. Summary sleep measures

Four summary sleep measures were calculated from the outputs of PSG, the wireless sleep-staging system and both activity monitors:

*Total sleep time (TST)* = the number of minutes asleep in bed;

*Sleep efficiency* = the percentage of time asleep between lights off and lights on;

*Wake after sleep onset (WASO)* = the number of minutes spent awake after sleep onset and before final awakening; and,

*Sleep onset latency (SOL)* = the number of minutes between lights off and sleep onset.

For PSG, sleep onset was defined as the first of three consecutive epochs of Stage 1 sleep, or one epoch of any other stage of sleep (i.e., stages 2, 3, 4 or REM) (Carskadon et al., 1986). As the wireless sleep-staging system collapses stages 1 and 2 together, sleep onset for this device was defined as the first of two consecutive epochs of light sleep or one epoch of deep sleep or REM sleep. Actiware sleep software calculated sleep onset for activity monitors as the first epoch of 10-min of immobility (CamNTEch Ltd., 2008).

Statistical tests of agreement were used to determine how accurate the devices were at estimating the summary measures. As the four summary measures were not normally distributed, Wilcoxon Signed-Rank Tests were conducted to identify which devices and/or thresholds significantly differed from PSG on each of the four measures.

### 3.2.4.3. Bland-Altman technique.

The Bland-Altman technique is a way of comparing alternative measurement methods with a gold standard by plotting the differences between them and analysing the distribution of differences (Bland & Altman, 1986). The differences from TST and WASO, as determined by PSG, were plotted for the wireless sleep-staging system and both activity monitors at their optimal threshold (as determined by post hoc analyses). TST and WASO were chosen

because they are measures that separately describe large proportions of sleep and wake during time in bed and allow for a clear comparison of devices against PSG. Differences in TST and WASO, between devices and PSG, were calculated such that a positive score indicated an overestimation by the device/threshold, and a negative score indicated an underestimation. Pearson correlations were calculated to determine the consistency of differences from PSG, i.e., whether there is a relationship between TST or WASO duration and how much each device differs from PSG.

### **3.3. Results**

Of the 42 nights recorded, one night each of PSG and sleep/wake monitor data and two nights of data for the wireless system had to be excluded from analysis due to technical failure. Results from the remaining 38 complete datasets are reported here.

#### **3.3.1. Epoch-By-Epoch Comparisons**

Compared against PSG epoch by epoch, the sleep/wake monitor correctly identified  $83.5 \pm 6.0\%$  to  $88.0 \pm 9.0\%$  of epochs as sleep or wake, depending on the threshold employed (Table 3-2). Although utilising the high threshold for the sleep/wake monitor accurately identified the most sleep epochs overall, it had the worst specificity and positive predictive value (PPV) relative to the other thresholds for this device; i.e., it misidentified the highest proportion of wake epochs as sleep. The customised very low threshold resulted in the best specificity and the highest PPV for the sleep/wake monitor, but had the worst overall agreement, sensitivity to sleep epochs, and negative predictive value (NPV). In contrast to these extremes, the medium and low thresholds both maintained a high overall agreement, identified more wake epochs than the high threshold and identified more sleep epochs than the very low threshold. The medium threshold was more accurate than the low threshold.

In contrast to the sleep/wake monitor, altering the thresholds did not affect the overall agreement of the energy expenditure monitor. However, they did



influence its sensitivity, specificity, PPV and NPV. The high and medium thresholds were the most sensitive to sleep, but this was at the expense of identifying epochs of wake. In contrast, the low and very low thresholds were slightly less sensitive but had much greater specificity. Of these two thresholds, the very low threshold had the greater specificity and the best PPV.

On average, the wireless sleep-staging system did not define 9 ( $\pm 40.9$ ) epochs with a sleep or wake stage per night. Of these undefined epochs, 96.3% were aligned with an epoch classified as sleep by PSG. Despite this, it correctly identified 91.6% of epochs as either sleep or wake (Table 3-2) and had a sensitivity, specificity, PPV and NPV that were higher than for the sleep/wake monitor at a medium threshold and the energy expenditure monitor at a very low threshold.

**Table 3-2** Mean epoch-by-epoch sleep/wake percentage agreement with PSG for each device and activity threshold.

Devices	Agreement (%)		Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
	M	SD	M	SD	M	SD	M	SD	M	SD
Wireless Sleep-Staging System	91.6	5.1	97.4	4.5	42.2	23.5	93.1	4.4	79.6	23.6
Sleep/Wake Monitor										
<i>Very low</i>	83.5	6.0	87.6	5.6	61.5	16.2	92.8	7.9	39.2	18.1
<i>Low</i>	86.3	6.6	92.5	4.2	49.7	15.5	91.6	8.7	46.4	19.2
<i>Medium</i>	87.7	7.6	95.8	2.7	37.7	14.5	90.4	9.3	52.8	19.4
<i>High</i>	88.0	9.0	97.8	1.6	26.9	13.5	89.3	10.1	59.1	20.4
Energy Expenditure Monitor										
<i>Very low</i>	86.8	8.6	95.0	4.4	36.3	16.3	90.1	9.9	50.9	20.3
<i>Low</i>	87.6	9.1	97.1	2.9	28.1	14.1	89.3	10.1	58.7	21.8
<i>Medium</i>	87.8	9.7	98.5	1.8	19.5	11.3	88.6	10.4	64.5	21.9
<i>High</i>	87.6	10.3	99.2	1.1	12.4	8.6	88.0	10.6	69.4	22.3

Note. N = 38.

PPV, positive predictive value; NPV, negative predictive value.

### 3.3.2. Cohen's Kappa.

Following the criteria of Landis and Koch, Cohen's Kappa coefficients for the activity monitors describe slight to fair sleep/wake epoch agreement with PSG beyond what could be expected by chance (Table 3-3). For the wireless sleep-staging system, it describes a moderate agreement. The results are consistent with the overall agreement of the devices.

**Table 3-3** Mean Cohen's Kappa for each device and activity threshold.

Devices	Cohen's $\kappa$	
	M	SD
Wireless Sleep-Staging System	0.47	0.24
Sleep/Wake Monitor		
<i>Very low</i>	0.35	0.12
<i>Low</i>	0.37	0.12
<i>Medium</i>	0.35	0.12
<i>High</i>	0.30	0.13
Energy Expenditure Monitor		
<i>Very low</i>	0.31	0.12
<i>Low</i>	0.29	0.12
<i>Medium</i>	0.24	0.12
<i>High</i>	0.17	0.11

*Note.*  $N = 38$ .

### 3.3.3. Summary Sleep Measure Comparisons

Mean ( $\pm$  SD) sleep and wake durations determined by each monitoring device are summarised in Table 3-4. For the activity monitors, higher thresholds for wake resulted in longer TST, decreased sleep efficiency, and less WASO (Table 3-4). As SOL for activity monitors is calculated as the duration from bedtime until 10 minutes of consecutive immobility, it remained unchanged irrespective of the sleep/wake threshold. Estimations of TST, sleep efficiency, and WASO using the wireless sleep-staging system were closest to the estimates of the sleep/wake monitor and the energy expenditure monitor when they were calculated using the medium and very low thresholds, respectively.

Significant differences from PSG, as determined by Wilcoxon Signed-Rank Tests (Bonferroni correction,  $p < .006$ ), are indicated in Table 3-4. SOL as determined by PSG was significantly longer than the SOL estimated by the three alternative devices. Even where summary measure estimates were not significantly different from PSG, standard deviations for each device and threshold were large.

At low and medium thresholds, there were no significant differences from PSG in terms of TST and sleep efficiency for the sleep/wake monitor (Table 3-4). The sleep/wake monitor also did not differ from PSG in terms of WASO at medium and high thresholds. For the energy expenditure monitor, low and very low thresholds did not result in significant differences from PSG in WASO, and the very low threshold did not result in significant differences from PSG in TST and sleep efficiency. The wireless sleep-staging system was not significantly different from PSG regarding WASO, but did significantly overestimate TST and sleep efficiency.

**Table 3-4** Mean summary sleep statistics for each device and threshold.

Devices	Total Sleep Time (min)		Sleep Efficiency (%)		Wake After Sleep Onset (min)		Sleep Onset Latency (min)	
	M	SD	M	SD	M	SD	M	SD
PSG	496.2	61.8	86.9	10.8	41.3	47.1	27.1	28.5
Wireless Sleep-Staging System	519.0 *	61.5	90.7 *	10.8	36.0	58.6	11.0 *	11.0
Sleep/wake Monitor								
<i>Very low</i>	461.1 *	42.7	80.9 *	7.5	92.9 *	36.2	11.1 *	12.3
<i>Low</i>	492.0	36.5	86.3	6.4	62.0 *	29.1	11.1 *	12.3
<i>Medium</i>	514.3	30.1	90.3	5.3	39.7	21.5	11.1 *	12.3
<i>High</i>	530.2 *	23.7	93.1 *	4.1	23.7	13.3	11.1 *	12.3
Energy Expenditure Monitor								
<i>Very low</i>	519.2	31.7	91.1	5.5	43.2	28.2	5.1 *	7.6
<i>Low</i>	533.9 *	24.6	93.7 *	4.3	28.4	20.6	5.1 *	7.6
<i>Medium</i>	545.2 *	17.8	95.7 *	3.1	17.2 *	13.7	5.1 *	7.6
<i>High</i>	552.6 *	13.8	97.0 *	2.4	9.7 *	8.9	5.1 *	7.6

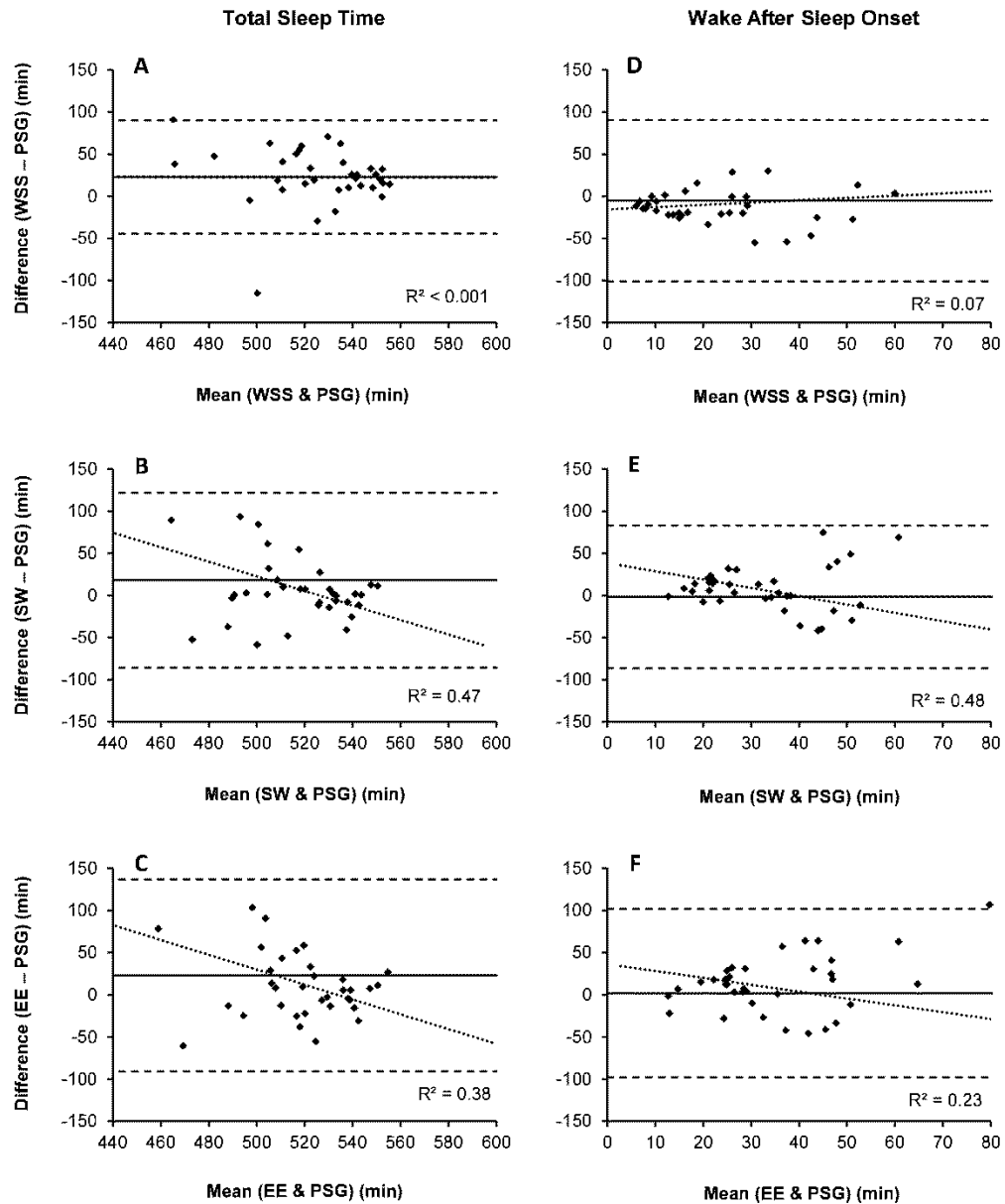
Note. N = 38.

\* $p < .05$ , compared to PSG (Bonferroni adjusted).

### 3.3.3.1. Bland-Altman plots.

The distribution of differences in TST and WASO from PSG is depicted, for all devices, in Figure 1. Plots for each activity monitor were created using its least biased threshold, i.e., the threshold that resulted in the fewest significant mean differences in TST and WASO from PSG (Table 3-4). The medium threshold had the fewest significant differences for the sleep/wake monitor, and the very low threshold had the fewest significant differences for the energy expenditure monitor.

The wireless sleep-staging system overestimated TST by a mean of 22.7 ( $\pm 33.7$ ) min and underestimated WASO by a mean of 5.4 ( $\pm 47.9$ ) min (Figure 3-1). In contrast, the sleep/wake and energy expenditure monitors overestimated TST, on average, by 18 ( $\pm 51.9$ ) min and 22.9 ( $\pm 56.9$ ) min, and underestimated WASO on average by 1.6 ( $\pm 42.4$ ) min and 1.9 ( $\pm 50.0$ ) min, respectively. The distribution of differences from PSG varied greatly for all devices and thresholds (Figure 3-1). However, the wireless sleep-staging system's differences from PSG were more consistent than for the activity monitors. For wireless sleep-staging, there were no significant ( $p > .10$ , two-tailed) correlations between the size of the difference from PSG and either TST ( $r < 0.01$ ) or WASO ( $r < 0.26$ ) duration (Figure 3-1). In contrast, for both activity monitors, differences from PSG were significantly ( $p < .05$ ) negatively correlated with the amount of TST (sleep/wake monitor:  $r = -0.69$ , energy expenditure monitor:  $r = -0.62$ ) and WASO (sleep/wake monitor:  $r = -0.69$ , energy expenditure monitor:  $r = -0.48$ ) obtained. That is, they progressively overestimated sleep for shorter durations of TST and underestimated wake for longer durations of WASO.



**Figure 3-1** Bland-Altman plots of total sleep time (TST) and wake after sleep onset (WASO). PSG is compared with: the wireless sleep-staging (WSS) system (A, D); the sleep/wake (SW) monitor at the medium threshold (B, E), and the energy expenditure (EE) monitor at the very low threshold (C, F). The x-axes indicate the average TST or WASO of each device and PSG. The y-axes describe the difference between each device and PSG in minutes, such that positive values indicate an overestimation of TST or WASO by the device compared to PSG, and negative values indicate an underestimation of the device compared to PSG. Solid horizontal lines indicate the mean bias from PSG and broken horizontal lines indicate the limits of agreement ( $\pm 2$  SD). Dotted lines and  $R^2$  indicate the slope and strength of the relationship between TST or WASO and the difference from PSG.

### 3.4. Discussion

In the present study, the ability of three devices to distinguish sleep from wake were evaluated in healthy young adults during night-time sleep periods. Our results confirm previous findings that sleep/wake monitors, energy expenditure monitors and wireless sleep-staging systems have high predictive value and agreement with PSG regarding sleep, but have relatively poor predictive value and agreement with PSG regarding wake (De Souza et al., 2003; Galland et al., 2012; Griessenberger et al., 2012; Kosmadopoulos et al., 2012; Kushida et al., 2001; Paquet et al., 2007; Robillard et al., 2012; Shambroom et al., 2012; Signal et al., 2005). Our results also confirm the large variability in differences from PSG previously found for individual sleep/wake estimates. As these alternatives to PSG were all used simultaneously in our study, we were also able to compare the sleep/wake monitor, the energy expenditure monitor, and the portable wireless sleep-staging system under the same conditions.

Due to the different methods used by the activity monitors to record activity counts (i.e., peak count/second vs mean count/second), counts per epoch for the sleep/wake monitor are higher than for the energy expenditure monitor. Consequently, at each threshold the former consistently detected more wake than the latter. However, consistent with previous validations, higher thresholds captured more sleep and lower thresholds captured more wake, irrespective of the monitor used (Kosmadopoulos et al., 2012; Kushida et al., 2001; Signal et al., 2005). Based on the epoch-by-epoch statistics and the comparisons of summary sleep measures with PSG, the default medium threshold for the sleep/wake monitor was found to have the optimum balance of agreement with PSG, compared to higher and lower thresholds. For the energy expenditure monitor, the optimum threshold was very low, suggesting that the pre-set low threshold previously used when validating it may not have fully reflected its capacity for sleep measurement (Kosmadopoulos et al., 2012; Weiss et al., 2010). At their optimum thresholds, the sleep/wake monitor performed only marginally better than the energy expenditure monitor in terms of epoch-by-epoch comparisons and summary measurement biases.



The wireless sleep-staging system agreed with PSG-determinations of sleep and wake more often than wrist actigraphy, even when set at their optimum thresholds. This superiority ranged from being only marginally better at identifying sleep and wake, to being far better at predicting wake (Table 3-2). Cohen's kappa coefficients suggest the wireless sleep-staging system had a moderate agreement with PSG beyond chance, while both activity monitors have a fair agreement with PSG. The mean biases of the wireless sleep-staging system for estimating TST and WASO only differed from both activity monitors at their best thresholds by a couple of minutes. However, the distribution of differences from PSG was smaller and more consistent for the wireless sleep-staging system. Activity monitors progressively overestimated sleep for shorter sleep durations and underestimated wake for longer wake durations. In contrast, biases of the wireless sleep-staging system were not affected by these durations. The activity monitors and the wireless sleep-staging system were equally very poor at estimating SOL.

#### 3.4.1. Implications for Field Research

As there is large variability in the differences of all device estimates from PSG, summary measures estimated for any one person may not be accurate, even when the mean results of many people are not significantly different from PSG. Therefore, these devices may be more appropriate for monitoring the average sleep/wake behaviours of groups, rather than individuals (Signal et al., 2005). Nonetheless, all of the devices satisfactorily distinguished sleep from wake on an epoch-by-epoch basis, having agreement rates within the accepted range of past validations (Galland et al., 2012; Kosmadopoulos et al., 2012; Paquet et al., 2007; Rupp & Balkin, 2011; Shambroom et al., 2012). Additionally, while the wireless sleep-staging system performed better than the activity monitors on several measures in this study, the accuracy of actigraphic sleep/wake assessments in other studies has been shown to improve when analysed in conjunction with sleep diaries (Acebo et al., 2005; Kushida et al., 2001). Activity monitors and the wireless sleep-staging system are better suited for use in different circumstances. Therefore, when PSG is not possible or practicable, the

primary consideration of which system to utilise is their theoretical and applied compatibility with the research question and the proposed research design.

Activity monitors are unobtrusive and can be worn both day and night for weeks and months, making actigraphy, together with sleep diaries, more conducive than a self-administered wireless system to long-term monitoring of patterns in sleep/wake behaviour (Roach et al., 2012a; Sargent et al., 2014). As the sleep/wake monitor that we evaluated is specifically developed for estimating sleep/wake states, threshold changes can be used to accommodate research populations with different sleep behaviours. For example, the default threshold, which is the most appropriate in a healthy population, could be lowered for sleep-disordered populations as this has been found to increase wake detection (Hyde et al., 2007; Kushida et al., 2001). Given that the threshold we found best for the energy expenditure monitor is already very low, it is effectively limited to use with non-clinical populations. However, in research involving the concurrent analysis of sleep and other behaviours, such as exercise, using an energy expenditure monitor to measure both sleep/wake patterns and energy expenditure has been found to be both practical and cost effective (Evans et al., 2011).

Unlike actigraphy, the wireless sleep-staging system employed in this study requires participants to wear a headband within close range of the base-station, making it more suited to shorter research protocols focused primarily on planned night-time sleeps. Its ability to correctly predict wake suggests wireless sleep-staging may be better than actigraphy for use with participants who frequently wake up due to sleeping disorders. Therefore, in research where sleep staging information is required but PSG is not possible, validated systems like this would be more suitable than actigraphy.

### 3.4.2. Limitations

Activity monitors are typically used over multiple 24-h periods. Given their relatively low rates of wake detection and overestimation of sleep, a limitation of this study is that activity monitors were only validated for sleep/wake

estimation during sleep periods at night. Future validation studies may consider evaluating the sleep/wake agreement of activity monitors, with a portable PSG system, across longer periods of time, at both normal and non-normal times for sleep (i.e., during the night and day).

We were able to concurrently evaluate two types of activity monitors and a wireless sleep-staging system. However, many other products, including a variety of different types of activity monitors and algorithms, are also used as alternatives to PSG (Van de Water et al., 2011). Due to poor standardisation across these alternatives, brand-specific differences in design may reduce the generalisability of our findings beyond the devices validated here (Te Lindert & Van Someren, 2013).

### 3.4.3. Conclusion

In conclusion, although the wireless sleep-staging system performed better than sleep/wake and energy expenditure monitors for some measures of agreement with PSG, the alternatives to PSG all performed well. The energy expenditure monitor was not developed for sleep monitoring, but when a very low threshold was applied its capacity for capturing sleep and wake was similar to devices that were. Provided the optimum thresholds are applied for the activity monitors, there are no definitive recommendations that any one of the three validated devices should be used over the others. Instead, when selecting a sleep-monitoring alternative, the primary consideration for researchers is which one will best address their research aim whilst being suitable for their research design.

## **Chapter 4.**

### **Developing a Tool to Discern Wrist Accelerometer Non-Wear from Inactivity**

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**Peer-reviewed publication associated with this chapter (Appendix G):**

**Kosmadopoulos, A.,** Darwent, D., & Roach, G. D. (2016). Is it on? An algorithm for discerning wrist-accelerometer non-wear times from sleep/wake activity. *Chronobiology International*, 33(6), 599-603.  
<http://dx.doi.org/10.3109/07420528.2016.1167720>.

## 4.1. Introduction

Actigraphy with wrist-worn activity monitors is widely employed in sleep research, both as a convenient alternative to gold-standard polysomnography in lengthy field-based studies (Darwent et al., 2008; Lastella et al., 2015; Rigney et al., 2015) and as a participant screening tool for laboratory protocols (Kosmadopoulos et al., 2015; Matthews et al., 2015; Sargent, Ferguson, Darwent, Kennaway, & Roach, 2010; Zhou et al., 2012). Although these devices do not measure sleep directly, they contain accelerometers and record movement associated with sleep/wake states. Algorithms have been validated which estimate sleep/wake based on the activity recorded during self-reported bedtimes (Kosmadopoulos, Sargent, Darwent, Zhou, & Roach, 2014b).

Before sleep/wake analyses are conducted, bedtimes reported in sleep diaries are cross-validated against wrist-activity data capturing sleep/wake behaviour (Darwent et al., 2008). Using this method, periods of high activity indicate 'wake' and periods of low activity indicate 'sleep'. Typically, disagreements between reported bedtimes and activity levels (i.e., high activity during reported bedtimes or low activity during reported wake times) are resolved by adjusting reported bedtimes. This is done on the assumption that activity monitors are more likely to accurately reflect rest/activity patterns than sleep diaries which are prone to reporting errors. Activity monitors in conjunction with sleep diaries yield a more accurate estimate of rest/wake activity than self-report sleep diaries alone. However, obtaining self-reported bedtimes is still important to distinguish between sleep periods and periods of quiescent wake times (e.g. lying still while watching a movie).

Confidence in the accuracy of sleep/wake estimates derived using this methodology is contingent on (1) devices being worn throughout the protocol, and (2) researchers being able to discern non-wear times when they occur. Periods of non-wear almost exclusively yield periods of zero activity counts. However, it can be difficult to distinguish between periods of non-wear, sleep and quiescent wakefulness, since all these states are associated with periods of

zero activity and can occur for similar durations that are not mutually exclusive (Evenson & Terry, 2009).

Though some wrist-worn activity monitors contain temperature or capacitive sensors that can assist with off-wrist detection (Chen & Bassett, 2005), a common method employed to identify removal is to apply a reasonable definition of non-wear time based on observed patterns of inactivity (Evenson & Terry, 2009; Masse et al., 2005). The chosen definition describes the minimum duration of inactivity required to make a determination of non-wear. In the exercise and physical activity literature, recommended definitions for non-wear time typically range from 60 min to 180 min of inactivity (Choi, Liu, Matthews, & Buchowski, 2011; Hutto et al., 2013; King, Li, Leishear, Mitchell, & Belle, 2011; Oliver, Badland, Schofield, & Shepherd, 2011). However, activity monitors in this field are generally worn around the waist to measure purposeful whole body movement rather than incidental limb movement (Kumahara, Tanaka, & Schutz, 2004; Trost, McIver, & Pate, 2005). Thus, these definitions may not be suitable to discern non-wear from sleep or quiescent wakefulness measured with wrist-actigraphy. The question remains: how long must an activity monitor be motionless before one can reasonably assume it is not being worn?

The challenge with a fixed definition of non-wear is that any chosen duration of inactivity will result in some misclassification. For example, minimising the misclassification of quiescent wakefulness or sleep with a high threshold of non-wear (i.e., a longer period of inactivity), comes at the expense of not detecting shorter periods of non-wear. The aim of this study was to develop an algorithm which can define periods of inactivity as non-wear time based on their likelihood of occurring during time in bed. This approach would allow researchers to choose a definition of non-wear consistent with an accepted margin of error or determine the margin of error associated with a given definition of non-wear.

## **4.2. Methods and Materials**

### **4.2.1. Participants**

Thirty-two healthy male volunteers aged  $22.84 \pm 2.94$  years (mean  $\pm$  SD; range = 19 – 29 years) with a body mass index (BMI) of  $22.33 \pm 2.16$  kg/m<sup>2</sup> (range = 18.5 – 25.0 kg/m<sup>2</sup>) participated in this study and provided written informed consent. Ethics approval was provided by the Central Queensland University Human Research Ethics Committee.

### **4.2.2. Protocol**

Participants resided in a sleep laboratory for 13 consecutive days. Days 1–3 were reserved for training and determining baseline performance on neurobehavioural tasks (the results of which are reported in Chapter 5 and Chapter 6). For the subsequent 9-day study period, 16 participants obtained time in bed equivalent to 8 h per 24 h and 16 participants obtained time in bed equivalent to 4 h per 24 h. A closed-circuit television system and in-person monitoring allowed researchers to ensure participants complied with study protocols. Participants wore activity monitors on their non-dominant wrist during the entire study except when showering. Wear was confirmed by researchers during sedentary wake periods and at bedtimes. Further details about the protocol are described in the General Methods, section 2.3.2., p.84.

### **4.2.3. Actigraphy**

The wrist-worn activity monitor employed in the study was the Actical (Philips Respironics, Murrysville, PA, USA), which has been validated for estimating both energy expenditure and sleep/wake states (Heil, 2006; Kosmadopoulos et al., 2014b). This device contains an omnidirectional piezoelectric transducer that converts accelerations (0.05 G to 2.0 G) in wrist movement to digital activity counts at 32 Hz. Activity counts were summed into 1-min epochs, with larger values indicating greater movement. Epochs with zero-counts represent 1-min of inactivity.

#### 4.2.4. Data Analyses

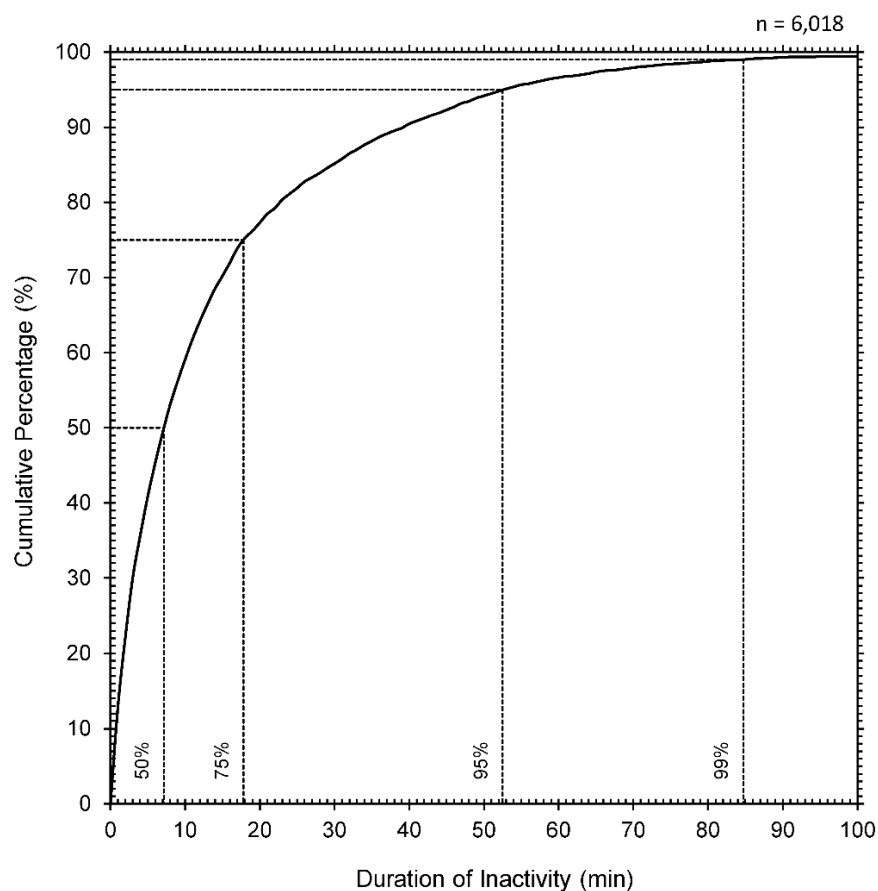
Only accelerometer data recorded during the 9-day study period were included in analyses. Data from two participants were removed due to technical failure. T-tests were conducted to determine whether durations of inactivity differed between time in bed and sedentary wake periods. The frequency of all consecutive zero epochs  $\geq 1$  min during time in bed were tabulated to derive a cumulative distribution function of inactivity.

### 4.3. Results

Across the 9-day study period, a total of 353,840 minutes of data were recorded. Zero activity counts were recorded in 91.7% of the epochs during time in bed and 43.6% of the epochs during sedentary wake periods. There were 6,018 distinct periods of inactivity  $\geq 1$  min during time in bed, averaging  $14.7 \pm 18.5$  min (range = 1 to 41 min). In comparison, periods of inactivity ( $n = 41,581$ ) during sedentary wake times averaged  $2.7 \pm 2.7$  min in duration (range = 1 to 145 min).

The cumulative distribution function of inactivity during time in bed is shown in Figure 4-1. During time in bed, periods of inactivity lasting only 1 min comprised the largest proportion (12.8%) of all cases. Over half (53.1%) of the instances of inactivity were  $\leq 8$  min in duration, 75.2% were  $\leq 18$  min, 95.1% were  $\leq 53$  min, and 99.0% were  $\leq 85$  min. The maximum duration of consecutive epochs with zero activity was 145 min (not shown in figure).





**Figure 4-1** Cumulative distribution function of all periods of inactivity  $\geq 1$  minute recorded during time in bed. The y-axis represents the cumulative frequency percentage. The x-axis represents durations of inactivity up to 100 min (99.5%). Dashed lines indicate the durations of inactivity at 50%, 75%, 95% and 99%.

#### 4.4. Discussion

An algorithm was developed from the cumulative distribution of bedtime inactivity to provide an objective basis upon which to discern activity monitor non-wear times from wear times. This was based on the assumption that the likelihood of non-wear increases as the number of consecutive epochs of zero-activity recorded by a monitor rises. Only inactive periods during time in bed were included because they produce more conservative definitions of non-wear that are less reliant on the accuracy of self-reported bedtimes and wake times. The likelihood threshold used to define non-wear time can be adjusted depending on the needs of the task and the desired level of certainty. Alternatively, researchers can use this tool to determine the likelihoods of non-wear associated with definitions chosen in advance (e.g., 10, 20, 60, or 90 min) for convenience.

A threshold of 50% (i.e., when the device is more likely to be off than on) is likely to be satisfactory for determining non-wear in routine rest/activity monitoring. When faced with periods of inactivity during self-reported wake times, this definition would detect short periods of removal  $\geq 8$  min (e.g., during showers). However, since long periods of inactivity are expected during reported bedtimes, a higher threshold (e.g., 95% or 99%) might be more appropriate for defining non-wear when cross-validating sleep diaries against activity data. This is because the threshold used to define non-wear can influence how discrepancies are resolved. For example, if a period of inactivity extended beyond a participant's self-reported get-up time and did not meet the definition for non-wear, it might be reasonable to assume the participant remained in bed longer than stated and the diary would be adjusted to reflect this. However, if it did meet the definition for non-wear, this period of inactivity would be removed from sleep analyses.

The thresholds of non-wear reported here are based on the bedtime activity profiles of young healthy male adults under normal and sleep-restricted conditions. Their suitability for female participants, children, older adults, or people with sleep disorders is unknown and would require separate

investigation. The definitions derived with this algorithm are specific to the activity monitor used in this study, but they may still be useful guides for other brands. The approach described for determining non-wear times is applicable to other devices and would likely produce similar distributions of inactivity, slightly shorter or longer, depending on their sensitivity to movement (Troost et al., 2005). As activity monitoring capabilities are increasingly incorporated into a plethora of lifestyle devices (e.g., fitness monitors, watches, mobile phones) the application of these and similar algorithms, separately or together with temperature/capacitive sensors, is likely to increase in scope.

## **Chapter 5.**

### **Effects of a Split Sleep-Wake Schedule on Performance and Subjective Ratings**

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**Peer-reviewed publication associated with this chapter (Appendix H):**

**Kosmadopoulos, A.,** Sargent, C., Darwent, D., Zhou, X., Dawson, D. & Roach, G. D. (2014). The effects of a split sleep-wake schedule on neurobehavioral performance and predictions of performance under conditions of forced desynchrony. *Chronobiology International*, 31(10), 1209-1217.  
<http://dx.doi.org/10.3109/07420528.2014.957763>.

## 5.1. Introduction

There is increasing expectation and demand for services that are available around the clock (Costa, 2003). As a consequence, more employees are undertaking shiftwork outside traditional daytime work hours. However, despite the need for it, shiftwork is associated with suboptimum performance and an increased risk of fatigue-related injuries and accidents, particularly at night (Folkard et al., 2005; Folkard & Tucker, 2003; Muller, Carter, & Williamson, 2008). The increase in risk has largely been explained by circadian misalignment, difficulty in obtaining sufficient recuperative sleep, and long shift duration (Folkard et al., 2005; Folkard & Tucker, 2003; Philip & Åkerstedt, 2006). Furthermore, there is evidence to suggest that assessments of one's capacity to perform during a week of simulated night shifts may only be moderately correlated with one's actual performance (Dorrian et al., 2003).

Sleep and wake are largely regulated by two interacting physiological processes: (1) a homeostatic process that progressively increases a drive for sleep (or 'sleep pressure') during wakefulness, which then declines after sleep onset, and (2) an endogenous circadian rhythm that increases the biological propensity for sleep during the night and wakefulness during the day (Borbély, 1982; Minors et al., 1991). For day workers, these two processes typically align such that the sleep drive, accumulated since waking, peaks in the late evening. Sleep is then promoted and maintained by the circadian process over the course of the night until it is time to wake the next morning. For shiftworkers who work outside traditional 0900 h–1700 h office hours, the homeostatic and circadian processes are often in conflict. Those rostered on night shifts are required to work long hours during times when they are biologically primed for sleep, with sleep opportunities available to them when primed for wake. The interaction of these processes help explain the reduced recuperative value of daytime sleep (Ferguson et al., 2012b) and form the basis of many fatigue and performance models (e.g., Åkerstedt & Folkard, 1997; Borbély & Achermann, 1999; Jewett & Kronauer, 1999; Roach, Fletcher, & Dawson, 2004) that predict declining, more variable, performance at night and with increasing homeostatic sleep pressure (Arnedt, Owens, Crouch, Stahl, & Carskadon, 2005; Matthews et al., 2012a; Scott

et al., 2007). In safety-critical industries that operate around the clock, such as emergency services, mining, and transport, there is a significant risk of harm both to the public and to the employees themselves.

In theory, splitting the work schedule into multiple short shift rotations per day (e.g., 2 × 6 h on/6 h off), instead of fewer longer shifts per day (e.g. 12 h on/12 h off), could help sustain operational performance capacity and minimise sleepiness around the clock. There are two primary reasons for this. First, a split work-rest schedule would truncate the duration of wake required between sleep opportunities, reducing the homeostatic component of performance decline and sleep pressure (Dijk et al., 1992; Zhou et al., 2010). Second, although it would compromise the beneficial circadian attributes of daytime shifts, these shorter rotations would facilitate increased opportunities for night-time sleep and daytime work compared to long night shifts. Indeed, applied research in the laboratory and the field provide credence to these reasons supporting a split work-rest schedule. For instance, dividing sleep opportunities into multiple short periods does not appear to disrupt daytime neurobehavioural performance, provided that the time allocated per 24 h is sufficient, or total sleep duration (Mollicone et al., 2007; Mollicone et al., 2008). Further support comes from mining operators and lead smelters on schedules consisting of long 12-h shifts (Baulk, Fletcher, Kandelaars, Dawson, & Roach, 2009; Ferguson, Kennaway, Baker, Lamond, & Dawson, 2012a) and bridge officers working simulated 4 h on/8 h off maritime watch systems (Van Leeuwen et al., 2013). For these workforces, performance was shown to vary across the day in accordance with expectations based on circadian physiology; however, in contrast to those working long 12-h shifts, performance by bridge officers did not decline across consecutive shifts in a manner indicative of circadian maladaptation.

However, despite findings that suggest short work-rest cycles may be feasible alternatives to consolidated schedules, research to-date has confounded the effects of time-of-day and prior wake. Therefore, it is not clear how a split work-rest schedule may impact neurobehavioural performance and sleepiness at

different times of day, particularly at night, compared to a consolidated schedule. In the current study, two forced desynchrony (FD) protocols were employed to identify and compare the individual contributions of prior wake and circadian phase on neurobehavioural performance, sleepiness, and self-assessed ability to perform, in both consolidated and split sleep-wake schedules. FD protocols impose on participants a sleep-wake cycle that has a period significantly longer or shorter than the 24-h chronological day (e.g., Czeisler et al., 1999; Sargent et al., 2010; Wright et al., 2002; Wyatt et al., 1999). As it cannot entrain to this period, the endogenous circadian pacemaker is able to 'free run' at its intrinsic near-24-h period and desynchronise from the imposed sleep-wake cycle. Thus, homeostatic and circadian factors can be assessed separately. So far, neurobehavioural performance and sleepiness have been evaluated in FD protocols with a single consolidated sleep period per 28 h (Darwent et al., 2010; Matthews et al., 2012b; Silva et al., 2010; Wright et al., 2002; Zhou et al., 2011, 2012); however, none have investigated the neurobehavioural and sleepiness outcomes of splitting the FD schedule in half. Similarly, none have investigated how splitting the schedule affects self-monitoring of one's capacity to perform. In this context, the aims of this study were to establish whether splitting the sleep-wake cycle has an effect on neurobehavioural performance, subjective sleepiness or individuals' perceptions of their ability, and to determine the relative circadian and homeostatic contributions of any such effects.

## **5.2. Methods and Materials**

### **5.2.1. Participants**

Participants were 29 healthy males aged  $22.52 \pm 2.56$  years (mean  $\pm$  SD; range = 18 – 29 years) and had a body mass index (BMI) of  $22.12 \pm 1.97$  kg/m<sup>2</sup> (range = 18.9 – 24.9 kg/m<sup>2</sup>). Volunteers were required to pass a screening process that involved an interview, questionnaires, and a week of wrist actigraphy. Exclusion criteria included smoking, excessive consumption of caffeine or alcohol, physical or medical disorders, irregular sleep patterns, or

transmeridian travel / shiftwork in the previous two months. For a week prior to admission, participants were required to maintain consistent bedtimes between 2200 h – 2400 h and sleep durations of 7 – 9 h per night. This was verified with wrist activity monitors (Actiwatch and Actical; Philips Respironics, Bend, Oregon, USA) and sleep diaries.

#### *5.2.1.1. Ethics*

The University of South Australia and Central Queensland University Human Research Ethics Committees granted ethical approval for this study. The study was conducted in accordance with the guidelines of the National Health and Medical Research Council of Australia. Participants provided informed written consent and were remunerated with an honorarium for their involvement.

#### *5.2.2. Setting*

Participants lived in the laboratory in groups of three or four, under conditions of temporal isolation. Each participant was assigned to a bedroom, living room, workstation for testing sessions, and bathroom facilities. A communal dining area was available for meal times. The laboratory was windowless, sound attenuated, and free of external time cues. Lighting was maintained at 10-15 lux during wake periods, and <.03 lux during sleep periods, at the angle of gaze. The target ambient temperature throughout the study was 21-23°C. Participant behaviour was monitored in person and via closed circuit television cameras in the laboratory to ensure compliance with study protocols.

#### *5.2.3. Measures*

Neurobehavioural performance was measured using a 10-min psychomotor vigilance test (PVT). The PVT is a simple response time task performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA) (Dinges & Powell, 1985; Wilkinson & Houghton, 1982). Four metrics were derived from the 10-min task. The first of these was the number of lapses, that is response times (RT) >500 milliseconds (ms). Others



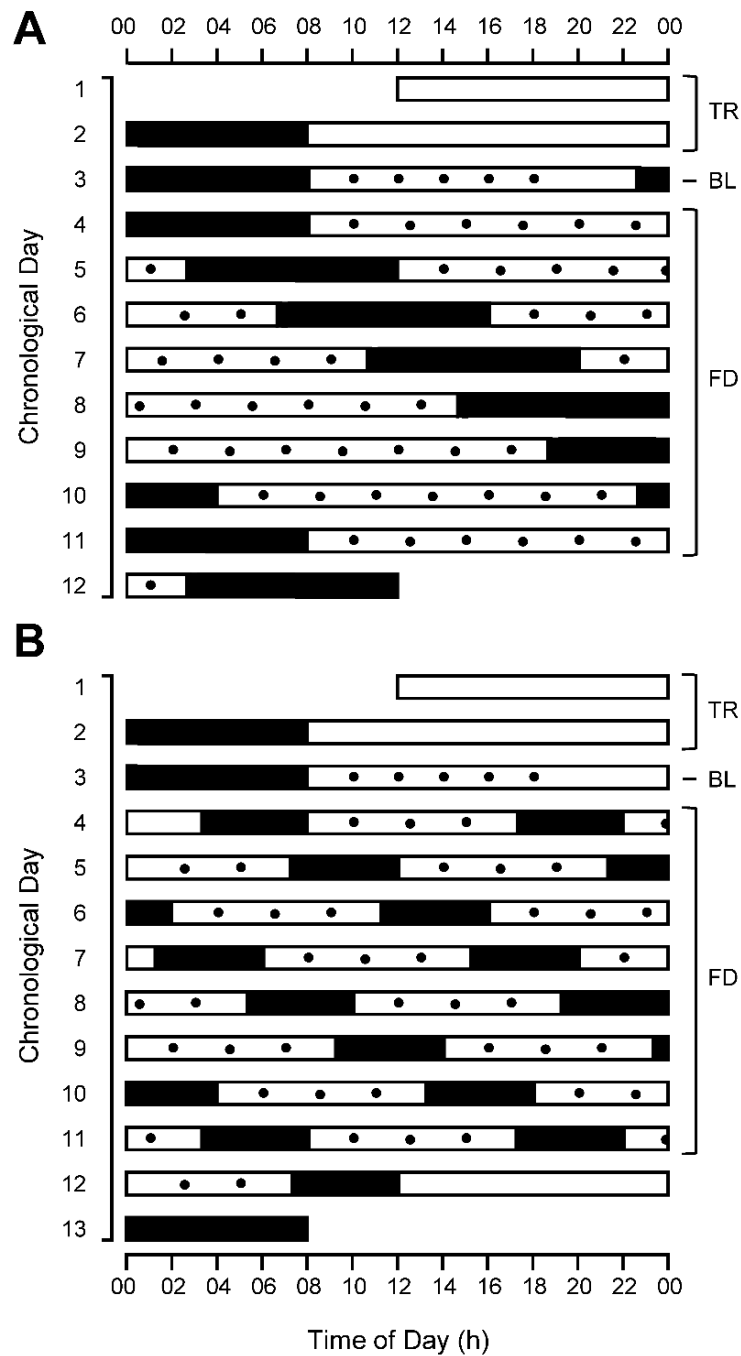
were the mean reciprocal response times (RRT;  $\text{ms}^{-1} \times 10^{-3}$ ), mean slowest 10% of RRT ( $\text{ms}^{-1} \times 10^{-3}$ ), and mean fastest 10% RT (ms). Reciprocals were used for mean and slowest speeds to lessen the contribution of long lapses (Jewett et al., 1999a). Subjective sleepiness was measured using the 9-point Karolinska Sleepiness Scale (KSS; Åkerstedt & Gillberg, 1990). Participants were required to rate their sleepiness by circling a number from 1 ('Extremely alert') to 9 ('Very sleepy, great effort to keep awake, fighting sleep'). Self-assessed ability was measured by asking participants to predict 'How well do you think you will perform?' on a 100-mm visual analogue scale (VAS performance), anchored by the statements 'Extremely poorly' and 'Extremely well'.

Sleep was monitored with standard polysomnography, using the E-Series and Graef PSG/EEG Systems (Compumedics, Melbourne, Victoria, Australia) and a montage of Grass<sup>TM</sup> gold-cup electrode leads (Astro-Med, Inc., West Warwick, Rhode Island, USA). The montage included two EEG channels (C3-M2, C4-M1), right and left EOG, and three channels of chin EMG. Sleep-wake stages were scored in 30-s epochs by a trained technician following standard criteria (Iber et al., 2007). Three sleep measures were employed for analyses: (i) total sleep time (TST) – the total amount of sleep of any stage obtained between lights out and lights on in minutes; (ii) REM sleep – the total amount of REM sleep obtained between lights out and lights on in minutes; and (iii) slow wave sleep (SWS) – the total amount of SWS obtained between lights out and lights on in minutes.

Core body temperature (CBT) was continuously recorded throughout the study in 1-min intervals via a rectal thermistor (Steriprobe 491B; Cincinatti Sub-Zero Products, Cincinnati, Ohio, USA) connected to an ambulatory recording device (Mini-logger series 2000, Mini-Mitter, Bend, Oregon, USA) worn around the waist. The thermistor was self-inserted and only removed for bowel movements and showers. Physical activity was monitored throughout the study with wrist-worn activity monitors (Actiwatch and Actical; Philips Respironics, Bend, Oregon, USA) (Kosmadopoulos et al., 2014b; Robillard et al., 2012).

#### 5.2.4. Protocol

Two FD schedules were run to assess the independent and combined effects of prior wake and circadian phase. Participants were assigned to either a consolidated sleep-wake schedule ( $n = 13$ ; age  $22.5 \pm 2.2$  years) or a split sleep-wake schedule ( $n = 16$ ; age  $22.6 \pm 2.9$  years) (Figure 5-1). Each protocol began with two 24-h training days and a baseline day. Training days involved familiarising participants with the PVT and other procedures involved in the study. On the baseline day participants completed five 1-h test batteries, including the VAS performance rating and PVT, beginning 1.5 h after waking. Following this, participants were scheduled to  $7 \times 28$ -h FD periods with an enforced rest-to-wake ratio of 1:2 (equivalent to an 8-h sleep opportunity in 24 h). The FD periods for the consolidated schedule comprised a single cycle of 9.33 h time in bed (TIB) and 18.67 h of wake. In contrast, the FD periods for the split schedule were subdivided into two alternating cycles of 4.67 h TIB and 9.33 h of wake (essentially, a 14-h FD protocol). During FD periods, 1-h test batteries also occurred 1.5 h after waking, with subsequent testing conducted every 2.5 h thereafter. Participants were permitted to read, watch DVDs, and listen to music in their living rooms between testing bouts. They were not permitted to undertake any strenuous activities or sleep outside designated periods, and social interaction between participants was limited to meal times. Prior to each sleep period, a montage of PSG electrodes was applied to participants for sleep monitoring.



**Figure 5-1** Diagrams of both the consolidated and split 28-h forced desynchrony schedules. Protocol A depicts the consolidated sleep-wake schedule, and Protocol B depicts the split sleep-wake schedule. The x-axis indicates clock time across a 24-h period and the y-axis plots successive 24-h periods chronologically. Identical training (TR) days and a baseline (BL) day were followed by a period of forced desynchrony (FD). Total sleep opportunity, depicted by black rectangles, was identical for both protocols. Testing sessions during wake periods are indicated by black circles.

#### 5.2.4.1. *Circadian phase estimates*

Circadian phase estimates were derived for each participant by means of a five-step de-masking process that incorporated PSG and activity monitor data to account for the effects of sleep and physical activity on the circadian rhythm of CBT (see Darwent et al., 2010). Circadian estimates (i.e., ranging from 0-360°, with 0° representing the nadir of the CBT curve) were assigned to each minute of the protocol for each participant (section 2.5, p.99, of General Methods).

### 5.2.5. Data Analysis

#### 5.2.5.1. *Sleep*

Polysomnographic data were analysed for the baseline sleep and the forced desynchrony sleeps for each of the three sleep measures (TST, REM sleep, and SWS). For the period of forced desynchrony, mean values for each participant were calculated for each measure from sleep episodes that occurred during a single beat period on days 5 to 11. This beat period included  $6 \times 9.33$ -h sleep episodes in the consolidated schedule and  $12 \times 4.67$ -h sleep episodes in the split schedule. A set of independent samples t-tests was used to compare the two conditions at baseline, and another set of t-tests was used to compare the schedules during the forced desynchrony phase.

#### 5.2.5.2. *Neurobehavioural performance, sleepiness and self-assessed ability*

PVT performance metrics and KSS and VAS performance ratings were expressed relative to participants' mean scores on the baseline day. For these relative scores, negative values indicated poorer performance, more sleepiness, and worse self-assessments of ability. Positive values indicated better performance, less sleepiness, and improved self-assessments of ability. Data from each protocol were assigned to 1 of  $6 \times 60^\circ$  circadian phase bins (i.e., centred at 0°, 60°, 120°, 180°, 240°, 300°) and to 1 of 7 levels of prior wake for the consolidated protocol (i.e., 2 h, 4.5 h, 7 h, 9.5 h, 12 h, 14.5 h, 17 h) or 1 of 3 levels of prior wake for the split schedule (i.e., 2 h, 4.5 h, 7 h). For each measure, data were reduced by means of averaging all data points for each participant

assigned the same combination of circadian phase and prior wake. This enabled an equal contribution by each participant to subsequent analyses. Differences between minimum and maximum scores across circadian phases were calculated to determine circadian amplitudes of performance and ratings. Similarly, differences between scores at 2 h and 7 h of prior wake were calculated to determine change as a function of wake.

Mixed-model analyses of variance (ANOVA) were conducted, with sleep-wake schedule (2 levels), circadian phase (6 levels), and prior wake (split schedule: 3 levels; consolidated schedule: 7 levels) included as fixed terms. The four PVT metrics, the KSS and VAS performance ratings were entered as the dependent variables. A random term of 'Participant' was also included. First tested were the main effects of sleep-wake schedule, circadian phase, and prior wake in each schedule. Two-way schedule x circadian phase interactions were then tested to evaluate the performance contributions of each schedule at different times of day. T-tests were conducted to determine whether the circadian amplitude of performance and ratings, and the size of the changes in performance and ratings with prior wake, varied between schedules.

## **5.3. Results**

### **5.3.1. Participants**

Participants in the consolidated sleep schedule ( $n = 13$ ; age =  $22.46 \pm 2.22$  years; BMI =  $22.25 \pm 2.14$  kg/m<sup>2</sup>) and those in the split schedule ( $n = 16$ ; age =  $22.56 \pm 2.87$  years; BMI =  $22.03 \pm 1.88$  kg/m<sup>2</sup>) were not significantly different in terms of age [ $t(27)=0.10$ ,  $p=.918$  (2-tailed)] or BMI [ $t(27)=0.29$ ,  $p=.773$  (2-tailed)].

### **5.3.2. Sleep**

For the baseline sleep episode, all participants had 8 h in bed. During this time, the mean TST obtained by those in the consolidated condition ( $445.4 \pm 23.0$  min) did not significantly differ from the mean TST obtained by those in the split

condition ( $442.6 \pm 14.9$  min) [ $t(26)=0.4$ ,  $p=.673$ ]. Similarly, at baseline the amount of REM sleep obtained in consolidated schedule ( $108.0 \pm 28.3$  min) and the split schedule ( $104.2 \pm 22.6$  min) did not differ [ $t(26)=0.4$ ,  $p=.690$ ], and the amount of SWS obtained in the consolidated schedule ( $122.4 \pm 22.6$  min) and the split schedule ( $134.5 \pm 28.3$  min) also did not differ [ $t(26)=1.3$ ,  $p=.214$ ].

During the forced desynchrony phase, participants in both schedules were allocated a total of 9.33 h in bed per '28-h day'. On average, the mean TST obtained per 28 h in the consolidated schedule ( $456.4 \pm 45.4$  min) did not significantly differ from the TST obtained in the split schedule ( $475.4 \pm 28.0$  min) [ $t(27)=1.4$ ,  $p=.183$ ]. In terms of sleep stages, the average amount of REM sleep obtained per 28 h in the consolidated schedule ( $109.8 \pm 23.5$  min) and the split schedule ( $100.2 \pm 15.1$  min) did not differ [ $t(27)=1.3$ ,  $p=.209$ ]. However, those in the consolidated schedule obtained significantly less SWS than those in the split schedule ( $133.3 \pm 25.2$  min vs.  $169.1 \pm 28.0$  min) [ $t(27)=3.6$ ,  $p=.001$ ].

### 5.3.3. Performance, Subjective Sleepiness, and Self-Assessed Ability

Independent samples t-tests revealed that on the baseline day consolidated and split sleep-wake schedules did not significantly differ on any of the PVT metrics, the KSS, or VAS performance ratings (Table 5-1).

#### 5.3.3.1. Neurobehavioural performance

Mixed-models ANOVA indicated no main effects of schedule on any of the PVT metrics, including lapses, RRT, slowest 10% RRT, and fastest 10% RT, relative to baseline; average performance across one schedule was not significantly better or worse than in the other (Table 5-2). A main effect of circadian phase was present for all PVT metrics. Around the circadian acrophase ( $180^\circ$ ,  $240^\circ$ ), lapses were less frequent and response times (RRT, slowest 10% RRT, and fastest 10% RT) were faster than they were around the circadian nadir ( $0^\circ$ ,  $60^\circ$ ) (Figure 5-2, left panel).

**Table 5-1** Results of t-test comparisons of PVT, KSS, and VAS performance ratings during each sleep-wake schedule on the baseline day.

Measure	Consolidated (n=13)		Split (n=16)		t (27)	p
	Mean	SD	Mean	SD		
Lapses	0.48	0.72	0.28	0.33	0.94	.362
RRT	4.45	0.41	4.68	0.40	1.54	.136
Slowest 10% RRT	3.09	0.40	3.34	0.34	1.77	.088
Fastest 10% RT	182.73	15.32	179.74	15.88	0.51	.612
KSS	4.05	1.43	4.03	1.27	0.04	.967
VAS performance	68.19	13.24	63.87	10.86	0.97	.342

RRT, reciprocal response time; RT, Response time; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.

A main effect of prior wake was also present for all PVT metrics in each schedule (Table 5-3). Performance decline as a function of prior wake is depicted in Figure 5-2 (right panel). T-tests between schedules revealed that the consolidated schedule had significantly ( $p < .017$ , Bonferroni adjusted) faster mean RRT [ $t(170) = 2.79$ ,  $p = .006$ ] and faster slowest 10% RRT [ $t(170) = 3.48$ ,  $p = .001$ ] at 2 h of wakefulness than the split schedule. The schedules converged by 7 h of wakefulness.

Although schedules did not differ on average, all PVT metrics exhibited schedule x circadian phase interactions (Table 5-2). Bonferroni post hoc analyses of these interactions revealed significant ( $p < .05$ ) differences between schedules around the circadian nadir for lapses and slowest 10% RRT. For these performance metrics, the consolidated schedule was significantly worse, relative to baseline, than the split schedule at this time (Figure 5-2). Differences between the schedules in mean RRT approached, but did not reach, the  $p < .05$  significance threshold around the nadir. Analysis of the simple effects revealed that there was a circadian effect present for lapses only during the consolidated schedule [ $F(5,796) = 15.84$ ,  $p < .01$ ], not the split schedule [ $F(5,795) = .31$ ,  $p = .91$ ]. Simple effects of circadian phase were present in both schedules, however, for mean RRT, slowest 10% RRT, and fastest 10% RT.

T-tests comparing the amplitudes of performance on each measure revealed that the size of the circadian effect was significantly larger for the consolidated schedule than the split schedule in terms of lapses [ $t(27)=2.13$ ,  $p=.043$ ] and fastest 10% RT [ $t(27)=2.30$ ,  $p=.030$ ]. The schedules did not differ in the amplitude of RRT or fastest 10% RT. Regarding the size of the decline between 2 h and 7 h of prior wake, t-tests revealed a greater effect on the consolidated schedule than the split schedule for mean RRT [ $t(27)=2.55$ ,  $p=.017$ ], slowest 10% RRT [ $t(27)=2.33$ ,  $p=.027$ ], and fastest 10% RT [ $t(27)=2.12$ ,  $p=.043$ ].

#### 5.3.3.2. *Subjective sleepiness and self-assessed ability*

Mixed-models ANOVA indicated no main effect of schedule on KSS or VAS performance ratings (Table 5-2). Significant main effects of circadian phase were present indicating that the KSS and VAS performance were better around the circadian acrophase than around the circadian nadir (Figure 5-2). There were no circadian x schedule interactions for either measure. T-tests comparing the amplitudes of subjective ratings across circadian phases revealed no differences between the consolidated schedule and the split schedule for either the KSS [ $t(27)=0.68$ ,  $p=.502$ ] or VAS performance [ $t(27)=0.41$ ,  $p=.683$ ].

Both schedules exhibited main effects of prior wake on KSS and VAS performance ratings (Table 5-3) such that they declined with time awake (Figure 5-2). T-tests revealed that the magnitude of the decline between 2 h and 7 h of prior wake was not significantly different between schedules for the KSS [ $t(27)=0.36$ ,  $p=.725$ ] or VAS performance [ $t(27)=0.01$ ,  $p=.991$ ]. However, KSS ratings were significantly ( $p<.017$ , Bonferroni adjusted) lower in the split schedule than in the consolidated schedule at 2 h [ $t(172)=5.34$ ,  $p<.001$ ], 4.5 h [ $t(172)=6.61$ ,  $p<.001$ ], and 7 h [ $t(172)=5.51$ ,  $p<.001$ ]. Similarly, VAS performance ratings were significantly ( $p<.017$ , Bonferroni adjusted) poorer for the split schedule than the consolidated schedule at 2 h [ $t(169)=4.82$ ,  $p<.001$ ], 4.5 h [ $t(171)=6.17$ ,  $p<.001$ ], and 7 h [ $t(171)=4.85$ ,  $p<.001$ ].



**Table 5-2** Results of mixed-effects ANOVAs on PVT, KSS, and VAS performance.

	Schedule		Phase		Schedule x Phase	
	F	df	F	df	F	df
Lapses	2.20	1,30	7.62***	5,795	3.80**	5,795
RRT	0.22	1,27	24.96***	5,792	3.34**	5,792
Slowest 10% RRT	0.46	1,27	23.45***	5,792	2.48*	5,792
Fastest 10% RT	0.06	1,27	18.51***	5,792	3.81**	5,792
KSS	0.62	1,27	21.37***	5,792	1.64	5,792
VAS performance	1.19	1, 26	12.23***	5, 787	0.37	5, 787

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

Phase, circadian phase; RRT, reciprocal response time; RT, response time; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.

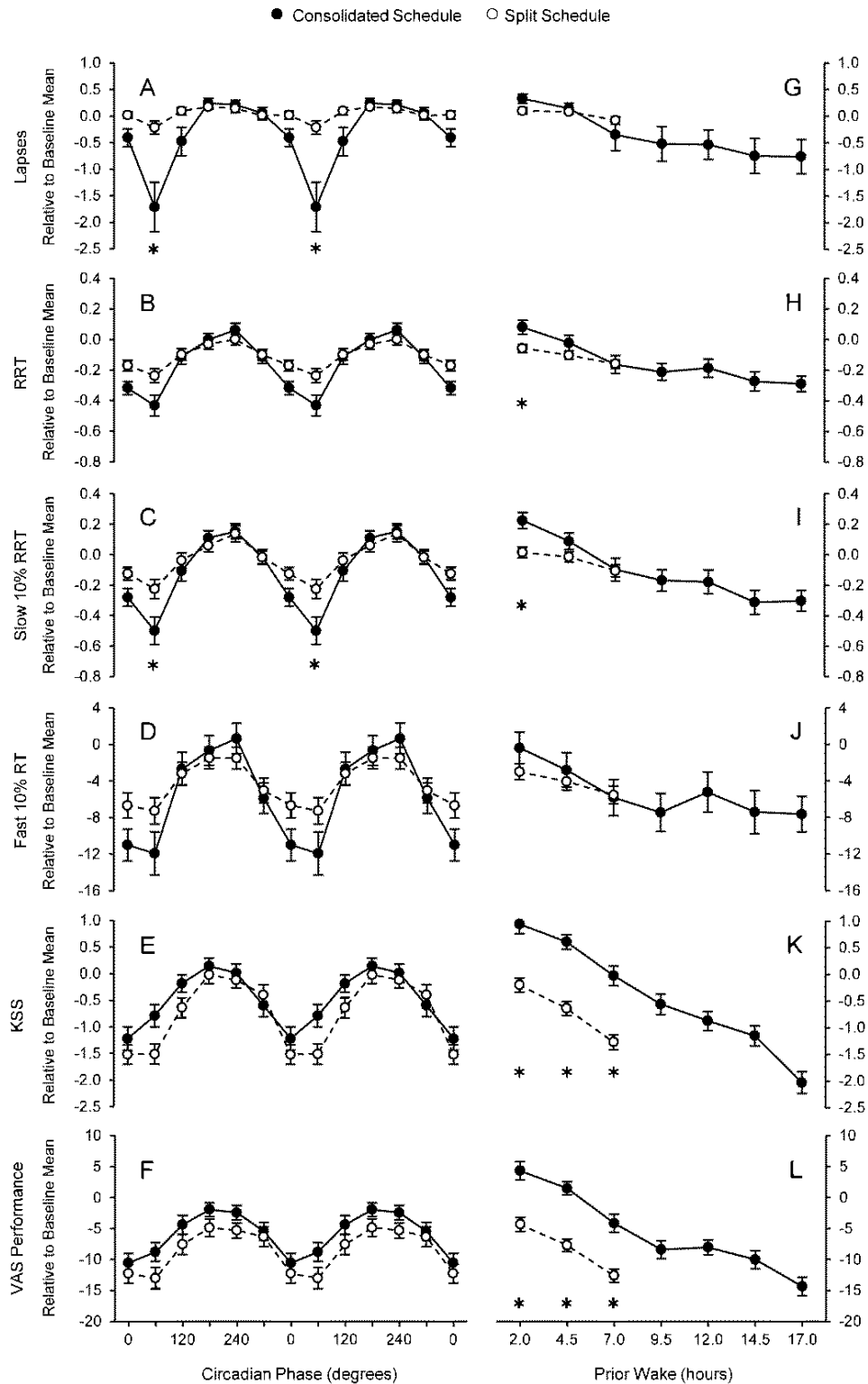
**Table 5-3** Main effects of prior wake in each sleep-wake schedule on PVT, KSS and VAS performance.

	Consolidated Schedule		Split Schedule	
	F	df	F	df
Lapses	2.88*	6, 524	4.80*	2, 270
RRT	9.66**	6, 524	9.74**	2, 270
Slowest 10% RRT	11.06**	6, 524	6.31**	2, 270
Fastest 10% RT	3.84**	6, 524	5.50**	2, 270
KSS	45.89***	6, 524	25.75***	2, 270
VAS performance	26.76***	6, 520	29.53***	2, 270

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

RRT, reciprocal response time; RT, response time; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.

## Effects of a Split Sleep-Wake Schedule on Performance and Subjective Ratings



**Figure 5-2** Psychomotor vigilance performance, KSS and VAS performance ratings, relative to baseline, during consolidated and split sleep-wake schedules.

Panels A-F depict results at different circadian phases (double-plotted), and panels G-L depict results across hours of wakefulness. Asterisks indicate significant differences ( $p < .05$ ) between schedules. Data are presented as mean  $\pm$  SEM.

## 5.4. Discussion

Two forced desynchrony (FD) protocols were implemented to investigate the circadian and homeostatic contributions to neurobehavioural performance and subjective assessments of sleepiness and ability to perform during consolidated and split sleep-wake schedules. This is the first such study where each of the conditions compared had the same rest-to-wake ratio but different periods for the imposed sleep-wake cycle. Specifically, the consolidated sleep condition employed a 28-h FD protocol and the split sleep condition employed a 14-h FD protocol (i.e., a “split” 28-h FD), which halved the period of the sleep-wake cycle. As a result, the same total duration of time in bed was obtained in one 28-h period or split into two equally divided 14-h periods. The results here suggest that splitting sleep opportunities does not reduce the amount of sleep that can be obtained and may even increase SWS. Overall, the results also indicate that splitting the sleep-wake schedule is not detrimental to neurobehavioural performance, sleepiness or self-assessed ability. Indeed, it appears to dampen the circadian and homeostatic contributions to neurobehavioural performance such that response times around the circadian nadir in split schedules do not decline to the extent of consolidated sleep-wake schedules. Sleepiness and self-monitoring of performance ability exhibited the same circadian variation and rate of homeostatic decline in both schedules.

The main effects of circadian phase on neurobehavioural performance found here have been well documented (e.g., Matthews et al., 2012a; Wright et al., 2012; Wyatt et al., 1999). In both schedules, best performance, similar to baseline levels, occurred around the circadian acrophase, and worst performance occurred around the circadian nadir. This pattern was also displayed, unsurprisingly, in subjective sleepiness and assessments of ability to perform. That the variation between best and worst performance in the split schedule was dampened compared to the consolidated schedule is demonstrative of the established relationship between accruing wakefulness and circadian phase (Dijk et al., 1992; Wyatt et al., 1999). Our finding that performance around the nadir was significantly worse for the consolidated schedule than the split schedule is most likely attributable to the additional

accumulated wakefulness in the former at this time. Support for this is evident in the number of performance lapses, which increased at a similar rate from 2 h to 7 h of prior wake in both conditions, despite being more frequent overall in the consolidated sleep-wake schedule around the nadir. As a greater amount of SWS occurred in the split schedule than the consolidated schedule, it is possible this may also have had a role in sustaining performance throughout the day. Incidentally, that schedules significantly differed around the nadir in terms of the number of lapses and slowest response times, while maintaining similar mean and fastest responses times, lends further support to the state-instability hypothesis (Doran et al., 2001).

Consistent with previous findings (Wright et al., 2002; Wyatt et al., 1999; Zhou et al., 2011), neurobehavioural decline occurred with increasing wakefulness in both consolidated and split schedules. The longer sleep episodes permitted in the consolidated schedule appeared to result in significantly better performance, compared to the split schedule, over the first few hours of prior wake. This was despite the same total amount of time in bed being provided to all participants over the course of each schedule. Given that testing sessions began 1.5 h after waking and no improvement in performance was evident in subsequent testing sessions, it is unlikely that this initial difference between schedules is attributable to sleep inertia (Jewett et al., 1999b). Instead, it is postulated that this difference, and the subsequent convergence of the schedules, reflects the competing influences of prior sleep duration and prior wake within a critical preceding period (Åkerstedt & Folkard, 1997; Ferguson, Paech, Dorrian, Roach, & Jay, 2011). At 2 h of prior wake, the longer duration of prior sleep in the consolidated schedule elicited better neurobehavioural performance than in the split schedule; however, by 4.5 h to 7 h of prior wake, it provided no additional benefit and performance continued to decline with increasing prior wake. This convergence of schedules in performance was reflected neither in subjective sleepiness nor individuals' assessments of their own capacity to perform, both of which were consistently better in the consolidated schedule than the split schedule at comparable durations of prior wakefulness. This suggests that objective performance is dependent, to a greater extent, on the total duration of

sleep obtained each day, whereas subjective assessments of sleepiness or ability may be more strongly influenced by the duration of the most recent sleep episode. Although participants in the split schedule reported feeling more sleepy than those in the consolidated schedule at 2 h to 7 h of prior wake, sleepiness ratings did not decline as far as those in the consolidated schedule at 17 h of prior wake.

#### 5.4.1. Implications for Practice

In practical terms, the findings of this study suggest that multiple shorter shifts per day have potential for sustaining neurobehavioural performance in the workplace around the clock, notwithstanding inconsistencies with the subjective measures. While the fragmentation of non-work hours caused by this shift type may not suit all industries or employees, due to its potential disruption of social and family life, it may be necessary or preferable in certain situations. For example, where the task is important enough (e.g., a short-term multi-day firefighter response) or where disruption to social or family life would be minimal and employees live on or near the site (e.g. fly-in, fly-out industries), splitting the work-rest schedule in this way may be more effective than current shift schedules in sustaining operational performance. Indeed, similar schedules of 4 h on/8 h off and 6 h on/6 h off are regularly employed in maritime watch systems, and alternating 8-h shifts, termed 'relay van work', are currently employed in sectors of the Australian rail industry, to ensure efficient 24-h operations (Darwent et al., 2008; Eriksen et al., 2006; Härmä et al., 2008; Van Leeuwen et al., 2013).

However, there are some considerations to be made regarding the application of these findings outside the laboratory. While shorter shifts may assist in the maintenance of neurobehavioural function around the clock, it is possible that splitting the schedule may also facilitate other opportunities for error. For example, the implementation of a split work-rest schedule would simultaneously increase the opportunities for sleep inertia (Tassi & Muzet, 2000) and the number of hand-overs required between employees of contiguous shifts

(Smith, Folkard, Tucker, & Macdonald, 1998a), both of which could enable miscommunication.

#### 5.4.2. Limitations and Future Research

The main limitation of this study is related to generalisability. Participants were all healthy young males who, for the duration of the study, lived in a time-isolated environment free of social and technological disruptions. This environment facilitated substantial durations of undisturbed sleep, not often achievable outside the laboratory. Therefore, the degree to which performance and subjective assessments of ability can be generalised to female, less healthy, and/or older people in a natural setting is not known. However, this is not a serious limitation given that young males represent a large demographic in the types of industries which could effectively utilise split work-rest schedules.

Reported in this paper are results from protocols with an enforced rest-to-wake ratio of 1:2, equivalent to 8 h of time in bed and 16 h of wake every 24-h day. Given that sleep loss affects performance and coexists with shiftwork (Åkerstedt, 2003), it is critical to understand how the circadian and homeostatic processes interact under conditions of moderate and severe sleep restriction. Some objective and subjective performance data have been reported for forced desynchrony protocols in which participants lived on consolidated sleep-wake schedules with sleep restriction (Buxton et al., 2012; Ferguson et al., 2012b; Heath et al., 2012; Matthews et al., 2012a; Matthews et al., 2012b; Paech, Ferguson, Sargent, Kennaway, & Roach, 2012; Sargent et al., 2012a; Sargent, Darwent, Ferguson, & Roach, 2012b; Zhou et al., 2011, 2012), but no data have yet been reported for forced desynchrony protocols in which sleep-wake schedules are split and sleep is restricted.

An additional avenue for enquiry exists in the finding that those in the split schedule acquired about 27% more SWS than those in the consolidated schedule. With a current understanding of sleep homeostasis, one would expect those acquiring similar ratios of sleep and wake to obtain equivalent amounts of SWS (Borbély, 1980, 1982). While it is unclear why those in the split schedule

acquired more SWS, on average, than those in the consolidated schedule there are a few possible explanations for this finding. A possible reason for the difference is that splitting the sleep-wake cycle has an impact on sleep homeostasis that is manifest in an increased duration of SWS of reduced intensity. Another possible explanation for the increased duration of SWS in the split schedule is the propensity for SWS to predominate at the beginning of sleep episodes (Carskadon & Dement, 2011). Since split sleep-wake schedules produce a greater number of individual sleep episodes, they might facilitate more opportunities to initiate SWS. In future, these explanations could be tested with spectral analyses of slow wave activity, to measure the intensity of sleep, and investigate changes in sleep architecture across successive sleep episodes.

#### 5.4.3. Conclusion

Neurobehavioural performance did not differ between schedule types overall. However, halving the duration of wakefulness between sleep episodes in the split schedule resulted in a smaller, less variable, decline in performance around the circadian nadir. The results suggest that improvement in performance at the nadir, relative to the consolidated schedule, may be attributable to a reduction of scheduled prior wake and potentially an increase in SWS. Additionally, splitting the sleep-wake schedule does not appear to have the same influence on subjective assessments of sleepiness or ability as it has on objective performance measures. The longer sleep episodes in the consolidated schedule coincided with reduced sleepiness and better assessments of ability than the shorter sleeps of the split schedule, despite facilitating better neurobehavioural performance for only a few hours after waking. Despite this, and provided sleep opportunities are properly utilised, these findings suggest that shorter work-rest shift cycles (e.g., 6 h on/6 h off) can be satisfactorily implemented in place of longer work-rest shift cycles (e.g., 12 h on/12 h off) to sustain performance at all times of day.

## **Chapter 6.**

# **Effects of Sleep Loss and Circadian Misalignment on Predictors of Driving Performance**

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### **Peer-reviewed publication associated with this chapter (Appendix I):**

**Kosmadopoulos, A.**, Sargent, C., Zhou, X., Darwent, D., Matthews, R. W., Dawson, D. & Roach, G. D. (2017). The efficacy of objective and subjective predictors of driving performance during sleep restriction and circadian misalignment. *Accident Analysis & Prevention*, 99(B), 445-451.  
<http://dx.doi.org/10.1016/j.aap.2015.10.014>.



## 6.1. Introduction

Demand for 24-h access to services and goods has led to an increase in the number of employees engaged in shiftwork (McMenamin, 2007). Despite its economic benefits, shiftwork has social and public health costs. Shiftworkers, especially those who work at night, are among the most fatigued demographic in society, frequently obtaining inadequate durations of sleep, and work in conflict with their body clocks (Åkerstedt, 2003). Insufficient sleep, extended wakefulness, and working during the circadian nadir are associated with an increased risk of workplace and motor vehicle accidents (Folkard et al., 2006; Philip & Åkerstedt, 2006). An estimated 20% of on-road accidents are attributed to fatigue (Horne & Reyner, 1995). Given the necessity of driving for many shiftworkers, whether it is for the purpose of commuting or a requirement of the job itself (e.g., trucking, mining, courier and postal services), this demographic is particularly susceptible to accidents on the road (Åkerstedt, Peters, Anund, & Kecklund, 2005). Thus, the ability to assess risk and predict driving impairment on the job is of great importance in fatigue management.

Numerous fatigue-detection technologies have been developed and released with the aim of providing reliable assessments of accident risk and driving performance capacity (Dawson et al., 2014). These range from embedded lane-tracking systems which detect performance deterioration while on the road, to devices that monitor physiological correlates of fatigue – such as the frequency and duration of eye-blinks or specific patterns of brain activity in EEG tracings (Balkin et al., 2004; Dawson et al., 2014). However, these technologies are not suitable for use by all individuals and all industries, where numerous issues must be considered – including financial cost, safety, convenience, comfort and privacy.

The measures of drowsy driving likely to be most feasible for the broader driving population are those derived from simple objective and subjective performance tasks (Balkin et al., 2004). To be effective and convenient, these measures must be sensitive to fatigue-inducing factors (e.g., sleep restriction and time of day), demonstrate a strong association with a relevant driving

performance metric, and should be portable, affordable, and brief (Balkin et al., 2004; Dorrian et al., 2005). A simple neurobehavioural task or subjective assessment of alertness or one's capacity to perform could meet all these criteria. Indeed, these tasks are often used in the laboratory and in the field as proxies for 'real-world' functioning on the basis that they capture basic constructs required for the performance of complex tasks (Basner & Dinges, 2011; Jackson et al., 2013) and are highly responsive to sleep and circadian processes (Balkin et al., 2004; Kosmadopoulos et al., 2014a; Lamond, Petrilli, Dawson, & Roach, 2006; Van Dongen, Baynard, Maislin, & Dinges, 2004; Zhou et al., 2011).

Neurobehavioural tasks requiring sustained attention, processing speed and working memory, as well as self-reflective subjective assessments of sleepiness, have all been associated with driving performance (Ingre et al., 2006; Szlyk, Myers, Zhang, Wetzel, & Shapiro, 2002). Recent studies conducted on-road and with laboratory-based simulators have indicated sustained attention measured with a psychomotor vigilance test (PVT) is strongly associated with driving performance following total sleep deprivation – more so than performance on tasks of executive function (Baulk et al., 2008; Jackson et al., 2013; Jongen et al., 2015). However, while attention is critical for a safe commute, it is not necessarily evident that performance on a PVT would constitute the best predictor of drowsy driving at all times of day. Shiftworkers, generally, tend to be chronically sleep-restricted rather than totally sleep-deprived (>24 h) and are employed around the clock, not just during the day. Notwithstanding individual differences in performance (Van Dongen et al., 2004), driving, neurobehavioural tasks, and subjective assessments all vary in their resilience to sleep and circadian manipulation depending on their duration, difficulty and complexity (Balkin et al., 2004; Burke et al., 2015; Matthews et al., 2012b; Schmidt, Collette, Cajochen, & Peigneux, 2007; Zhou et al., 2012). Thus, the driving performance of shiftworkers and any given assay used to predict it may not have consistently strong associations, following partial sleep restriction, at all times of day.

The aim of this study was twofold: First, to establish the sensitivity of a simulated driving task, several commonly-used neurobehavioural tasks, and subjective measures of sleepiness and self-assessed ability to perform, to circadian phase and sleep dose; and, second, to determine how well these neurobehavioural and subjective measures predict simulated driving performance at different circadian phases and sleep durations. To accomplish this, two forced desynchrony protocols, one with sleep restriction and one without, were employed.

## **6.2. Methods and Materials**

### **6.2.1. Participants**

Participants were 32 healthy males aged  $22.84 \pm 2.94$  years (mean  $\pm$  SD; range = 19 – 29 years) and had a body mass index (BMI) of  $22.33 \pm 2.16$  kg/m<sup>2</sup> (range = 18.5 – 25.0 kg/m<sup>2</sup>). Volunteers were required to pass a screening process that involved an interview, questionnaires, and a week of wrist actigraphy. Exclusion criteria included smoking, excessive consumption of caffeine or alcohol, physical or medical disorders, irregular sleep patterns, or transmeridian travel / shiftwork in the previous two months. For a week before admission, participants were required to maintain consistent bedtimes between 2200 h – 2400 h and sleep durations of 7 – 9 h per night, verified by activity monitors (Actical; Philips Respironics, Bend, Oregon, USA) and sleep diaries (Kosmadopoulos et al., 2014b).

#### **6.2.1.1. Ethics**

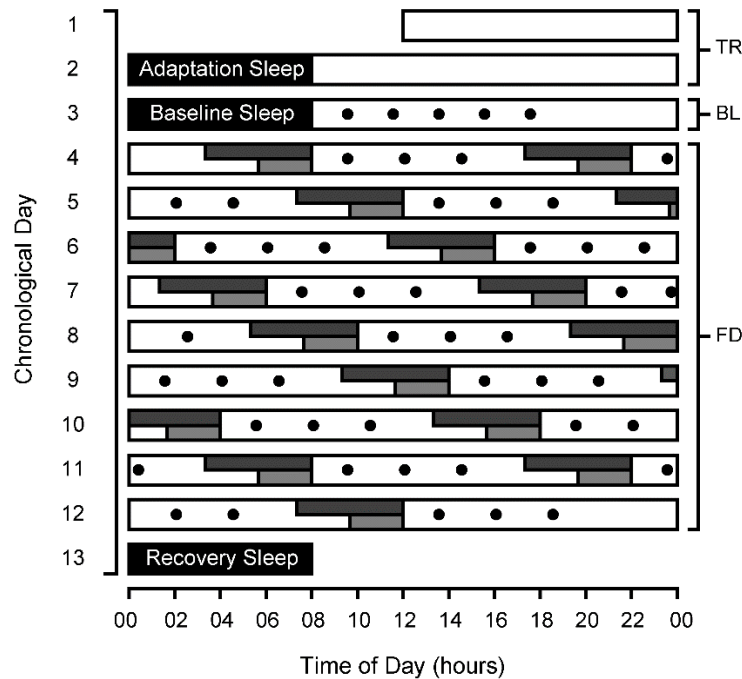
The study was conducted in accordance with the Declaration of Helsinki and guidelines of the National Health and Medical Research Council of Australia. All participants provided informed written consent prior to admittance into the study and were remunerated with an honorarium for their involvement. The Central Queensland University Human Research Ethics Committee approved the protocol.

### 6.2.2. Setting

Participants lived in the Appleton Institute time-isolation laboratory in groups of four. Each participant was assigned their own bedroom, living room, workstation, and bathroom facilities. A communal dining area was available for meal times. The laboratory was windowless, sound attenuated, and free of external time cues. Lighting was maintained at 10-15 lux during wake periods, and  $<.03$  lux during sleep periods. The target ambient temperature was 21-23°C. Participant behaviour was monitored in person and via closed circuit television cameras in the laboratory to ensure compliance with study protocols.

### 6.2.3. Protocol

Two protocols were conducted to assess the independent effects of circadian phase, controlling for prior wake. Participants were assigned to either a control condition ( $n = 16$ ) or a sleep restriction (SR) condition ( $n = 16$ ) (Figure 6-1). Both began with two 24-h training days, during which participants practiced neurobehavioural and subjective tasks to minimize learning effects. On the baseline day, participants completed five 1-h test sessions, scheduled at 2-h intervals, beginning 1.5 h after waking. Following this, participants in each condition underwent a 28-h FD schedule. During FD, sleep and wake was split into two 14-h cycles with an enforced rest-to-wake ratio of 1:2 (equivalent to an 8-h sleep opportunity in 24 h) in the control condition, and 1:5 (equivalent to 4-h sleep opportunity in 24 h) in the SR condition. During wake periods, 1-h test sessions began 1.5 h after lights on, with subsequent testing conducted every 2.5 h. Participants were permitted to read, watch DVDs, and listen to music in their living rooms between testing bouts, but were not permitted to undertake any strenuous activities or sleep outside designated periods. Interaction between participants was limited to meal times. A montage of PSG electrodes was applied to participants 30 min prior to sleep episodes.



**Figure 6-1** Protocol diagram of the control and sleep restriction (SR) forced desynchrony conditions. The x-axis indicates clock time across a 24-h period and the y-axis plots successive chronological days. Training days (TR) and a baseline day (BL) are followed by a period of forced desynchrony (FD). Control condition sleep opportunities are depicted by dark grey rectangles, and SR condition sleep opportunities are depicted by light grey rectangles. Black circles during wake periods indicate test sessions.

## 6.2.4. Measures

### 6.2.4.1. Simulated driving task

Driving was assessed using the York Driving Simulator (YDS; York Computer Technologies, Kingston, Ontario), conducted on a desktop computer, with a wheel mounted to the desk and acceleration and brake pedals fixed to the floor. The simulation was 10 min in duration and emulated a night-time rural drive on a single carriageway, two-lane road with target speeds of 100 km/h on straight sections alternating with target speeds of 80 km/h on winding sections. Participants were required to overtake a single car appearing 7 min into the task. Participants were instructed to keep as close to the speed limit as possible and to stay within the left lane (standard in Australia). Performance was expressed as the standard deviation of lateral position (SDLAT) within the lane,

with increased variability indicative of worse performance, as it is sensitive to fatigue (Matthews et al., 2012a). Lateral position was calculated as the distance in meters from the centre point of the car to the centre of the road.

#### *6.2.4.2. Neurobehavioural performance measures*

Three measures of fatigue and neurobehavioural function were selected for their potential utility as predictors of SDLAT in operational settings. The first of these was the psychomotor vigilance test (PVT), a 10-min simple response time task performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA) (Dorrian et al., 2005). The PVT has minimal learning effects and measures sustained attention, requiring constant vigilance to detect stimuli presented at random intervals. Increased mean response times on the PVT indicate reductions in the ability to sustain attention. The mean reciprocal response time (RRT;  $\text{ms}^{-1} \times 10^{-3}$ ) was derived as the performance metric as it has been shown to be the most sensitive to partial sleep deprivation (Basner & Dinges, 2011). The Serial Addition/Subtraction Test (SAST), was included as a cognitive throughput measure capturing changes in declarative working memory (Darwent et al., 2010; DeStefano & LeFevre, 2004). Conducted on a desktop computer, performance was determined by the number of addition and subtraction sums correctly answered in 5 min. The final task was the Digit Symbol Substitution Test (DSST), a cognitive throughput measure dependent on processing speed, memory, and visuomotor coordination (Joy et al., 2004). A different version of the DSST was used in each test session to minimize learning effects. Performance was determined by the number of correct digit-symbol pairs created in 90 sec.

#### *6.2.4.3. Subjective measures of sleepiness, alertness, and ability.*

Subjective sleepiness was measured using a 9-point Karolinska Sleepiness Scale (KSS) (Åkerstedt & Gillberg, 1990). This scale requires participants to rate how sleepy they feel, from 1=“Extremely alert” to 9=“Very sleepy, great effort to keep awake, fighting sleep”, with intermediate levels labeled in 1-unit increments. Alertness and self-assessed ability to perform were assessed using 100mm

visual analogue scales (VAS). The question, 'How alert do you feel?' (VAS Alert) was anchored left-to-right by the statements 'struggling to remain awake' and 'extremely alert and wide awake'. Similarly, the question, 'how well do you think you will perform?' (VAS Performance) was anchored with 'extremely poorly' and 'extremely well'.

#### *6.2.4.4. Core body temperature, sleep, and physical activity*

Core body temperature (CBT), sleep, and physical activity were recorded to derive estimates of circadian phase. CBT was continuously recorded via a rectal thermistor (Steriprobe 491B; Cincinatti Sub-Zero Products, Cincinnati, Ohio, USA) connected to a waist-worn ambulatory recording device (Mini-logger series 2000, Mini-Mitter, Bend, Oregon, USA) in 1-min intervals. Sleep was monitored with standard polysomnography, using the Graef PSG/EEG Systems (Compumedics, Melbourne, Victoria, Australia). Sleep-wake stages were scored in 30-s epochs by a trained technician according to standard criteria (Iber et al., 2007). Physical activity was monitored with wrist-worn activity monitors (Actical; Philips Respironics, Bend, Oregon, USA).

#### *6.2.4.5. Circadian phase estimates*

Circadian phase estimates were derived from the CBT of each participant by means of a five-step de-masking process to control for the effects of sleep and physical activity. Circadian phase estimates (i.e., ranging from 0-360°, with 0° representing the nadir of the CBT curve) were assigned to each minute of the protocol for each participant (section 2.5, p.99, of General Methods).

#### *6.2.5. Data Analysis*

Prior to data analyses, all metrics collected during the forced desynchrony period were standardized within individuals against their respective average during the five test sessions on the baseline day. Standardized scores were derived such that negative values indicated declines, and positive values indicated improvements, relative to baseline. Data from each condition were

assigned to one of 6x60° circadian phase bins (i.e., centred at 0°, 60°, 120°, 180°, 240°, 300°).

#### *6.2.5.1. Sensitivity of tasks to sleep dose and circadian phase*

Mixed-model analyses of variance (ANOVAs) were conducted, with sleep dose (two levels) and circadian phase (six levels) included as fixed terms. Performance measures were entered as the dependent variables and a random term of 'Participant' was also included. Main effects of sleep dose and circadian phase were tested first, followed by a test of any sleep dose x circadian phase interactions. Effect sizes were interpreted with Cohen's  $f^2$ , calculated with the formula:  $f^2 = F \times (n / d)$ , where n and d are the respective numerator and denominator degrees of freedom of the F-statistic derived in the analysis (Cohen, 1988, pp.408-410). Small, medium and large effect sizes were interpreted against the respective 0.02, 0.15, and 0.35 benchmarks (Cohen, 1988).

#### *6.2.5.2. Objective and subjective measures as predictors of driving*

To evaluate the relationship of all measures with SDLAT at each circadian phase, mean scores were derived for each participant for each circadian phase. Regression analyses were then conducted for each combination of sleep dose and circadian phase (2 sleep doses × 6 circadian phases) with SDLAT as the dependent variable and neurobehavioural and subjective measures as the predictors.

### **6.3. Results**

#### **6.3.1. Participant Characteristics**

Participants assigned to the control condition (n = 16; age = 22.56 ± 2.87 years; BMI = 22.03 ± 1.88 kg/m<sup>2</sup>) and the sleep restriction (SR) condition (n = 16; age = 23.13 ± 3.07 years; BMI = 22.63 ± 2.44 kg/m<sup>2</sup>) did not significantly differ in terms of age [t(30)=0.54, p=.597 (2-tailed)] or BMI [t(30)=0.77, p=.447 (2-



tailed)]. T-tests revealed no significant differences between conditions for any of the performance and rating scores on the baseline day (Table 6-1).

### 6.3.2. Main Effects and Interactions

#### 6.3.2.1. Circadian phase

Mixed models analyses revealed significant main effects of circadian phase for all driving, neurobehavioural, and subjective tasks (Table 6-2). Specifically, performance and subjective ratings were lower around the circadian nadir than at other circadian phases (Figure 6-2a-g). SDLAT was the measure most sensitive to circadian phase ( $f^2=0.58$ ). Large effect sizes of circadian phase were observed for all neurobehavioural and subjective tasks except the SAST ( $f^2=0.34$ ), for which a medium effect of circadian phase was found.

**Table 6-1** Baseline day results for objective and subjective measures.

Measures	Control		Sleep Restriction		t (30)	p
	Mean	SD	Mean	SD		
SDLAT	0.31	0.06	0.33	0.08	0.71	0.483
PVT	4.68	0.40	4.55	0.59	0.76	0.451
SAST	63.91	10.27	61.98	7.97	0.60	0.556
DSST	63.34	11.21	62.66	11.69	0.17	0.869
KSS	4.03	1.27	4.16	1.51	0.28	0.782
VAS Alert	61.47	11.87	58.15	15.12	0.69	0.495
VAS Performance	63.87	10.86	59.24	10.19	1.24	0.223

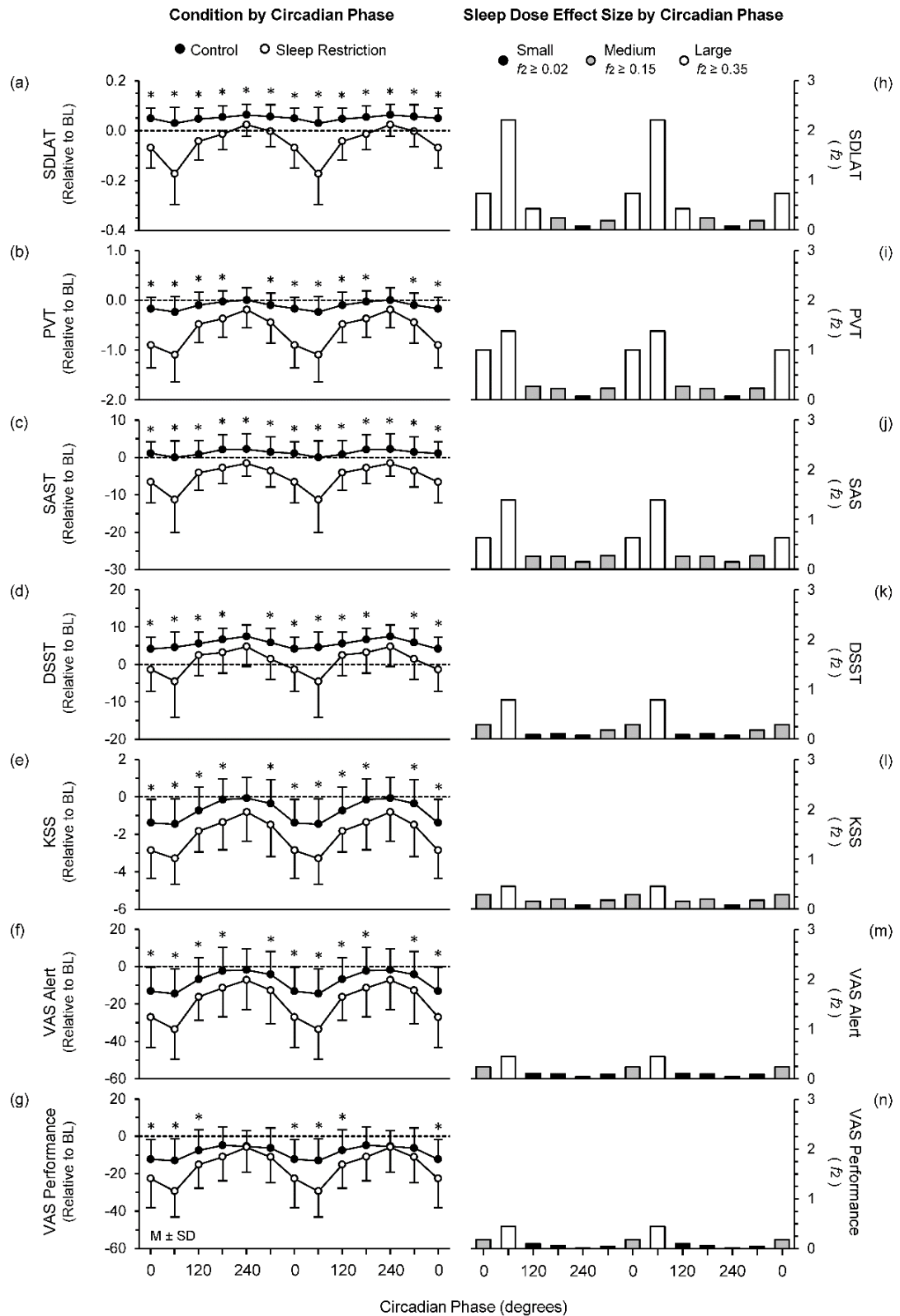
SDLAT, standard deviation of lateral position; PVT, psychomotor vigilance test; SAST, serial addition/subtraction test; DSST, digit symbol substitution task; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.

**Table 6-2** Results of mixed models ANOVAs for objective and subjective measures.

Measures	Phase	Sleep	Phase x Sleep
	F (5,534)	F (1,30)	F (5,534)
SDLAT	61.48***	38.52***	31.98***
PVT	59.18***	33.95***	21.54***
SAST	36.72***	26.97***	15.75***
DSST	37.93***	12.44**	10.54***
KSS	60.49***	13.24**	3.45**
VAS Alert	56.34***	8.96**	5.43***
VAS Performance	48.68***	5.67*	9.56***

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

Phase, circadian phase; Sleep, sleep dose condition; SDLAT, standard deviation of lateral position; PVT, psychomotor vigilance test; SAST, serial addition/subtraction test; DSST, digit symbol substitution task; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.



**Figure 6-2** Mean ( $\pm$ SD) relative-to-baseline scores for each task and condition by circadian phase (panels a-g) and effect sizes of sleep dose for each task by circadian phase (panels h-n). Asterisks indicate a significant difference between conditions.

### 6.3.2.2. *Sleep dose*

Mixed models analyses revealed significant effects of sleep dose for all tasks (Table 6-2). Specifically, performance and subjective ratings were worse during the SR condition than the control condition (Figure 6-2a-g). Effects of sleep dose were large for all driving and neurobehavioural tasks, with SDLAT ( $f^2=1.28$ ) and the PVT ( $f^2=1.13$ ) being the most sensitive and DSST ( $f^2=0.41$ ) being the least sensitive. There was a large effect of sleep dose on the KSS ( $f^2=0.44$ ) and medium effects on both VAS Alert ( $f^2=0.30$ ) and VAS Performance ( $f^2=0.19$ ).

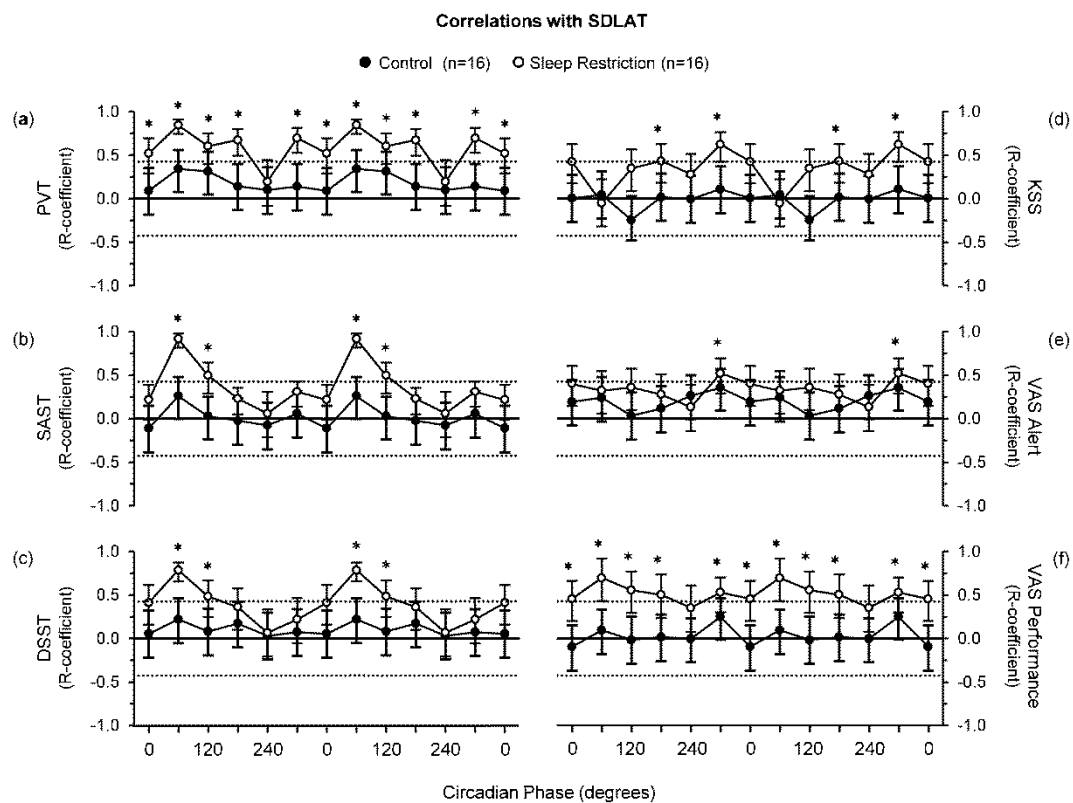
### 6.3.2.3. *Circadian phase x sleep dose interactions*

All of the tasks exhibited significant circadian phase x sleep dose interactions (Table 6-2). During the control condition, circadian phase had small ( $f^2<0.15$ ) effects on all driving, neurobehavioural, and all subjective measures except the KSS ( $f^2=0.18$ ), which exhibited a medium effect of circadian phase. During the SR condition, there were large ( $f^2>0.35$ ) effects of circadian phase on all performance and ratings; SDLAT ( $f^2=0.85$ ) and the PVT ( $f^2=0.71$ ) were most sensitive, followed by the SAST ( $f^2=0.47$ ) and VAS Performance ( $f^2=0.47$ ).

Effects of sleep dose were dependent on circadian phase (Figure 6-2h-n). In the SR condition, impairment in performance and ratings, relative to the control condition, was greater around the circadian nadir in CBT than around the circadian acrophase. Performance on the neurobehavioural tasks was more sensitive to SR around the nadir than subjective ratings. SDLAT ( $f^2=2.21$ ) was the measure most affected by sleep dose around the nadir.

### 6.3.3. Predictors of Driving Performance

During the control condition, there were no significant correlations between SDLAT and any measure at any circadian phase (Figure 6-3). During SR, there were strong to moderate significant positive correlations between SDLAT and PVT across all circadian phases except near the acrophase of CBT (240°) (Figure 6-3a). SDLAT was only correlated with the SAST and DSST metrics close to the nadir. Of the subjective measures, VAS Performance was similar to the PVT in that it was strongly associated with SDLAT at almost all circadian phases except 240° during SR (Figure 6-3f). Although VAS Alert was only correlated with SDLAT around the nadir (300°) during SR (Figure 6-3e), it was correlated with VAS Performance at all circadian phases ( $r=.69$  to  $r=.82$ ,  $p<.05$ , 1-tailed).



**Figure 6-3** Pearson's R-coefficients of correlations between SDLAT and each neurobehavioural task (panels a-c) and each subjective measure (panels d-f) at each circadian phase in both the control condition and the sleep restriction condition. Significant ( $p<.05$ , 1-tailed) correlation coefficients are those placed above the dotted lines, marked with asterisks.

## 6.4. Discussion

The aim of the current study was to establish the sensitivity of several potential predictors of driving impairment to chronic sleep restriction and circadian phase, and to evaluate their efficacy as predictors of driving, with and without sleep restriction, at different circadian phases. The main findings of this study were that the impact of sleep restriction on performance and subjective ratings is highly dependent on circadian phase and that psychomotor vigilance and self-assessed ability explain large proportions of the variance in simulated driving, across most circadian phases, during sleep restriction. These results reinforce previous findings that vigilance is a core component of driving performance (Jackson et al., 2013), and that fatigued people have some insight into their limitations and ability to perform (Dorrian, Lamond, & Dawson, 2000).

An advantage of the forced desynchrony protocol in this study was that it permitted the effects of sleep restriction to be assessed at all times of day. All measures of driving, neurobehavioural performance and subjective assessment were impaired by sleep restriction and varied across circadian phases parallel to the rhythm of CBT, consistent with previous findings (Matthews et al., 2012a; Wright et al., 2012; Zhou et al., 2012). In the current study, lane deviation and vigilance were the most vulnerable to the combined effects of sleep restriction and the circadian nadir in CBT. Mean performance on neurobehavioural tasks, with the exception of the DSST, tended to be more affected by chronic sleep restriction than subjective measures.

Past research has established vigilance as a strong predictor of drowsy driving resulting from extended wakefulness (Baulk et al., 2008; Jackson et al., 2013; Jongen et al., 2015). The current study extends these findings, showing that vigilance is a strong predictor of driving impairment at most times of day, following insufficient sleep, even when prior wake is low (limited to 7 h). The absence of any significant correlations between the PVT and driving performance throughout the control condition – when participants were well-rested – or around the acrophase of CBT during sleep restriction when participants were more alert, suggests that vigilance to road conditions is

critical for driving performance when fatigued. A similar pattern of correlations found between lane deviation and self-assessed ability is consistent with findings by Dorrian et al. (2003) that individuals can recognize the effect of insufficient sleep on their capacity to perform at night. The lack of a correlation between lane deviation and self-assessed ability around the acrophase may be an issue of restricted range, rather than indicative of reduced self-awareness. However, the strong relationship between measures of alertness and self-assessed ability at all circadian phases does support the notion that insight into one's ability to perform is influenced by circadian variations in alertness.

As the PVT and self-assessed ability explain large proportions of the variance in lane deviation when sleep-restricted at most times of day, they may provide useful indications of decline. However, the large inter-subject variability in drowsy driving and differences in the sensitivity of tasks to sleep restriction (Figure 6-2), mean that these measures may be limited in predicting the extent of impairment. Indeed, Baulk et al. (2008) found that although PVT performance and simulated driving were strongly correlated across a night of sleep deprivation, vigilance increasingly underestimated the magnitude of lane deviation as performance deteriorated. As such, these simple measures may not be appropriate for determining an individual's fitness to drive.

#### 6.4.1. Limitations and Future Directions

A limitation of this study is that driving performance was assessed with a simulated task, rather than with an on-road assessment in a real car. However, on-road assessments were not feasible in the current study, as forced desynchrony protocols must be conducted in controlled environments free of external time cues. Nevertheless, computer-based simulated driving tasks like the one used in the current study capture more skills required in driving than simple neurobehavioural measures (Jackson et al., 2013; Lee, Cameron, & Lee, 2003) and have been used extensively in clinical settings (Vakulin et al., 2014). Strong associations have also been found between simulated and on-road drives in well-rested and sleep-restricted groups (Lee et al., 2003; Philip et al., 2005).

It should be noted that there are many types of neurobehavioural tasks that could have been selected (Szlyk et al., 2002). The tasks used in the current study were selected on the basis that they are simple, brief, frequently used in fatigue research (Dorrian et al., 2003; Van Dongen et al., 2004; Zhou et al., 2011), and associated with driving (Ingre et al., 2006; Szlyk et al., 2002). The results of this study must be interpreted in the context that they represent only a subset of possible predictors. Additionally, the sample size in the current study was not powerful enough to detect weak correlations of performance and ratings with lane deviation that approached significance at several circadian phases. Beyond basic neurobehavioural function, there is an avenue for further research into the relative sleep and circadian influences on more complex, higher-order cognitive processes (Burke et al., 2015) and constructs, such as judgement and decision-making, in relation to driving.

A limitation regarding the analyses used to assess objective and subjective measures as predictors of driving performance was that data for each individual were averaged at the level of circadian phase. Thus, individuals' average scores at each phase were regressed against their respective average driving performance at that phase. In future, it would be useful to compare metrics directly, evaluating associations at each testing session.

#### 6.4.2. Conclusions

The results of this study highlight that the impact of sleep loss on driving and neurobehavioural performance is more detrimental during the night than it is during the day. Simple assessment tools of psychomotor vigilance and self-monitoring of one's own ability to perform are strong predictors of impaired driving following sleep loss. However, given the complexity of driving and the varying sensitivity of tasks to sleep restriction, these measures may not be sufficient on their own to evaluate the magnitude of driving impairment when fatigued. Thus, determining fitness to drive may require a battery of validated tasks to capture the range of processes and skills involved in driving.



## **Chapter 7.**

# **Evaluation of Sleep-Timing Strategies Used to Sustain Performance on Night Shifts**

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**Peer-reviewed publication associated with this chapter (Appendix J):**

**Kosmadopoulos, A.,** Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2015). Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times? In G. A. Kennedy & C. Sargent (Eds.), *The Time of Your Life* (pp. 32-37). Melbourne, Australia: Australasian Chronobiology Society.

## 7.1. Introduction

Consumer expectations and demands for 24-h service in a competitive global marketplace has led to an increase in the proportion of employees engaged in shiftwork (McMenamin, 2007). Approximately 16% of employees in Australia are shiftworkers, and 7% usually work at night (Australian Bureau of Statistics, 2013). However, despite its important role in the economy, shiftwork can have a negative impact on employee health, well-being, and performance (Costa, 1996; Folkard & Tucker, 2003). Night work, in particular, is disruptive to the sleep/wake system and the internal body clock. Night workers must sleep during the daytime when their body clock is promoting wake and they must stay awake to work at night when their body clock is promoting sleep. Combined, the resulting poor sleep quality, longer durations of wake, and increased sleepiness, mean that there is an increased likelihood of making errors, having an accident, or being injured on shift (Folkard & Tucker, 2003; Smith et al., 1994).

Numerous studies have investigated methods of promoting alertness during night shifts, through the use of caffeine, naps, bright light, and melatonin (Crowley, Lee, Tseng, Fogg, & Eastman, 2003; Garbarino et al., 2004; Purnell et al., 2002; Schweitzer, Randazzo, Stone, Erman, & Walsh, 2006). However, there is also research to suggest that the timing of sleep during breaks between consecutive night shifts may have an effect on night-time neurobehavioural performance and alertness (Åkerstedt, 1998; Santhi, Aeschbach, Horowitz, & Czeisler, 2008). Night workers could adopt a sleep strategy that maximises the amount of sleep obtained between consecutive night shifts or reduces the time spent awake before work (Åkerstedt & Landstrom, 1998; Tepas, 1982).

Currently, night workers generally adopt one of three main approaches when sleeping between shifts. Some choose to (i) have a single sleep in the morning immediately after work, (ii) others delay sleep until several hours after work in a manner similar to day workers, and (iii) others split their sleep episodes, obtaining some sleep in the morning and some in the evening (Åkerstedt, 1998; Roach et al., 2016). All these sleep strategies have advantages and

disadvantages, but their effectiveness at sustaining performance has not been systematically evaluated. The first approach, popular among many night workers, is often chosen because it immediately satiates the sleep pressure accumulated during the night (Åkerstedt, 1998; Ficca et al., 2010; Knauth & Rutenfranz, 1981; Tepas, 1982). However, sleep quality and duration at this time may be reduced due to the alerting influence of the circadian pacemaker (Åkerstedt & Landstrom, 1998; Sargent et al., 2012a). Additionally, it also increases the duration of wakefulness accumulated before the subsequent shift. The second approach, where sleep is delayed several hours, allows night workers to commence their shift refreshed with little accumulated prior wake (Chinoy, Harris, Kim, Wang, & Duffy, 2016; Santhi et al., 2008). However, this strategy may be of limited effectiveness and viability for two reasons: first, it requires night workers to remain awake during their break fatigued, which not all are able or willing to do; second, it can result in sleep overlapping the biological wake maintenance zone, which may affect its quality (Lavie, 1986; Strogatz et al., 1987). The split sleep strategy is an attempt to obtain some of the benefits of both immediate and delayed strategies, but it may be difficult to implement and its effectiveness at sustaining night-time performance has not been ascertained.

There is some evidence to suggest that delaying sleep is a more effective strategy than an immediate sleep for 8-h night shifts because it reduces the amount of prior wakefulness accumulated across the night (Santhi et al., 2008; Santhi, Duffy, Horowitz, & Czeisler, 2005). However, this may not be the case for the 35.8% of shiftworkers who usually work longer shifts (Australian Bureau of Statistics, 2010) with shorter breaks between them, such as 12-h on/12-h off systems. With little evidence to support one approach over another, workers typically arrange their daytime sleep episodes in a way that suits personal preferences and enables them to fulfil societal obligations. Smith et al. (2005) found that shiftwork-specific internality (i.e., the degree to which individuals believe they can control factors associated with shiftwork, including sleep quality and work performance) can explain 25-31% of the variance in fatigue, and 21% of the variance on night shift drowsiness. As such, it may be that an

individual worker's preference for a sleep strategy might have an influence on subsequent performance. This may mean that night workers who are not able to sleep at their preferred times may perform worse on shift than those who are able to obtain sufficient sleep at times of their choosing.

The primary aim of this study was to determine the best sleep strategy to adopt between consecutive night shifts by comparing the effectiveness of each at sustaining performance and maximizing sleep quality and duration. The secondary aim of this study was to determine whether preferences for a sleep strategy can indicate subsequent functioning. To achieve these aims, participants in this study completed three simulated shiftwork protocols. Each protocol comprised two identical 12-h night shifts with 7 h of time in bed arranged at different times between them.

## **7.2. Methods and Materials**

### **7.2.1. Participants**

Participants were 12 healthy males aged  $22.92 \pm 5.23$  years (mean  $\pm$  SD; range = 18 – 34 years) with a body mass index (BMI) of  $22.89 \pm 1.38$  kg/m<sup>2</sup> (range = 20.8 – 25.1 kg/m<sup>2</sup>) who successfully passed a screening process involving a general health questionnaire, an interview, and a week of wearing wrist activity monitors to measure sleep patterns. Participants did not have any physical or medical disorders, were non-smokers, had not undertaken transmeridian travel or shiftwork in the previous two months, and did not report excessive consumption of caffeine or alcohol. For the week immediately prior to admission, participants were required to maintain consistent night-time sleep schedules of ~8 hours initiated between 2200 h – 2400 h, verified by a week of wrist actigraphy and self-report sleep diaries. Ethical approval for the study was granted by the Central Queensland University Human Research Ethics Committee using guidelines established by the National Health and Medical Research Council of Australia.

### 7.2.2. Setting

The protocol was conducted in a sound-attenuated, windowless sleep laboratory at the Appleton Institute, Central Queensland University. The laboratory was configured to accommodate six participants at a time, each with their own bedroom, living room, and bathroom facilities. Participants had access to the time, but were isolated from external environmental cues and were not permitted to leave the laboratory during the protocol. Room temperature was maintained at 21-23°C. During wake periods, ambient light was maintained at normal indoor levels (~300 lux). Lights were extinguished (i.e., <.03 lux) during sleep periods.

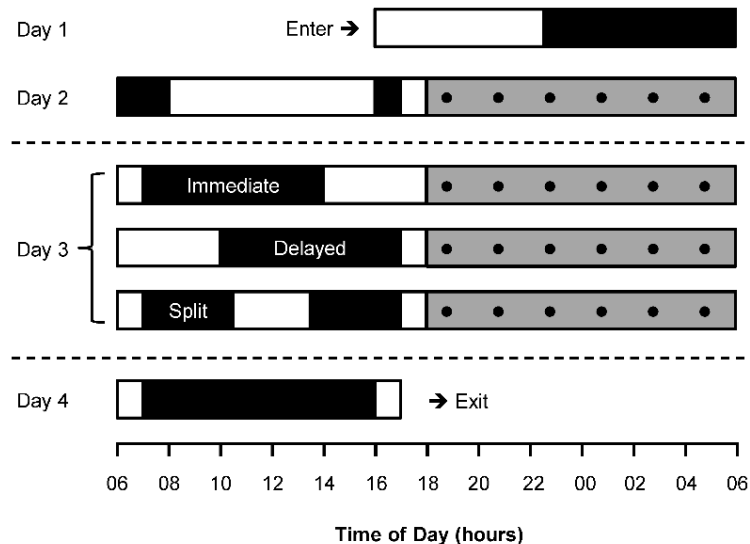
### 7.2.3. Protocol

The study employed a repeated-measures design with three randomised, completely counter-balanced, conditions. Participants attended the laboratory on three separate occasions, each covering a 4-day period, exactly one week apart. Each visit consisted of an adaptation night, two 12-h simulated night shifts separated by a 7-h sleep opportunity, followed by one daytime recovery sleep (Figure 7-1). The three conditions differed only in the timing of the 7-h sleep opportunity scheduled between the two night shifts.

The first evening and subsequent morning were used to train participants on the performance tasks. Participants were given 9.5 h in bed (2230 h – 0800 h) on the first night to familiarise them with the equipment used to monitor sleep and to eliminate any prior sleep debt. On the following afternoon, participants were scheduled a 1-h nap (1600 h – 1700 h) to prepare for the first night shift. After completing their first simulated night shift (1800 h – 0600 h), participants were provided a 7-h sleep opportunity. The timing of the sleep opportunity reflected one of three common sleep patterns exhibited by shiftworkers between night shifts – i.e., an immediate sleep (0700 h – 1400 h), a delayed sleep (1000 h–1700 h), or a split sleep (0700 h – 1030 h and 1330 h – 1700 h). These daytime sleeps were followed by a second night shift (1800 h – 0600 h)

and a 9-h recovery sleep (0700 h – 1600 h) before participants exited the laboratory at 1700 h.

During the simulated night shifts, participants completed a 30-min test battery every two hours (i.e., 6 in total), with the first test battery beginning 30 min after the start of the night shift. These test batteries comprised a number of tasks, including measures of neurobehavioural performance and alertness. Participants were kept free from distraction during test batteries by being seated alone in their living rooms in front of a blank wall. Participants had free time between testing bouts during which they could read, listen to music, draw or watch DVDs, but not sleep, exercise or leave their living rooms. Research staff monitored the participants' compliance with these instructions in person and via a closed-circuit television system. After having completed all three conditions, participants were asked to respond to the question, '*If you were working two night shifts in a row, which type of daytime sleep strategy would you most likely follow?*' by ranking them 1 to 3 in order of preference.



**Figure 7-1** Simulated consecutive night shift protocol with daytime sleep strategies. X-axis represents time of day (hours) and y-axis represents days in the protocol. Black rectangles represent time in bed (TIB), and shaded rectangles represent simulated night shifts. Black circles represent 30-min testing sessions. The temporal placement of TIB on Day 3 was dependent on whether participants were undergoing the Immediate, Delayed, or Split sleep strategy.

## 7.2.4. Measures

### 7.2.4.1. *Sleep*

Sleep was monitored with standard polysomnography (PSG), using the Grael PSG/EEG System (Compumedics, Melbourne, Australia) and a montage of Grass™ gold-cup electrode leads (Astro-Med, Inc., West Warwick, RI). The montage included two EEG channels (C3-M2, C4-M1), right and left EOG, and three channels of chin EMG. Sleep stages were scored in 30-s epochs by a trained technician following standard criteria (Iber et al., 2007). The sleep variables derived during time in bed were, in minutes, total sleep time (TST), stage N2 sleep, stage N3 sleep, and REM sleep.

### 7.2.4.2. *Neurobehavioural performance*

Neurobehavioural performance was assessed with a 10-min psychomotor vigilance test (PVT). The PVT, performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA), requires participants to respond to a visual stimulus appearing on a display at random 2-10 second intervals as quickly as possible with a button press. The dependent measures derived from the PVT were the mean reciprocal response time (RRT;  $\text{ms}^{-1} \times 10^{-3}$ ) and the number of lapses (i.e., response times >500 ms). A 5-min computerized serial addition and subtraction test (SAST) was included as a measure of cognitive throughput. The SAST requires participants to respond to a series of randomly presented single-digit arithmetic problems. Performance on the SAST was determined by the number of correct responses.

### 7.2.4.3. *Subjective sleepiness, alertness and self-assessed ability*

Subjective sleepiness was assessed using the Karolinska Sleepiness Scale (KSS; Åkerstedt & Gillberg, 1990). The KSS is a 9-point scale that requires participants to rate how they feel, from 1 ('Extremely alert') to 9 ('Very sleepy, great effort to keep awake, fighting sleep'). Subjective alertness was assessed using a visual analogue scale (VAS Alert; Dorrian et al., 2003). This required participants to rate how alert they felt by placing a vertical mark on a 100-mm

horizontal line, anchored by the statement 'struggling to remain awake' at one end and 'extremely alert and wide awake' at the other. Finally, a VAS scale was used to measure participants' assessments of their own ability to perform (VAS Performance). Participants had to respond to the question 'How well do you think you will perform' by placing a mark between the statements 'extremely poorly' and 'extremely well'.

#### 7.2.5. Statistical Analyses

Values more than three standard deviations from the mean were excluded from analyses as outliers. There was 1 outlier for PVT RRT and 4 outliers for PVT Lapse. There were no outliers for subjective measures. The effect of daytime sleep strategy on night-time performance was examined using mixed models ANOVAs, with sleep strategy (immediate, split, delayed) and time of test session (1830 h, 2030 h, 2230 h, 0030 h, 0230 h, 0430 h) included as fixed terms. Subject ID was included as a random term. First tested were the main effects of sleep strategy and time of day, followed by a two-way interaction. To evaluate whether there was any effect of strategy preference order on night-time performance, a second set of ANOVAs was conducted with preference (first, second, third) and sleep strategy included as fixed terms. These analyses tested the effect of preference and the interaction of preference with sleep strategy.

### 7.3. Results

#### 7.3.1. Sleep and Sleep Strategy Preferences

Repeated measures ANOVA revealed that sleep strategies did not significantly differ in terms of the amount of total sleep time (TST), stage N2 sleep, and REM sleep participants obtained (Table 7-1), but did differ in terms of stage N3 sleep. Bonferonni post hoc analyses showed that participants obtained significantly more stage N3 sleep during the split sleeps combined than during the immediate sleep.



The immediate sleep was ranked as most preferred by 50.0% of the participants, with the delayed and split sleeps ranked first by 33.3% and 16.7% of the participants, respectively. The split sleep was ranked last by 58.3% of the participants, followed by the delayed sleep (33.3%) and immediate sleep (8.3%).

**Table 7-1** Repeated measures ANOVA of sleep variables during each sleep strategy.

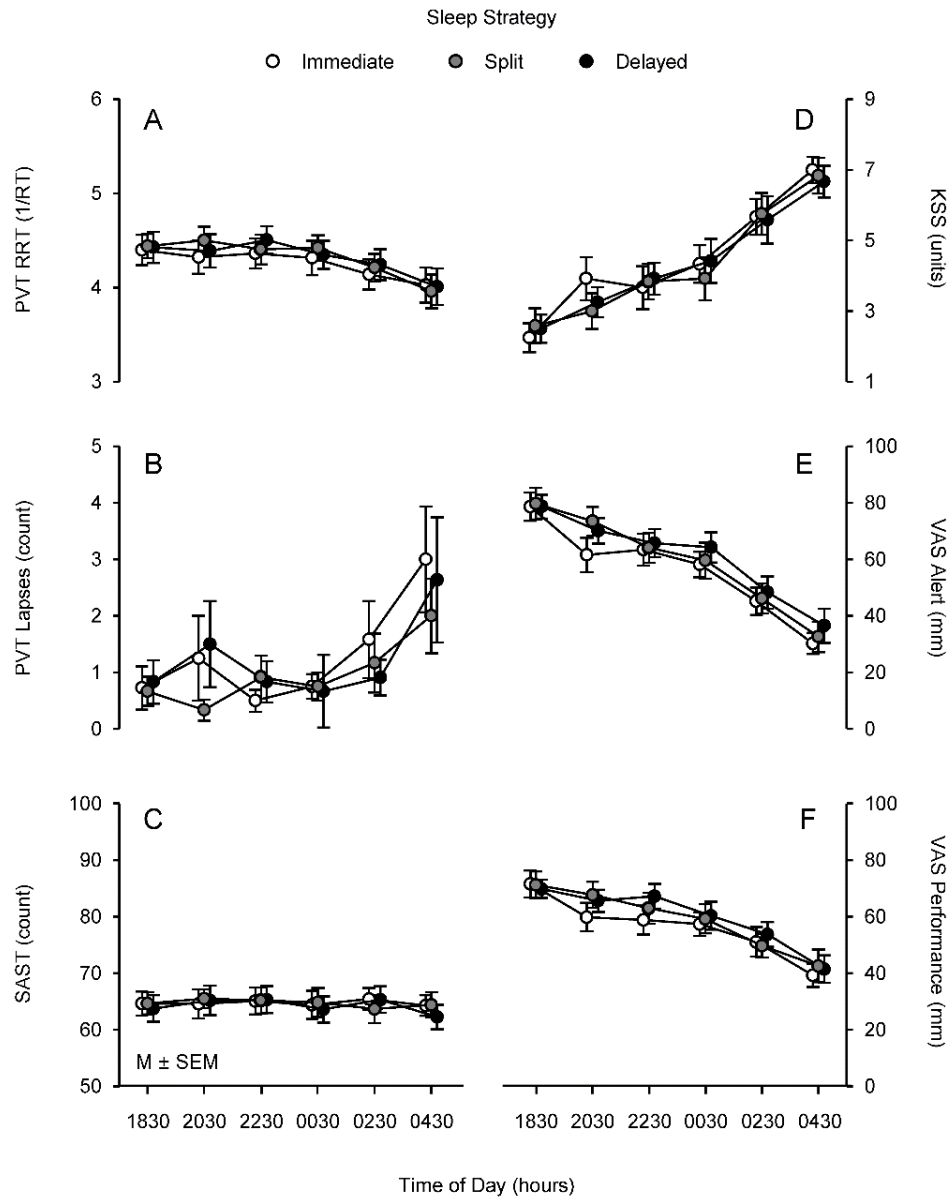
Sleep Stages	Sleep Strategy						F (2,22)
	Immediate		Delayed		Split		
	M	SD	M	SD	M	SD	
TST (min)	383.63	22.31	384.04	21.26	391.58	17.63	0.78
N2 (min)	160.00	13.32	156.45	27.58	145.46	23.74	1.63
N3 (min)	124.33	25.37	138.00	26.56	149.54	30.60	11.46***
REM (min)	82.96	25.98	71.83	27.77	81.13	27.87	1.24

\*\*\* $p < .001$

TST, total sleep time; N2, stage N2 sleep; N3, stage N3 sleep; REM, rapid eye movement sleep.

### 7.3.2. Sleep Strategy on Performance and Subjective Ratings

Mixed models ANOVAs revealed there were no main effects of sleep strategy on any of the performance tasks or subjective ratings. There were main effects of time for all measures, except the SAST (Table 7-2). These showed a trajectory of decline in performance and subjective ratings as the night progressed (Figure 7-2, p.176). There were no 2-way sleep strategy x time of day interactions (Table 7-2, p.177).



**Figure 7-2** Night-time neurobehavioural performance (panels A-C) and subjective ratings (panels D-F) following immediate, split, and delayed daytime sleep strategies. Mean ( $\pm$  SEM) results are depicted on the y-axis, and time of day is depicted on the x-axis. White = immediate strategy, grey = split strategy, black = delayed strategy.

**Table 7-2** Results of mixed models analyses with sleep strategy and time of day as fixed terms.

Measures	Strategy		Time		Strategy x Time	
	F	df	F	df	F	df
PVT RRT	1.52	2,186	12.62***	5,186	0.40	10,186
PVT Lapses	0.79	2,183	6.63***	5,183	0.44	10,183
SAST	0.47	2,187	1.02	5,187	0.57	10,187
KSS	0.25	2,187	55.19***	5,187	0.49	10,187
VAS Alert	2.30	2,187	60.98***	5,187	0.48	10,187
VAS Performance	1.83	2,187	32.89***	5,187	0.51	10,187

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

PVT, psychomotor vigilance test; SAST, serial addition and subtraction test; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.

### 7.3.3. Strategy Preference on Performance and Subjective Ratings

The second set of mixed models ANOVAs revealed there were no main effects of preference on performance or subjective ratings of sleepiness, alertness or self-assessed ability to perform (Table 7-3). Performance and ratings following participants' most preferred sleep strategies were not significantly better than results following their least preferred sleep strategy.

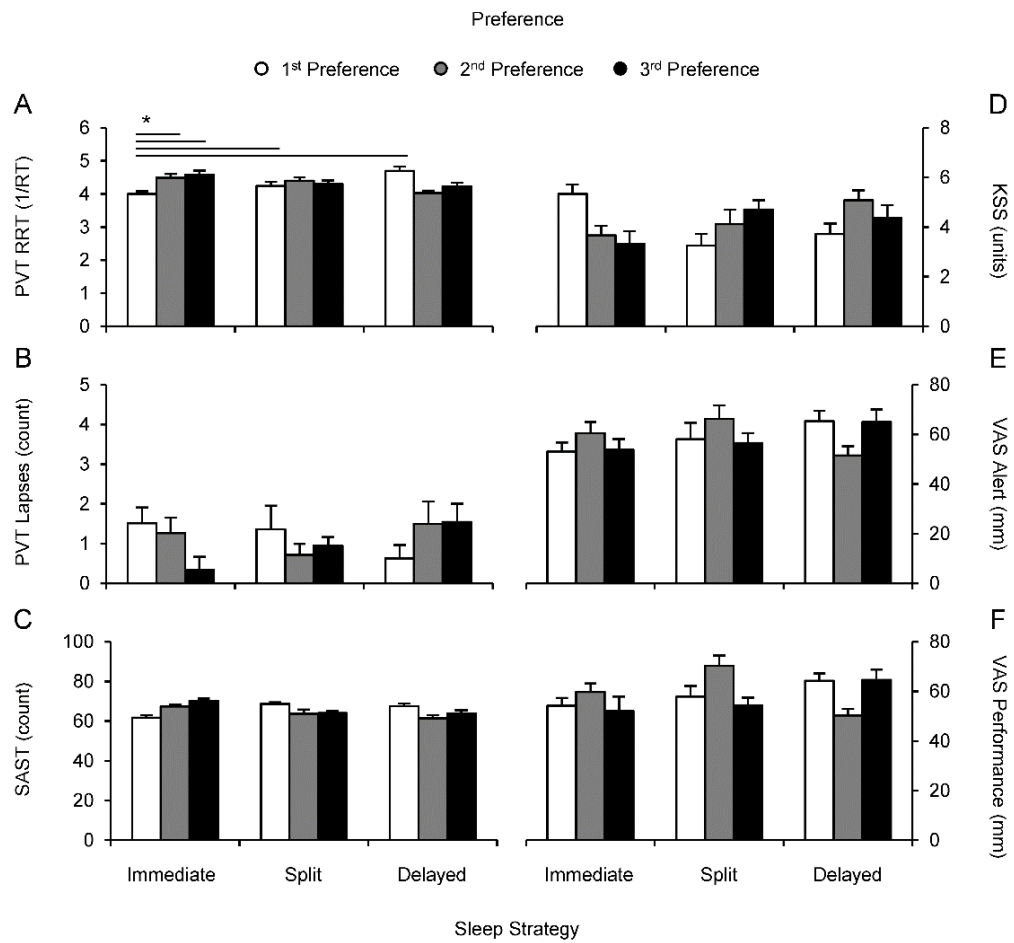
There was a significant two-way interaction between preference and sleep strategy for the PVT RRT (Table 7-3). Following the immediate sleep strategy, participants who ranked it as their first preference had a slower mean RRT on the consecutive night shift than those who ranked it second or third (Figure 7-3A). Participants who preferred the immediate sleep strategy performed worse during this condition than participants who favoured the delayed and split sleep strategies performed in their respective preferred conditions (Figure 7-3A).

**Table 7-3** Results of mixed models analyses with preference and sleep strategy as fixed terms.

Measures	Preference		Strategy x Preference	
	F	df	F	df
PVT RRT	0.56	2,198	2.88*	6,201
PVT Lapses	0.45	2,202	1.23	6,161
SAST	0.27	2,198	0.89	6,200
KSS	0.04	2,206	0.82	6,166
VAS Alert	<0.01	2,206	0.51	6,175
VAS Performance	0.20	2,204	0.86	6,190

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

PVT, psychomotor vigilance test; SAST, serial addition and subtraction test; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.



**Figure 7-3** Night-time neurobehavioural performance (panels A-C) and subjective ratings (panels D-F) during each sleep strategy according to preference ranking. Mean ( $\pm$  SEM) results are depicted on the y-axis and preference ranks for each strategy are depicted on the x-axis: white = 1<sup>st</sup>, grey = 2<sup>nd</sup>, and black = 3<sup>rd</sup>. Asterisks indicate a significant difference ( $p < .05$ ).

## 7.4. Discussion

In this study, sleep episodes were scheduled between two 12-h night shifts in the laboratory to simulate the immediate, delayed, and split sleep strategies commonly used by night workers. The primary aim of this study was to determine whether there is an optimum arrangement of daytime sleep that can maximise daytime sleep quality and duration and sustain night time function. In this study, sleep strategies did not affect the total amount of daytime sleep participants obtained. However, participants did obtain significantly more slow-wave stage N3 sleep for the split sleep strategy than the immediate strategy – similar to what was observed for the split-sleep schedule in Chapter 5. Measures of sustained attention and self-assessed ability to perform significantly declined with time on shift. Performance on the SAST did not decline across the shifts. It is possible this was because answers to the arithmetic sums were simple enough to retrieve from declarative memory rather than be calculated (Gunzelmann et al., 2012). Previous research indicates that the ability to retrieve domain-specific knowledge is resilient to the effects of sleep deprivation (Lim & Dinges, 2010). Regardless, neurobehavioural performance and subjective ratings of sleepiness and alertness following all sleep strategies were the same on the second night shift. As such, the results indicate that none of these sleep strategies are more effective at ameliorating declines in neurobehavioural function and alertness during a 12-h night shift than any of the others.

The absence of a significant effect of sleep strategy on night-time performance is in contrast with previous research by Santhi et al. (2008) that supports a delayed daytime sleep strategy. However, this discrepancy is most likely due to the different shift durations scheduled in each study. Santhi et al. (2008) evaluated the efficacy of immediate and delayed daytime sleep strategies during the 16-h break between consecutive 8-h night shifts. In the current study, sleep strategies were scheduled during the 12-h breaks between 12-h night shifts. As these breaks were shorter, the start and end times for the immediate and delayed sleeps differed by only 3 h. It is possible that a delayed sleep strategy is

not beneficial for shift schedules with long shifts (e.g., > 8 h) because there is not enough time during the break to differentiate it from other sleep strategies.

#### 7.4.1. Effect of Sleep Strategy Preferences

Given that night workers can generally sleep during their breaks at times of their choosing, a subsequent aim was to evaluate whether neurobehavioural function and alertness is influenced by the alignment of participants' preferred sleep strategies with their scheduled sleep times (Smith et al., 2005). No main effect was found for preference ranking, suggesting that neurobehavioural performance and alertness during 12-h night shifts may not be adversely affected if night workers are not able to obtain their daytime sleep episodes at their preferred times.

##### 7.4.1.1. *A split-sleep advantage?*

Interestingly, a significant interaction between scheduled sleep strategy and preferred sleep time was present for mean RRT on the PVT. This interaction showed that, following the immediate sleep strategy, those who most preferred it were poorer at sustaining attention on the second shift than participants who preferred the delayed or split sleep strategies (Figure 7-3A). In contrast, preferred sleep times had no effect on mean RRT following the delayed or split sleep strategies. A possible explanation for this is that people who prefer to satiate their sleep drive immediately following a night shift may be more vulnerable to the homeostatic drive for sleep than people who are content to delay or split their sleep episodes. If this is the case, workers who prefer to sleep immediately after a night shift may benefit from adopting a split sleep strategy, as this would provide them some immediate relief and also alleviate sleep pressure before the subsequent night shift.

#### 7.4.2. Limitations

There are a few limitations in this study to consider when interpreting the results. The first is that the protocol simulated only two consecutive night shifts.

It is possible that with more consecutive night shifts, differences between sleep strategies may have a more pronounced influence on performance, sleepiness, and alertness. It must also be considered that because lighting during the night was set at ~300 lux to simulate office conditions, any differing effects of the sleep strategies on neurobehavioural performance may have been muted by its alerting influence. Another limitation is that the sleep time preferences were assessed by asking participants to rank three broad, pre-determined approaches, rather than allowing participants to choose when they slept. Given a free choice, participants may have preferred to sleep for a different duration or at different times. In terms of generalisability, a limitation of this study was that it was conducted in laboratory conditions that facilitated undisturbed sleep. Future research could build on the findings of this study by evaluating performance during 8-h shifts across multiple consecutive nights.

#### 7.4.3. Conclusion

In conclusion, the findings of this study indicate that neurobehavioural performance, sleepiness and alertness during 12-h night shifts are not affected by the timing of daytime sleeps. Similarly, the results suggest performance on 12-h night shifts is not adversely affected if night workers are not able to sleep at their preferred times. Workers who prefer to sleep immediately after a night shift may benefit from adopting a split sleep strategy to alleviate sleep pressure on the subsequent shift. It is not clear whether these findings would apply to shorter night shifts or schedules with more than two consecutive night shifts.



## **Chapter 8.**

# **Facilitating the Transition onto the First Night Shift with a Prophylactic Nap**

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**Peer-reviewed publication associated with this chapter (Appendix K):**

**Kosmadopoulos, A.,** Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2016). No first night shift effect observed following a nocturnal main sleep and a prophylactic 1-h afternoon nap. *Chronobiology International*, 33(6), 716-720.  
<http://dx.doi.org/10.3109/07420528.2016.1167727>.

## 8.1. Introduction

Although night shifts play an integral role in the functioning of a modern 24-h society, it is well-established that their opposition to ingrained biological drives for night-time sleep and daytime wakefulness increase fatigue, reduce alertness (Åkerstedt, 2003; Folkard et al., 2005) and impair performance across a number of domains (Kosmadopoulos et al., 2014a; Matthews et al., 2012a; Sargent et al., 2010). In what has been coined the ‘first night shift phenomenon’, sleepiness and neurobehavioural impairment are often reported to be particularly poor on the first night shift in a roster (Folkard, 1992; Hansen et al., 2010; Purnell et al., 2002, p.226). The declines associated with this shift have been equated with a blood alcohol concentration of 0.10% (Lamond et al., 2004). Considering that as much as 7% of the Australian workforce is engaged in night work on a regular basis (Australian Bureau of Statistics, 2013), risks associated with the first night of work are of significant concern to occupational health and safety and need to be addressed.

Poor performance on the first night has been attributed to an interplay between sleep loss and circadian factors (Santhi et al., 2007). Indeed, in addition to forcing a misalignment between sleep/wake behaviour and physiological drives, the transition from daytime to night-time work is frequently associated with acute sleep deprivation (Knauth et al., 1980; Lamond et al., 2003; Santhi et al., 2007; Tepas et al., 1981). The amount of sleep obtained in the preceding 24 h is a strong indicator of performance (Ferguson et al., 2011), yet most sleep prior to the first night shift is obtained during the previous night (Knauth et al., 1980). Up to as many as 50% of workers do not nap before the first night shift and end the shift having spent at least 24 h awake (Knauth et al., 1980; Rosa, 1993; Sallinen et al., 2003; Tepas et al., 1981). In comparison to the first night, shiftworkers obtain an average ~6 h daytime sleep between consecutive night shifts (Knauth et al., 1980; Pilcher, Lambert, & Huffcutt, 2000; Roach et al., 2003), thus starting successive shifts with a reduced homeostatic drive for sleep.

The primary approaches for mitigating fatigue at night either rely on stimulants such as caffeine or target the circadian and homeostatic processes of sleep

regulation. That is, they focus on the circadian phase-shifting properties of bright light or melatonin, or encourage long daytime sleeps (Crowley et al., 2003). However, these approaches are limited during the transition to night work, where circadian adaptation can take several days to have a noticeable effect (Bjorvatn et al., 2007; Boudreau, Dumont, & Boivin, 2013; Ferguson et al., 2012a; Folkard, Arendt, & Clark, 1993) and sleep pressure has not sufficiently accumulated to override the alerting signal of the circadian pacemaker (Sargent et al., 2012a).

In the absence of circadian adaptation or a long recuperative daytime sleep, an afternoon nap scheduled before work, in conjunction with a long night-time sleep the previous day, might ameliorate fatigue-related decline on the first night shift (Ruggiero & Redeker, 2014). Purnell et al. (2002) found that a 20-min nap during the night can mitigate performance decline associated with the first shift, but the effectiveness of prophylactic naps at facilitating the transition to night work is less clear. Several studies regarding the efficacy of napping before night work show that it can improve performance across various periods of extended wakefulness (Bonnet et al., 1995; Schweitzer et al., 2006). However, these studies have not compared improvements on the first night shift with performance on subsequent shifts. Conversely, studies that have evaluated performance across multiple night shifts (both simulated and real), and have identified performance on the first night to be particularly poor, have not evaluated the efficacy of a prophylactic nap (Hansen et al., 2010; Lamond et al., 2004; Santhi et al., 2007). The aim of this study was to determine whether a 1-h afternoon nap opportunity before a 12-h night shift schedule is sufficient to produce neurobehavioural, sleepiness and alertness outcomes comparable to those of a subsequent night shift preceded by a sufficient daytime sleep.

## 8.2. Methods and Materials

### 8.2.1. Participants

Twelve male volunteers aged  $22.92 \pm 5.23$  years (mean  $\pm$  SD; range = 18 – 34 years) with a body mass index (BMI) of  $22.89 \pm 1.38$  kg/m<sup>2</sup> (20.8 – 25.1 kg/m<sup>2</sup>) participated in the study. Participants underwent a screening process that involved in-person interviews, the completion of several questionnaires, and a week of wrist actigraphy to monitor sleep patterns. From these, participants were determined to be free of psychiatric disorders, endocrine disorders, and sleep disorders. They were non-smokers, medication free, and did not consume excessive doses of caffeine (< 350 mg/day) or alcohol (< six standard drinks/week). Participants had not undertaken shiftwork or flight across more than two time zones in the two months prior to the study. Once selected, participants were required to maintain consistent sleep-wake schedules with ~8 h of sleep per night for the week prior to study admission. This was verified with activity monitors and self-report sleep diaries (Kosmadopoulos et al., 2014b).

#### 8.2.1.1. Ethics

Ethics approval for the study was provided by the Central Queensland University Human Research Ethics Committee in accordance with National Health and Medical Research Council of Australia guidelines. All participants provided written, informed consent.

### 8.2.2. Setting

The study was conducted in a sound-attenuated, windowless sleep laboratory at the Appleton Institute. This laboratory accommodated six participants at a time, providing each with separate bedroom, living room and bathroom facilities. Ambient lighting was maintained at ~300 lux, 183 cm above the floor in the horizontal plane (i.e., normal office lighting) during wake periods, and extinguished during sleep periods. The target room temperature was 21-23°C.

Participants had access to clocks inside the laboratory, but were isolated from environmental time cues, such as sunlight. Participants were not permitted to leave the laboratory during the protocol. A closed-circuit television system in the laboratory allowed researchers to monitor participant compliance with study protocols, in conjunction with in-person monitoring.

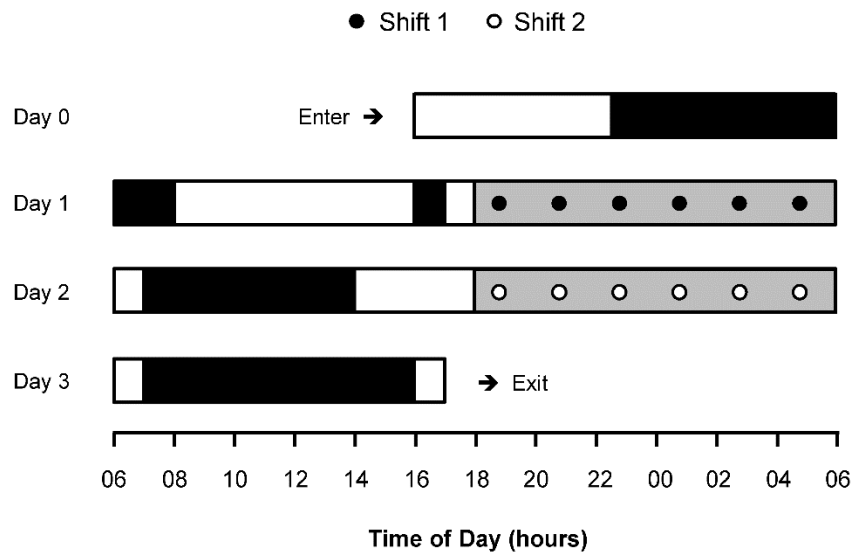
### 8.2.3. Protocol

Participants resided in the laboratory for three days. These comprised a baseline night sleep, an afternoon nap, and two 12-h simulated night shifts separated by a 7-h daytime sleep opportunity (Figure 8-1). The evening of day 0 and morning of day 1 were used to train participants on the performance tasks and eliminate any learning effects.

Participants were provided 9.5-h time in bed (TIB) (2230 h – 0800 h) at the end of day 0 to eliminate any prior sleep debt. Participants had a 1-h nap opportunity (1600 h – 1700 h) during the afternoon of day 1 to prepare for the first simulated night shift. During the first shift (1800 h – 0600 h), participants completed six 30-min test batteries at 2-h intervals, beginning 30 min after the start of the shift. At the start of day 2, participants were provided 7 h of TIB (0700 h – 1400 h), followed by the second nightshift (1800 h – 0600 h) in the evening. Participants were provided a recovery sleep opportunity (0700 h – 1600 h), at the beginning of day 3, before departing.

#### 8.2.3.1. Test batteries

Test batteries were simultaneously administered to all participants by two research staff members. Participants were isolated from each other in their own rooms during test sessions to keep them free from distraction. During the breaks between test sessions, participants were free to read, listen to music, draw or watch DVDs; participants were not allowed to sleep, exercise or leave their living rooms.



**Figure 8-1** Protocol diagram of simulated consecutive night shifts. Black rectangles represent time in bed and grey rectangles represent the simulated night shifts. White and black circles represent test sessions during the first shift and second shift, respectively. The x-axis represents time of day (hours) and the y-axis represents successive 24-h periods in the laboratory.

## 8.2.4. Measures

### 8.2.4.1. Sleep

Sleep was monitored with standard polysomnography, using the Grael PSG/EEG Systems (Compumedics, Melbourne, Victoria, Australia) and a montage of Grass<sup>TM</sup> gold-cup electrode leads (Astro-Med, Inc., West Warwick, Rhode Island, USA). The montage included two EEG channels (C3-M2, C4-M1), right and left EOG, and three channels of chin EMG. Sleep-wake stages were scored in 30-s epoch by an experienced technician (Iber et al., 2007). The duration of TIB spent in any stage of sleep was used to derive total sleep time (TST) in hours. Sleep stages N2, N3 and R were calculated as percentages of TIB.

#### 8.2.4.2. Neurobehavioural performance

Sustained attention was measured using a 10-min psychomotor vigilance test (PVT; Dorrian et al., 2005). This is a simple response time task performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA) with a four-digit LED display and two push-button response keys. Participants were required to press the appropriate response key as quickly as possible after the presentation of a visual stimulus on the LED display, appearing at random 2-10s intervals. Dependent measures derived from the PVT included the number of lapses, which are response times (RT) >500 ms, and the mean reciprocal response time (RRT;  $\text{ms}^{-1} \times 10^{-3}$ ) (Basner & Dinges, 2011). The reciprocal was used to lessen the contribution of long lapses (Jewett et al., 1999a). A 5-min computerized serial addition/subtraction test (SAST) was used as a measure of declarative memory (Gunzelmann et al., 2012). The SAST requires participants to respond to a series of randomly presented single-digit arithmetic problems whose answers are simple enough to be retrieved from declarative memory rather than calculated. Performance was determined by the number of correct responses in the allocated time.

#### 8.2.4.3. Sleepiness, alertness, and self-assessed ability

Subjective sleepiness was assessed using the Karolinska Sleepiness Scale (KSS; Åkerstedt & Gillberg, 1990). The KSS is a 9-point scale that requires participants to rate how they feel, from 1 ('Extremely alert') to 9 ('Very sleepy, great effort to keep awake, fighting sleep'). Subjective alertness was assessed using a visual analogue scale (VAS Alert; Dorrian et al., 2003). This required participants to rate how alert they felt by placing a vertical mark on a 100-mm horizontal line, anchored by the statement 'struggling to remain awake' at one end and 'extremely alert and wide awake' at the other. A VAS scale was also used to measure participants' self-assessed ability to perform (VAS Performance). Participants had to respond to the question 'How well do you think you will perform' by placing a mark between the statements 'extremely poorly' and 'extremely well'.

### 8.2.5. Data Analyses

Outliers more than three standard deviations from the mean of any variable were excluded from inferential analyses. The removal of several outliers by one participant reduced the sample size to 11 for the PVT RRT, PVT Lapses, and SAST. There were no outliers for subjective measures. Remaining data for the dependent variables were analysed with separate repeated measures ANOVAs including two within-subjects factors – night shift (first, second) and time of test session (1830 h, 2030 h, 2230 h, 0030 h, 0230 h, 0430 h). The main effects and interaction of these were assessed. Violations identified by Mauchly's test of sphericity were corrected with Greenhouse-Geisser adjusted degrees of freedom, but the original degrees of freedom are reported.

## 8.3. Results

### 8.3.1. Sleep

Participants slept an average of 8.23 h ( $\pm 1.46$  h) during the 9.5-h night-time sleep opportunity (Stage N2,  $48.3 \pm 8.6\%$ ; Stage N3,  $29.3 \pm 9.6\%$ ; Stage R,  $19.1 \pm 4.4\%$ ) before their first simulated night shift. Participants slept for 0.89 h ( $\pm 0.05$  h) during their afternoon nap (Stage N2,  $35.6 \pm 15.6\%$ ; Stage N3,  $56.2 \pm 15.5\%$ ; Stage R,  $1.1 \pm 2.3\%$ ), and 6.39 h ( $\pm 0.37$  h) during the 7-h daytime sleep opportunity (Stage N2,  $41.8 \pm 3.9\%$ ; Stage N3,  $32.5 \pm 6.7\%$ ; Stage R,  $21.4 \pm 6.3\%$ ). During the recovery sleep opportunity, participants obtained 7.7 h ( $\pm 1.07$  h) of sleep (Stage N2,  $40.7 \pm 3.4\%$ ; Stage N3,  $33.3 \pm 5.3\%$ ; Stage R,  $22.0 \pm 5.7\%$ ).

### 8.3.2. Performance and Subjective Ratings

Repeated measures ANOVAs revealed no significant main effects of night shift for any of the neurobehavioural and subjective tasks (Table 8-1). Significant effects of time were evident for all tasks except the SAST, such that performance and ratings declined across the simulated night shift (Figure 8-2). The KSS, VAS Alert, and VAS Performance scores declined more steeply with time on shift



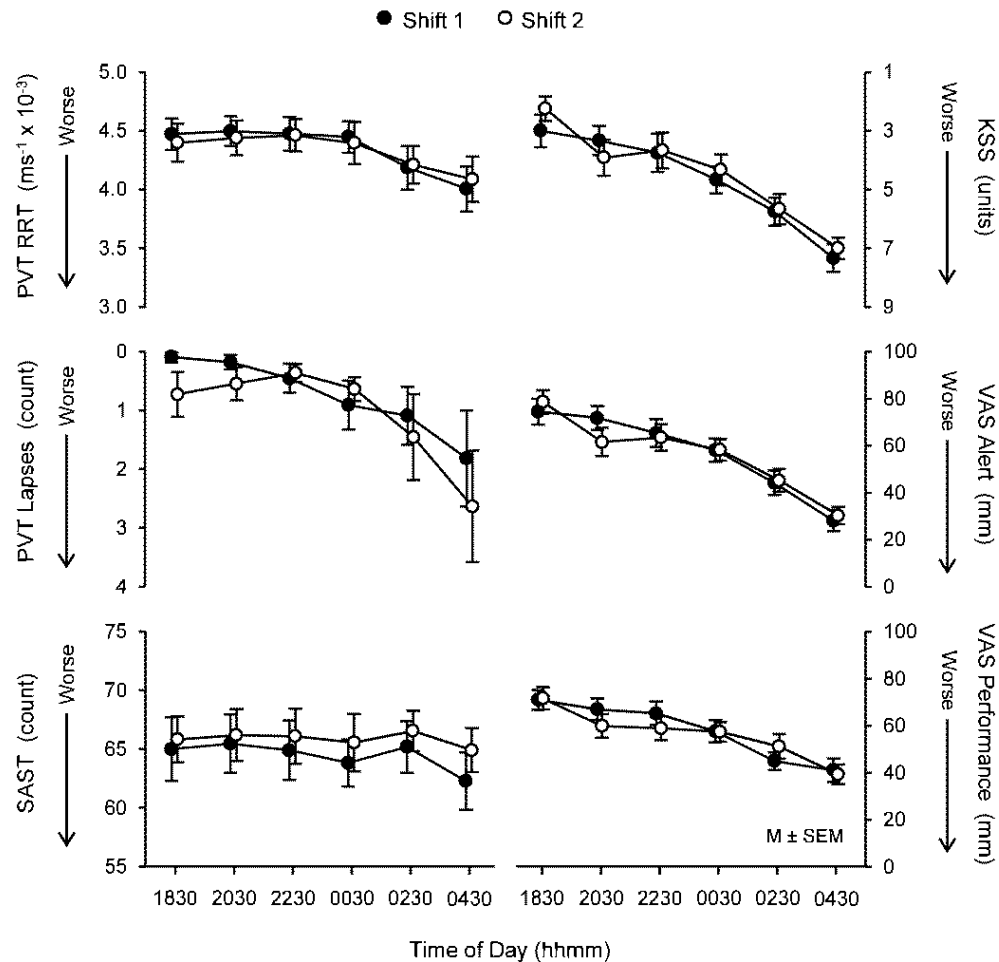
than PVT RRT or PVT Lapses. SAST performance remained constant across the night. There were no significant 2-way interactions of night shift and time on shift for performance or ratings.

**Table 8-1** Results from repeated measures ANOVAs for performance tasks and subjective ratings.

Variables	Shift		Time		Shift x Time	
	F	df	F	df	F	df
PVT RRT	0.1	1,10	13.1**	5,50	0.6	5,50
PVT Lapses	3.4	1,10	5.3*	5,50	0.5	5,50
SAST	4.7	1,10	2.1	5,50	0.2	5,50
KSS	0.5	1,11	31.1***	5,55	1.2	5,55
VAS Alert	0.1	1,11	36.8***	5,55	1.5	5,55
VAS Performance	0.4	1,11	32.4***	5,55	1.4	5,55

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

RRT, reciprocal response time; PVT, psychomotor vigilance test; SAST, serial addition and subtraction test; KSS, Karolinska Sleepiness Scale; VAS, visual analogue scale.



**Figure 8-2** Neurobehavioural performance and subjective ratings across simulated night shifts. Time of day is indicated on the x-axis and mean ( $\pm$  SEM) scores are indicated on the y-axis.

## 8.4. Discussion

All shiftworkers scheduled to work at night, whether on a permanent basis or on a rotating schedule comprising multiple consecutive night shifts, have to contend with the effects of circadian misalignment on neurobehavioural function and alertness. However, performance is particularly vulnerable to the effects of fatigue on the first night shift (Folkard, 1992; Lamond et al., 2004; Purnell et al., 2002) because it is often accompanied by sleep deprivation. In this study, a 1-h afternoon nap was scheduled before the first of two simulated night shifts, and neurobehavioural function and alertness during each shift were compared. The results revealed significant declines in sustained attention,

sleepiness, alertness, and self-assessed ability to perform across both nights. Shifts did not significantly differ from each other in terms of performance or subjective ratings at any time during the night. The mean durations of sleep obtained the night before the first shift ( $\sim 8.2$  h) and during the day between the shifts ( $\sim 6.4$  h) are comparable to what has previously been observed in the field (Knauth et al., 1980; Roach et al., 2003). With the inclusion of the prophylactic nap, participants gained an additional  $\sim 0.9$  h of sleep and reduced the amount of prior wake accumulated by the end of their first shift from 22 h to 13 h, less than the 16 h accumulated by the end of the second shift. These times are below the 17-h level equated with performance at a blood alcohol concentration (BAC) of 0.05% (Dawson and Reid 1997). Therefore, it is possible the 1-h nap afternoon opportunity before the first night shift ameliorated impairment by reducing prior wakefulness as well as increasing the amount of sleep obtained in the previous 24 h.

Sustained attention is sensitive to changes in fatigue (Dorrian et al., 2005), and performance on the PVT substantially declined accordingly with increasing time on shift. Standard deviations grew larger with time on shift as a consequence of individual variability in resilience to sleep deprivation. This is consistent with findings elsewhere (Howard et al., 2010; Lamond et al., 2004). In contrast to measures of sustained attention, the number of correct responses on the SAST, which utilises declarative memory, remained stable over both nights (Gunzelmann et al., 2012). While access to declarative memory can be diminished by insufficient sleep, these results are congruent with findings that accurate retrieval of arithmetic knowledge is robust to the effects of a night of total sleep deprivation (Gunzelmann et al., 2012; Kim et al., 2001).

Sleepiness, alertness and self-assessed ability on both shifts worsened with increasing time on shift, emulating the course of decline in sustained attention. The similar trajectory of both subjective sleepiness and alertness to sustained attention performance is consistent with past research and reflects their shared association in measuring fatigue (Howard et al., 2010; Schweitzer et al., 2006). As self-assessed ability corresponded to changes in sustained attention, the

results indicate that individuals have some insight their own ability to perform. However, that self-assessed ability did not also correspond to changes in SAST performance indicates that performance estimates may at least partially influenced by global assessments of alertness and fatigue.

#### 8.4.1. Practical Applications

Unlike stimulants such as caffeine, naps target the homeostatic sleep drive and can have a more stable and longer-lasting influence on performance (Bonnet et al., 1995). As performance on the first shift was no worse than performance on the second night, this study supports a 1-h prophylactic nap as a sufficient countermeasure to mitigate decline due to fatigue on the first night shift. However, encouraging shiftworkers who do not already integrate prophylactic naps into their routine to do so may prove difficult, particularly in the face of other competing familial, social and household obligations (Monk & Wagner, 1989). As it consumes 'personal' rather than 'work' time, the benefits of prophylactic napping to employees beyond an operational context may need to be advocated to be seriously considered over other priorities.

#### 8.4.2. Limitations and Future Directions

The main limitation of this study is the absence of a control condition, identical to the current protocol but without nap. A control condition would have indicated the precise contribution of the nap to performance during the first shift. Despite this, the effect of the nap can be approximated from previously established performance during a night of total sleep deprivation (Chang, Scheer, Czeisler, & Aeschbach, 2013; Chua et al., 2012; Dawson & Reid, 1997; Doran et al., 2001; Jung, Ronda, Czeisler, & Wright, 2011; Van Dongen & Dinges, 2005). The final test session of the first shift would have concluded following 21 h of wakefulness, rather than 12 h, if not for the 1-h nap opportunity. In other studies, 21 h of prior wakefulness at this time of day has been equated with mean lapse counts of ~12 to ~15 (Chang et al., 2013; Chua et al., 2012; Jung et al., 2011). Compared to these results, the mean lapse count following the

nap in the current study (i.e.,  $\sim 1.82$ ) was much lower. It is possible that light levels in the present study ( $\sim 300$  lux) may account for some of this difference in performance. However, given the mean lapse count of  $\sim 12$  observed by Chang et al. (2013) in  $\sim 150$  lux (187 cm above the ground) is comparable to means of  $\sim 13$  to  $\sim 15$  observed in  $<5$  lux (Jung et al., 2011; Chua et al., 2012), it is not clear the additional  $\sim 150$  lux in the present study alone would have been sufficient to reduce the count to  $\sim 1.82$ . A recently published study by Chinoy et al. (2016) supports this interpretation. They found that evening sleeps and bright lighting during the second half of consecutive simulated night shifts improved alertness and performance relative to a control group.

A further limitation is that of generalisability. Participants in the current study were all healthy young males, residing in an environment that was conducive to sleep and were isolated from external distraction. Given this, it is possible those working night shifts who are female, older, or overweight may be differently affected by sleep deprivation and have a different response to the nap. Future research could benefit from a field-based protocol with more diverse pool of participants, including women, and the implementation of a control condition.

#### 8.4.3. Conclusion

Those who work night shifts continually have to contend with impaired neurobehavioural performance resulting from fatigue due to the misalignment of sleep/wake behaviour with endogenous circadian processes. The first night shift in a roster is particularly vulnerable to the effects of fatigue because it is often also accompanied by sleep deprivation. For the current study, neurobehavioural performance and subjective assessments during a simulated 12-h night shift preceded by a 1-h prophylactic afternoon nap did not differ from performance and subjective assessments on the subsequent night shift. These findings reinforce the role of recent prior sleep history in the 'first night shift phenomenon', and suggest that a nap opportunity as short as 1-h, in conjunction with a long night-time sleep the preceding night, may be sufficient to mitigate it.

## **Chapter 9.**

### **General Summary and Discussion**

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## 9.1. General Summary

This thesis examined the sleep and circadian components of performance, with particular focus on those aspects relevant to shiftwork, such as sleep timing and duration. The objectives of Chapters 3 and 4 were to evaluate and improve the utility of technologies employed for monitoring sleep and sleep-wake patterns in the laboratory and the field. The remaining experimental chapters (Chapters 5 to 8) were designed to evaluate the effects of different sleep-wake schedules on neurobehavioural performance and subjective self-assessments under laboratory conditions. Specifically, Chapters 5 and 6 examined the contributions of homeostatic and circadian processes during split-sleep schedules by means of forced desynchrony. Chapters 7 and 8 examined the effects of different daytime sleep strategies on performance and alertness in relation to simulated night shifts. Following is a general overview of the objectives, methods, results and conclusions of each of the six studies in this thesis.

### 9.1.1. Sleep Monitoring Technologies

#### *9.1.1.1. Chapter 3 – Validation of alternative sleep monitoring devices*

The gold-standard for measuring sleep is PSG, but it is not always practical, convenient or cost-effective for use in the field; therefore, various alternatives are often used instead. The objective of Chapter 3 was to assess the validity of three different commercially available devices for measuring sleep and wake under identical conditions. These devices included two types of wrist-worn activity monitors (a sleep/wake activity monitor and an energy expenditure monitor) and a wireless partial-PSG system. Secondary aims were to evaluate sleep/wake thresholds for the activity monitors and to compare all the devices.

To achieve these aims, two nights of sleep were simultaneously recorded with the three alternative sleep-monitoring devices and PSG in the laboratory. Agreement with PSG was evaluated epoch-by-epoch and with summary measures including total sleep time and wake after sleep onset. All devices had high agreement rates with PSG for identifying sleep and wake, but the partial-

PSG system was the best, with an agreement of  $91.6 \pm 5.1\%$ . At their best thresholds, the sleep/wake monitor (medium threshold,  $87.7 \pm 7.6\%$ ) and the energy expenditure monitor (very low threshold,  $86.8 \pm 8.6\%$ ) had similarly high rates of agreement. Summary sleep measures were similar to those determined by PSG, but the partial-PSG system again provided the most consistent estimates.

While the partial-PSG system was the most accurate device, both activity monitors were also valid for sleep estimation, provided the appropriate thresholds were selected. Each device has advantages for use in different environments and to achieve different goals, so the primary consideration for researchers is to determine which best suits a given research design.

#### *9.1.1.2. Chapter 4 – Discerning accelerometer non-wear times*

Validated algorithms derive estimates of sleep and wake from wrist-worn sleep/wake monitors based on the amount of activity recorded by sensitive piezoelectric accelerometers. However, the accuracy of these estimates is often contingent on researchers being able to discern activity monitor non-wear by participants in the field, when it occurs, from either sedentary wakefulness or sleep. Though some wrist-activity monitors contain temperature or capacitive sensors that can assist with off-wrist detection, not all have this capability. The objective of Chapter 4 was produce a simple decision-making tool for objectively estimating non-wear when this is not known – assuming it could be inferred from continuous periods of inactivity unlikely to occur while in bed. A period of inactivity that is not likely to occur while asleep is even less likely to occur during wake. Thus, the approach of this study was to derive a frequency distribution of bedtime inactivity that would allow decisions about non-wear to be made probabilistically.

In this study, participants living in the laboratory for 13 days wore activity monitors on their non-dominant wrists and slept only during scheduled bedtimes. Following the protocol, periods of consecutive zero-activity epochs  $\geq 1$  min were extracted from the accelerometer data. Inactive periods during time in bed were then tabulated to derive a cumulative frequency distribution



function. Data collected suggest that more than 50% of inactive periods during time in bed are < 8 min in duration. This duration may be an appropriate minimum threshold for routine, “more likely than not”, non-wear classification during self-reported wake. For self-reported bedtimes where it is expected that participants would be sedentary, higher thresholds could be chosen to estimate non-wear depending on the desired level of certainty. For instance, thresholds of 75%, 95% and 99% would require periods of inactivity to be  $\geq 18$  min,  $\geq 53$  min and  $\geq 85$  min, respectively, to determine non-wear.

### 9.1.2. Split-Sleep Schedules

#### *9.1.2.1. Chapter 5 – The impact of split and consolidated sleep-wake schedules on neurobehavioural performance*

Extended wakefulness, sleep loss, and circadian misalignment are factors associated with an increased accident risk in shiftwork. Splitting shifts into multiple shorter periods per day may mitigate these risks by alleviating prior wake. However, the effect of splitting the sleep-wake schedule on the homeostatic and circadian contributions to neurobehavioural performance and subjective assessments of sleepiness or one’s capacity to perform are not known. The study reported in Chapter 5 facilitated the examination of these issues with twenty-nine male participants assigned to one of two 28-h forced desynchrony schedules in a time isolation laboratory.

Depending on the assigned schedule, participants were provided the same total time in bed each 28-h cycle, either consolidated into a single period (9.33 h time in bed) or split into two equal halves ( $2 \times 4.67$  h time in bed). Neurobehavioural performance was regularly assessed with a psychomotor vigilance test, sleepiness was measured with the Karolinska Sleepiness Scale, and self-assessed ability to perform was measured with a visual analogue scale. Polysomnography was used to assess sleep, and core body temperature was recorded to assess circadian phase.

On average, participants obtained the same amount of sleep on both schedules, but those in the split schedule obtained more slow wave sleep on forced desynchrony days. Mixed effects ANOVAs indicated no overall difference between the consolidated and split schedules in neurobehavioural performance, sleepiness or self-assessed ability. Main effects of circadian phase and prior wake were present for both schedules, such that performance and subjective ratings were best around the circadian acrophase, worst around the nadir, and declined with increasing prior wake. There was a schedule by circadian phase interaction for all neurobehavioural performance metrics such that performance was better in the split schedule than the consolidated schedule around the nadir. There were no such interactions for sleepiness or self-assessed ability to perform. Performance during the consolidated schedule was significantly better than the split schedule at 2 h of prior wake, but declined at a steeper rate such that the schedules converged by 4.5-7 h of prior wake.

Overall, the results indicate that when the total opportunity for sleep per day is satisfactory, a split sleep-wake schedule is not detrimental to sleep, performance, or subjective measures. Indeed, splitting the schedule may be of some benefit, given its reduction of neurobehavioural impairment at night and its association with increased slow wave sleep. Therefore, for some industries that require operations to be sustained around the clock, implementing a split work-rest schedule may be of assistance.

#### *9.1.2.2. Chapter 6 – The effect of sleep-restricted schedules on driving impairment and the ability to predict performance*

Fatigue is a significant contributor to motor-vehicle accidents and fatalities. Shiftworkers are particularly susceptible to fatigue-related risks as they are often sleep-restricted and required to commute around the clock. Simple assays of performance could provide useful indications of risk in fatigue management, but their effectiveness may be influenced by changes in their sensitivity to sleep loss across the day. The aim of the study in Chapter 6 was to evaluate the sensitivity of several neurobehavioural and subjective tasks to sleep restriction

at different circadian phases, and their efficacy as predictors of performance during a simulated driving task.

Thirty-two volunteers were time-isolated for 13-days and participated in one of two 14-h FD protocols with sleep opportunities equivalent to 8 h per 24 h (control) or 4 h per 24 h (severe sleep restriction). At regular intervals during wake periods, participants completed a 10-min simulated driving task, several neurobehavioural tasks, including the PVT, and subjective ratings, including a self-assessment measure of ability to perform. Scores were transformed into standardised units relative to baseline and folded into 60° circadian phase bins based on core body temperature.

Sleep dose and circadian phase effect sizes were derived via mixed models analyses. Predictors of driving were identified with regressions. Performance was most sensitive to sleep restriction around the circadian nadir. The effects of sleep restriction around the circadian nadir were larger for simulated driving and neurobehavioural tasks, especially the PVT, than for subjective ratings. None of the tasks significantly predicted driving performance during the control condition, or around the acrophase during the sleep restriction condition – likely an issue of restricted range. The PVT and self-assessed ability were the best predictors of simulated driving across circadian phases during severe sleep restriction. These results show that simple performance measures and self-monitoring explain a large proportion of variance in driving when fatigue is high.

### 9.1.3. Simulated Night Shifts

#### *9.1.3.1. Chapter 7 – Strategically timing sleep between night shifts*

Night shift workers often employ daytime sleep strategies between consecutive shifts that may generally be divided into three main approaches. These include (i) sleeping immediately after work, (ii) delaying sleep several hours after work, and (iii) splitting sleep episodes such that some sleep is obtained both at the beginning and at the end of the break. Each strategy has its own advantages and disadvantages, and workers may prefer different strategies for various reasons.

The aim of this study in Chapter 7 was to determine the best sleep strategy for night-time performance to adopt between consecutive 12-h night shifts.

Twelve healthy males participated in a repeated-measures laboratory study with three counterbalanced sleep conditions. Conditions differed only in the timing of 7-h sleep opportunities between two consecutive simulated night shifts (1800 h – 0600 h). Sleep opportunities were scheduled either (i) immediately following the simulated night shift, 0700 h – 1400 h; (ii) delayed until, 1000 h – 1700 h; or (iii) split across the break, 0700 h – 1030 h and 1330 h – 1700 h. PVTs were conducted to assess response time performance and visual analogue scales were employed to rate alertness. At the end of the study, participants ranked the sleep conditions in order of preference.

The results revealed no main effects of sleep strategy (immediate, delayed, or split) on the amount of sleep participants obtained, but they did show participants obtained more recuperative stage N3 sleep during the split strategy than the immediate strategy. There were no significant main effects of sleep strategy for the performance and subjective sleepiness measures. Similarly, there were no significant main effects of strategy preference (first, second, third) on sustained attention or subjective sleepiness. These findings indicate that performance and subjective sleepiness during consecutive 12-night shifts may not be significantly affected by the adoption of different sleep strategies. For the majority of tasks, working at night following a preferred sleep time was no more beneficial to performance and alertness than following less preferred sleep times. It is not clear whether these findings would apply to shorter night shifts, where there is more time during breaks to accumulate homeostatic sleep pressure, or schedules with more than two consecutive shifts.

#### *9.1.3.2. Chapter 8 – Prophylactic napping before the first night shift*

Extended wakefulness and circadian misalignment associated with the transition onto the first night shift impairs neurobehavioural performance and alertness. Naps have demonstrated some success as countermeasures to fatigue when scheduled before or during night shifts. In Chapter 8, the aim was to

determine whether a 1-h afternoon nap prior to the first of two consecutive 12-h night shifts is sufficient to produce neurobehavioural performance at levels comparable to the second night shift.

Twelve healthy male participants resided in a sleep laboratory for four days. Following a baseline night sleep opportunity (2230 h – 0800 h), participants completed two consecutive simulated 12-h night shifts (1800 h – 0600 h). A nap opportunity (1600 h – 1700 h) was scheduled prior to the first simulated night shift and a daytime sleep opportunity (0700 h – 1400 h) was scheduled between the shifts. A battery of neurobehavioural tests, including the PVT, was used to assess performance at regular intervals across both nights. Subjective measures of sleepiness and alertness were also assessed. Repeated measures ANOVA revealed significant declines with increasing time awake for PVT response time, subjective sleepiness and alertness. Repeated measures ANOVA revealed no main effects of night shift (1st vs. 2nd) on any of the neurobehavioural tasks or subjective measures. Results from this study indicate that increasing total sleep duration and reducing prior wakefulness before the first night shift with a 1-h afternoon nap may facilitate the transition to night work. These findings reinforce the importance of recent sleep/wake history in counteracting the effects of the circadian pacemaker on performance at night.

## 9.2. General Discussion

### 9.2.1. Theoretical Implications

#### 9.2.1.1. *Is the human sleep-wake system polyphasic?*

The conventional wisdom in western nations has been that humans are predisposed to (and should) obtain their sleep in single, uninterrupted episodes at night (refer to literature review, section 1.3.3, p.47). This view of human sleep as monophasic largely stems from the results of early ‘free run’ studies, in which participants, isolated from time cues and social contact, generally maintained a routine of sleeping once per night (Aschoff, 1981). However, as discussed by Campbell and Murphy (2007) and mentioned earlier (p.49), this may simply

have been an artefact of the instructions given to participants – i.e., to maintain a “normal” rest-wake schedule with three meals per day and no naps. The results of later studies, where participants were permitted to eat and sleep ad libitum, revealed that major night-time sleeps tended to be supplemented by daytime naps (Campbell & Zulley, 1985, 1989). These studies and further research into the predisposition for napping during constant routines have allowed for the possibility that human sleep may be polyphasic, in contrast to the habits of many people in industrialised nations.

While the split-sleep schedule imposed on participants in Chapter 5 does not permit insight into how people are disposed to sleep voluntarily, it does provide support that the human sleep-wake system is adaptable if not strictly polyphasic or monophasic. Consistent with previous research, Chapter 5 indicates that splitting sleep into multiple episodes per day is not inherently detrimental to sleep or performance (Jackson et al., 2014; Mollicone et al., 2007; Mollicone et al., 2008; Short et al., 2016). However, while previously published studies have predominantly focused on the effects of split-sleep schedules on daytime function, this study investigated performance at all times of day by means of forced desynchrony. Expanding on previous research, Chapter 5 revealed that participants who had two short sleep episodes per day performed better at night and had potentially better sleep than participants who had the same total sleep opportunity in one episode. There was also support from the sleep strategy protocols in Chapter 7 that sleep need not be monophasic. While night-time performance and total sleep duration did not differ between strategies, splitting the daytime sleep opportunity into two equal halves resulted in significantly more slow-wave sleep overall compared to an immediate consolidated sleep strategy.

Combined, the evidence supporting a biological predisposition for polyphasic sleep suggests the absence of a ‘culture of napping’ in most western societies is due to social and occupational factors interfering with the sleep-wake system. Given that monophasic sleep is so prevalent, this does raise questions about whether there are any long-term consequences of not napping (Campbell &

Murphy, 2007). Normal day-to-day and interindividual variations in sleep timing and sleep duration are evidence of some flexibility in the sleep-wake system. However, too much variation, whether by chronic restriction or displacement of night-time sleep to the daytime, has clear costs for performance, fatigue, and well-being. Given that people generally perform well without regular napping, it appears that polyphasic sleep is not essential - that the sleep-wake system is flexible.

#### *9.2.1.2. Circadian and homeostatic considerations for daytime sleep strategies to maintain night-time function*

The daytime sleep strategies adopted by night workers between shifts broadly fall into three types, described in Chapter 7 as “immediate”, “delayed”, and “split” strategies. Each type of strategy has theoretical advantages and disadvantages, and it was the aim of Chapter 7 to explore their effectiveness at sustaining night-time function in practice. The putative advantage of the first strategy, to sleep in the morning shortly after the night shift, is the immediate satiation of homeostatic sleep pressure accrued during the night, allowing quick relief and recovery (Tepas, 1982). However, disadvantages associated with this approach include potentially significant reductions in sleep quality and sleep duration due to the alerting influence of the circadian pacemaker at this time of the morning (Åkerstedt & Landstrom, 1998; Sargent et al., 2012a). Furthermore, it also increases the duration of wakefulness accumulated before the subsequent shift. The second approach, to delay sleep for several hours, has the putative benefit of allowing night workers to commence their shifts refreshed with little accumulated prior wake. However, given this timing could coincide with or overlap the biological wake maintenance zone, this strategy also has the potential to affect sleep quality (Lavie, 1986; Strogatz et al., 1987). The third strategy, to split sleep, is an attempt to obtain some of the benefits of both immediate and delayed strategies, but it may be that doing so achieves neither.

In this study, none of the strategies were found to have any significantly different effects significant benefits to night-time performance or alertness. However, this is not to say that all the strategies are equally useful under all

circumstances. In the current study, sleep strategies were scheduled during 12-h breaks between shifts. This meant the amount of homeostatic sleep pressure accrued following the immediate and delayed strategies differed by only 3 h. In other circumstances, where rest-breaks permit a larger difference in the temporal placement of sleep episodes, circadian and homeostatic differences between strategies could have a greater role in moderating night-time performance. So far, findings by Santhi et al. (2008) indicate that, for 8-h night shifts, the advantage of reduced homeostatic pressure following a delayed sleep strategy outweighs the putative benefit of early sleep satiation in the immediate strategy. However, as Santhi and colleagues did not investigate the effect of split strategies, it remains to be seen whether it is necessary to delay a *whole* sleep episode to improve performance or whether it might be sufficient to supplement an immediate sleep with an evening nap before work.

## 9.2.2. Practical Considerations

### 9.2.2.1. *Split work-rest schedules*

The split sleep–wake schedule employed in this thesis (Chapter 5) did not harm sleep and resulted in sustained attention being better than normal during the night-time. Based on these findings, it is plausible that split work–rest schedules may have some utility. One of the main arguments made against split-shift schedules, such as those employed in the hospitality industry, is that working twice a day is disruptive to shiftworkers' family/social lives (Bohle et al., 2004; Costa, 2016). While this may true in many cases, split schedules might be practical or warranted where optimal performance around the clock is essential and such disruptions are either not applicable or of secondary importance. For instance, these schedules may be suitable for safety-critical environments such as fly-in fly-out mines where shiftworkers are isolated from their normal social obligations. Similarly, they may be usefully employed for short-term emergency responses to disasters, such as floods and bushfires, where less urgent and time-sensitive matters may be temporarily put aside. Potential difficulties in the implementation of the schedules may include: resistance by workers to



appropriately utilising their breaks for sleep; increased miscommunication due to the greater number of hand-overs between consecutive shifts; and more instances of sleep inertia from which to recover (Hilditch et al., 2016).

#### *9.2.2.2. Sleep advice for night workers*

The usefulness of advice is dependent on a mutual understanding of the desired goal. For instance, any response to a night worker's enquiry about the best time to sleep between night shifts must be consistent with what it is they wish for their sleep to achieve. While the study in Chapter 7 sought to determine the best daytime sleep strategies for night-time alertness and performance on shift, another legitimate avenue of enquiry would be to investigate which strategies are best for improving alertness and performance during the break.

If the goal of sleep between night shifts is to simply recover and improve daytime functioning, sleeping immediately – a choice popularly adopted by night workers, supplemented or not by an evening nap (Ficca et al., 2010; Tepas, 1982) – is likely the best strategy. However, with night-time function as the primary goal, the results from Chapter 7 suggest the arrangement of daytime sleep is not especially important for 12-h night shifts, provided a sufficient opportunity to sleep is scheduled. Results from other studies, however, such as one by Santhi et al. (2008), indicate that for shorter 8-h night shifts– where the duration of the rest break is longer - delaying sleep might be the better option for night-time performance. It remains to be seen whether splitting sleep across the break is equally viable, better, or worse for 8-h night shifts. Other options for sleep, such as work-allocated rest-breaks during the night, may also be useful strategies in some industries (Purnell et al., 2002).

### **9.3. General Limitations**

The studies reported in this thesis provide valuable insight into the effects that the temporal arrangement and duration of sleep have on neurobehavioural performance. However, the implementation of these protocols in a controlled laboratory setting, with laboratory-based tasks and a homogenous participant

demographic, means there are questions about the extent to which findings may be applied to the 'real world'. The following sub-sections discuss some of the limitations of these studies and factors that may affect the overall generalisability of the findings.

### 9.3.1. Participant Demographics

Since interindividual differences can influence performance, participants were chosen according to a set of criteria to limit the effect of potential confounders. This was done so results could more confidently be attributed to manipulation of the independent variable. Except for the equipment validation study reported in Chapter 3, all participants in the studies included in this thesis were male. Participants were aged 18 to 35 years, had no recent history of shift work, and entered the laboratory well-rested and healthy (as determined by body mass index and self-report questionnaire). However, notwithstanding the advantages of a homogeneous sample, the characteristics of these participants are important to consider when trying to generalise findings to the broader population or to specific subsets of people, like shiftworkers.

The exclusion of women as participants in several of the studies is consistent with similar previous laboratory protocols involving multiple days of sleep restriction (Jackson et al., 2014; Wyatt et al., 2004; Zhou et al., 2011). However, there are some small sex differences in neurobehavioural decline due to sleep loss that are important to consider (Blatter et al., 2006). During sleep deprivation, Blatter et al. observed women exhibited slower response times than men but tended to commit fewer errors, suggesting they utilised a different strategy to sustain performance. As such, the absence of female participants could affect the extent to which results may be generalised towards female shiftworkers.

A clear majority of shiftworkers are older than the participants in this thesis, with 54.8% of Australians regularly engaged in shiftwork in 2012 aged over 35 years (Australian Bureau of Statistics, 2013). This percentage is an increase from 19 years earlier, when 47.2% of shiftworkers were aged over 35 years

(Australian Bureau of Statistics, 1994). Age is an important factor to consider because it is associated with significant differences in sleep, circadian adjustment, and performance independent of the effects of shiftwork (Blatter et al., 2006; Dijk et al., 1999; Scullin, 2012; Van Cauter, Leproult, & Plat, 2000). For instance, adults typically sleep for shorter durations as they get older and find it more difficult to adjust to disruptions of their circadian rhythms (Bonnefond et al., 2006; Matsumoto & Morita, 1987). In terms of performance, younger males tend to have faster response times on neurobehavioural tasks than older males, but older adults are more resistant to the effects of sleep deprivation, demonstrating smaller declines (Adam, Retey, Khatami, & Landolt, 2006; Blatter et al., 2006; Bonnefond et al., 2006). Aside from differences in neurobehavioural performance, older shiftworkers have more experience regarding the real-world demands of their work, so it is possible they have developed better strategies than younger shiftworkers to cope with them (Avolio, Waldman, & McDaniel, 1990).

### 9.3.2. The Laboratory Setting

The benefit of conducting research in a laboratory is the wide latitude it provides to manipulate and systematically control for extraneous behavioural and environmental factors which can affect dependent variables – such as lighting, temperature, time cues, food intake, physical activity and social interaction. This control helps to elucidate the relationships between variables and determine the validity of theoretical mechanisms. However, since this artificial environment often eliminates or simplifies the factors to which people are usually exposed, it can also inhibit the ability to generalise findings beyond the four walls of the laboratory.

An example of this is that the sleeping conditions for participants in all the studies in this thesis were likely more conducive to sleep than those of typical shiftworkers (Barton, 1994; Knauth & Rutenfranz, 1975; Lee, 1992). Participants were allocated periods of uninterrupted sleep in separate bedrooms that were dark, sound-attenuated, and temperature-controlled. In

contrast, shiftworkers must often combat disruptions to sleep (e.g., daylight streaming in through the curtains, loud traffic noise, telephone ringing, social or family demands). Changes in sleep quality/quantity resulting from such environmental differences could have implications for individuals' feelings of fatigue and subsequent performance.

Another issue is the confounding influence laboratory procedures and environments can have on participants' boredom and motivation to perform (Paterson, Dorrian, Ferguson, Jay, & Dawson, 2013). Paterson et al. (2013) reported findings from a laboratory study conducted over multiple days in which participants were scheduled 9 h of time in bed each night. Despite no sleep loss, they found participants' performance, mood, alertness, and sleep all significantly declined across successive days. These results have implications for other laboratory studies, particularly those where sleep timing and duration *are* manipulated. To wit, even in highly controlled studies, there must be caution when attributing cause as multiple factors may be responsible for the results.

### 9.3.3. Laboratory-Based Performance Tasks

Another aspect that needs to be considered when trying to generalise the findings of this thesis is the laboratory tasks used to measure performance. Investigations into the impairment associated with sleep restriction, prior wakefulness and circadian misalignment often use laboratory-based tasks as proxies for 'real-world' tasks for their convenience and simplicity. This thesis employed a variety of computer- and paper-based tasks to capture effects on various domains of neurobehavioural function. For instance, tasks such as the psychomotor vigilance test predominantly focused on domains of sustained attention (Dorrian et al., 2005), while the serial addition/subtract task and digit symbol substitution test also captured features of working memory, processing speed, and visuomotor coordination (DeStefano & LeFevre, 2004; Imbo & Vandierendonck, 2007; Joy et al., 2004; Salthouse, 1978). However, while useful, restraint is required when extrapolating findings from laboratory-based tasks to the 'real world' because they bear little resemblance to activities employed in

occupational settings. There is no guarantee that they utilise all the requisite cognitive functions and skills to successfully complete job demands or that they will be affected by work conditions in the same way or to the same extent.

Further to the issue of the generalisability of laboratory-based tasks is that fatigued performance is mediated by factors such as task complexity, task difficulty and participants' motivation (Drummond et al., 2004; Harrison & Horne, 2000; Horne & Pettitt, 1985). This is supported by the differing effects of sleep restriction and circadian misalignment that have been demonstrated on various measures in this thesis (Chapter 6) and elsewhere (Burke et al., 2015; Jongen et al., 2015; Lo et al., 2012). For those measures that were significantly affected by sleep restriction and circadian phase, patterns of impairment were usually similar but the magnitudes of impairment differed. As such, while these tasks can provide an indication of how real-world performance may be affected, they should not be considered definitive.

Given the practical and ethical constraints involved in experimentally investigating real-world activities such as driving, studies aiming to produce more accurate estimates of performance often employ simulators that mimic task conditions. Simulators go some way to address the limited ecological validity of other laboratory-based neurobehavioural tasks, but they do have their own limitations (Reed & Green, 1999). An issue often raised in relation to simulators is the incentive to perform. Within the laboratory, there is no risk of physical harm. In contrast to on-road driving, where poor driving could result in fatalities, there are few if any personal consequences in a simulator and little to motivate effort apart from goodwill. Compounding this issue in this thesis is that the driving task described in Chapter 6 was not conducted in a high fidelity simulator. Rather, it was presented as a lane-tracking task on a personal computer, with a steering wheel attached to the desk and pedals fixed to the floor. As such, it is possible that the results overestimated the declines associated with sleep restriction and circadian misalignment in the laboratory.

## 9.4. Future Directions

### 9.4.1. Improving Generalisability

Given the aforementioned limitations to generalisability, there are multiple avenues for further research. The questions in this thesis have been examined under controlled conditions, so future research could investigate how well these findings translate in the field. For instance, the benefits of different daytime sleep strategies between night shifts (Chapter 7) and prophylactic naps before the first night shift (Chapter 8) could be further assessed with respect to real shiftworkers before and after their shifts. Similarly, the relative influences of sleep and the circadian pacemaker during split sleep-wake schedules (Chapter 5 and 6) could be examined for more complex higher-order cognitive constructs, such as judgement and decision-making (Burke et al., 2015), and for applied competency-based workplace skills and tasks. Future studies would also do well to examine the effects of sleep timing and duration with a more diverse participant sample – including women, older adults, and adults who are less healthy than those recruited here. To decrease any variance unrelated to experimental manipulation during the protocols, female participants could be studied at the same phase of the menstrual cycle.

### 9.4.2. Expanding Knowledge

Chapter 5 supports previously published research that having multiple sleep episodes per day is not inherently harmful (Jackson et al., 2014; Mollicone et al., 2008; Short et al., 2016). In this thesis, it is suggested that split sleep-wake schedules may be more beneficial than consolidated schedules for night-time performance due to a reduction in prior wake. However, the results are from protocols with enforced bedtime durations equivalent to 8 h each day, and it is possible the benefits of split schedules found in this thesis do not extend to individuals who are not well rested. Given sleep loss affects performance and often coincides with shiftwork (Åkerstedt, 2003), it is critical to understand how the circadian and homeostatic processes interact under conditions of moderate and severe sleep restriction. Some objective and subjective performance data

have been reported for forced desynchrony protocols in which participants lived on consolidated sleep-wake schedules with sleep restriction (Buxton et al., 2012; Ferguson et al., 2012b; Heath et al., 2012; Matthews et al., 2012a; Matthews et al., 2012b; Sargent et al., 2012a; Sargent et al., 2012b; Zhou et al., 2011, 2012), but no data have yet been reported for forced desynchrony protocols in which sleep-wake schedules are split and sleep is restricted.

An additional avenue for enquiry in Chapter 5 exists in the finding that participants in the split schedule acquired about 27% more slow-wave sleep than those in the consolidated schedule. With a current understanding of sleep homeostasis, one would expect those acquiring similar ratios of sleep and wake to obtain equivalent amounts (Borbély, 1980, 1982). A possible reason for the difference is that splitting the sleep-wake cycle has an impact on sleep homeostasis that is manifest in an increased amount of SWS of reduced intensity. In future research, analysis of slow wave activity, a measure of the intensity of sleep, could determine whether there is support for this explanation.

In Chapter 7, results indicated no significant advantages to any daytime sleep strategy (i.e., sleeping immediately after a night shift, delaying sleep after a night shift, or splitting sleep during the day) for performance the following night. However, this protocol simulated only two consecutive shifts. It is possible that a given sleep strategy might have a more pronounced effect on performance over more nights. Similarly, since the simulated night shifts were 12-h long, the breaks may not have been long enough to significantly differentiate the timing of the sleep strategies. As such, future research could build on the findings of this study by evaluating the effect of the different strategies on performance during 8-h shifts (with 16-h breaks) across multiple consecutive nights.

## 9.5. Conclusion

Several conclusions may be drawn from this dissertation. First, the wrist-worn accelerometers used in the studies were suitable for monitoring sleep/wake behaviour (Chapter 3 and 4). Second, provided sufficient time in bed, split sleep-wake schedules are not inherently detrimental to performance and may even be

beneficial for nocturnal performance due to the reduction of sustained wakefulness (Chapter 5). Third, during severe sleep restriction, performance-based tasks that require sustained vigilance exhibit the greatest circadian variation, the worst nocturnal deficits, and are the best neurobehavioural predictors of driving impairment (Chapter 6). Fourth, daytime sleep-timing strategies have no significant effects during 12-h night shifts, where the “window” in which to differentiate them is limited (Chapter 7). Finally, a prophylactic 1-h nap is likely to be sufficient to mitigate the effects of sleep deprivation on performance during the first night shift (Chapter 8).



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## **Appendix A: Recruitment Flyers**

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## Study 1

# VOLUNTEERS REQUIRED

Researchers at the **Appleton Institute** sleep laboratory are seeking volunteers to participate in a SLEEP STUDY.

We are looking for healthy non-smokers, aged 18-35 years, who would like to spend a night at our centre to test some new equipment.

During your time here, we will provide you dinner, breakfast and your own bedroom!

**For more information, please contact:**

Email: [a.kosmadopoulos@cqu.edu.au](mailto:a.kosmadopoulos@cqu.edu.au) or  
[greg.roach@cqu.edu.au](mailto:greg.roach@cqu.edu.au)

This project has been approved by the  
CQUniversity Human Research Ethics Committee

## Study 2

# VOLUNTEERS REQUIRED

Researchers at the Appleton Institute sleep laboratory are seeking volunteers to participate in a SLEEP STUDY. We are looking for healthy males, aged 18-35 years, who would like to live in our lab over **13 days**.

*The Appleton Institute is located at: 44 Greenhill Road, Wayville SA 5034*

Participants will be financially compensated for the inconvenience associated with their participation in the study (\$1500). During your stay in the lab, you will not have access to clocks, telephones/mobile phones, internet or live television/radio so you will be unaware of the time.

The next dates are:      **10<sup>th</sup> July - 22<sup>nd</sup> July**

**For more information, please contact Stas**

Email: a.kosmadopoulos@cqu.edu.au

Phone: 08 8378 4527

This project has been approved by the  
CQUniversity Human Research Ethics Committee

## Study 3

# VOLUNTEERS REQUIRED

Researchers at the Appleton Institute sleep laboratory are seeking volunteers to participate in a SLEEP STUDY. We are looking for healthy males, aged 18-35 years, who would like to live in our lab for **12 days**.

*The Appleton Institute is located at: 44 Greenhill Road, Wayville SA 5034*

Participants will be financially compensated for the inconvenience associated with their participation in the study (\$1500).

The next dates are:

- |   |           |
|---|-----------|
| 1) 29 <sup>th</sup> Nov – 2 <sup>nd</sup> Dec 2013  | } 12 Days |
| 2) 6 <sup>th</sup> Dec – 9 <sup>th</sup> Dec 2013   |           |
| 3) 13 <sup>th</sup> Dec – 16 <sup>th</sup> Dec 2013 |           |

**For more information, please contact Xuan**

Email: x.zhou@cqu.edu.au

Phone: 08 8378 4525

This project has been approved by the  
CQUniversity Human Research Ethics Committee

## **Appendix B: Information Sheets**

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## Study 1

### Validation of Wrist-Actigraphy Technologies Against Gold-Standard Polysomnography

#### INFORMATION SHEET

##### Project Overview

Actigraphs are wristwatch-like devices which contain accelerometers and measure movement. They are widely used to estimate sleep/wake behaviour in field and laboratory research when it is not practical to use the gold-standard technique to measure sleep (polysomnography). High activity recorded by actigraphs indicates wake, low activity indicates sleep. However, different types of actigraphs measure movement slightly differently so, unless researchers know how they relate to each other and to polysomnography, it is difficult for them to compare findings across studies which use different actigraphs. This project aims to close this knowledge-gap by comparing two types of actigraphs against polysomnography in a single-night protocol at the Centre for Sleep Research in CQUniversity's Appleton institute.

This study design will run over a single night from 7pm to 10am, with three participants taking part at a time. Dinner and breakfast will be provided and participants will each have a separate bedroom to sleep in. During sleep periods, participants will wear two actigraphs on their non-dominant arms and also have electrodes taped to their heads and face to detect electrical signals in the brain; these will be scored into sleep/wake stages using standardised criteria.

##### Participation Procedure

Prospective participants, aged 18-35 years, will be asked to complete a demographic and general health questionnaire as part of the participant screening process. On arrival for the study at 7pm, actigraph data will be checked for compliance. Participants will be provided an orientation of the facilities and safety procedures and will be provided consent forms to sign.

Demands placed on participants will be minimal. Essentially, the main events of the study will be dinner provided at 7.45pm, a 9.5-hour sleep period from 10pm to 7.30am, breakfast, and then a study debrief. At 8.30pm participants will be asked to prepare for bed. At 9pm participants will be given two actigraphs to wear and then, in their own bedrooms, will have electrodes placed in the standard array for polysomnography recording; this should be completed by 9.45pm. Participants will be in bed when the lights are turned off at 10pm and will be asked to remain in bed until lights are turned back on at 7.30am (unless they need to use the bathroom amenities). In the morning, participants will have their actigraphs and electrodes removed and be able to shower, get changed, have breakfast, and be debriefed. Estimated departure time is 9-10am. Research staff will be on site the whole night. Participation or non-participation will not affect the participants' employment or academic standing.

##### Benefits and Risks

It is possible that some participants may experience minor skin irritations as a result of the tape used to attach the electrode cups for polysomnography. This risk is unlikely as it occurs in a minority of people and usually only after multiple nights of sleep monitoring. If it does occur, moisturiser will be made available to participants. Aside from potential skin irritation,



no risks beyond those normally encountered in everyday life/work are anticipated in this study. There will be no financial compensation for participating, but all meals will be provided and all participants will have access to free car parking for the duration of the study if they need it.

**Confidentiality / Anonymity**

All data collected will be assigned a unique participant code so that it will remain anonymous. Data will be securely stored on a password-protected computer or locked away in a filing cabinet for five (5) years in accordance with the CQUniversity policy. No one will have access to the data except for research staff working on the project.

As three other participants will be involved in this study at the same time, it is requested that all participants' anonymity shall be respected and no one pass on the identity of other participants without their consent,

**Outcome / Publication of Results**

Results from this study will be analysed to assess the validity of the actigraphs. These findings will be disseminated in articles published in scientific journals and conference proceedings.

**Consent**

Any questions regarding the purpose, nature and procedures of this study can be discussed at any time. Informed consent will be requested in writing on the evening of the study.

**Right to Withdraw**

Participants have the right to withdraw participation and request that their data be destroyed at any time without penalty.

**Feedback**

Feedback will be given to participants in a debrief session in the morning and on request at a later stage.

**Questions/ Further Information**

If you have any questions or would like more information, please contact:

Anastasi Kosmadopoulos: a.kosmadopoulos@cqu.edu.au, or

A/Prof. Greg Roach: greg.roach@cqu.edu.au

**Concerns / Complaints**

*Please contact CQUniversity's Office of Research should there be any concerns about the nature and/or conduct of this research project. Tel: 07 4923 2607; E-mail: research-enquiries@cqu.edu.au; Mailing address: Building 32, CQUniversity, Rockhampton QLD 4702*

## Study 2

### INFORMATION SHEET

#### **Project Title: Should we go halves? The impact of split work-rest schedules on sleep and cognitive performance**

You have been invited to participate in a research study. Before agreeing to participate in the study, it is important that you read and understand the following explanation of the study and the procedures. This form describes the purpose, procedures, benefits, risks, discomforts and alternative procedures that are available to you. If you choose to participate, you have the right to withdraw from the study at any time.

#### **What is the study about?**

The aim of this study is to improve our understanding of how sleep and wake affect behaviour and cognitive function. That is, how they affect our memory, alertness and performance. The results we obtain from this study will help us to design better shiftwork schedules.

#### **Who can participate and how does the study work?**

Healthy, non-smokers who are aged between 18 to 35 years old, taking no medication and have a regular sleep pattern are eligible to participate in this study. Before commencing the study, potential participants will be required to attend a screening interview where they will complete a general health questionnaire. Participants will also be required to complete a 7-night sleep/wake diary and wear a wrist activity monitor (small device the same size as a wrist watch). These two measures will allow us to assess your sleep pattern.

#### **What happens during the study?**

All investigations will be carried out in the Appleton Institute's live-in sleep laboratory. If you are eligible to participate, you will be asked to attend the laboratory for thirteen consecutive nights/days. During this period, you will not have access to clocks, telephones (or mobile phones), internet or live television/radio, so you will be unaware of the time. You will be randomly allocated to either the **split sleep group** or the **ad libitum sleep** group, which will undergo distinctive experimental protocols.

**Split Sleep Group** – For this group, there will be three baseline nights and days, followed by nine study nights and days. If you are allocated to this group, you will be required to arrive at the lab no later than 12:00pm on the first baseline day. At this time, you will begin training on a number of performance tasks that will be used throughout the study (memory, concentration, alertness, performance tests) until your performance reaches a plateau. For the three baseline nights, your bedtime will be scheduled at 11:00pm and you will be woken at 7:00am the following morning.

Following the baseline period, you will then undergo nine study nights and days. On these nights and days, your sleep and wake periods will be set at times that are different to those in a normal 24h cycle. You will get a different amount of sleep than you would in a normal 24h day. Sleep laboratory staff will instruct you when it is time to go to sleep and when it is time to wake up. Because of these changes to your sleep and wake schedule, you may experience a range of symptoms, including excessive sleepiness and fatigue, irritability, and mild queasiness.

During all sleep periods (baseline and study nights) your sleep will be monitored using standard polysomnography, which involves placing electrodes on your face (taped to the skin) and scalp. During the daytime (baseline and study days), you will also be asked to complete a series of performance tasks at set times. When you are not completing these tasks, you may read, watch TV (i.e., DVDs), or listen to music etc. Your movement and activity during wake and sleep periods will be recorded using small, visible cameras that are located in the ceiling of each bedroom and living area. These cameras will not be located in any of the bathrooms. The Research Staff conducting this study will be the only group that will have access to this data to ensure your confidentiality.

Throughout the study, we will be monitoring your body temperature. Body temperature will be measured using two devices: (1) a rectal thermometer and; (2) a tiny capsule (which contains a temperature sensor) that you will be asked to swallow (about the size of a multi-vitamin). The capsule transmits a signal to a small monitor pack that will be worn around the waist. At all times, you will have one capsule traveling through your digestive system. The capsules take approximately two days to pass through your system (although this may vary between individuals) and you will be required to swallow approximately 10 capsules (1-2 capsules every second day depending on your bowel activity) over the course of the study.

All of your meals will be supplied during the study, and you will not be allowed to bring any food with you. If you have any special dietary requirements, please let the staff know so that we can accommodate you. It is important to remember that throughout the study, and in the 24hr prior to the first baseline night, you will be asked to refrain from consuming any alcohol or caffeine.

**Ad libitum Sleep Group** – If you are allocated to this group, you will be required to arrive at the lab no later than 03:00pm on the first day. During the study, you will be asked to sleep “ad libitum” – that is, you will be free to go to bed whenever you feel like sleeping and you can sleep for as long as you like. Your sleep and wake patterns will be monitored using wrist activity monitors (the same devices worn prior to participating in the study), and using small, visible cameras that are located in the ceiling of each bedroom and living area. These cameras will not be located in any of the bathrooms. The research staff conducting this study will be the only group that will have access to this data to ensure your confidentiality. When you are not sleeping, you will be free to read, watch TV (i.e., DVDs), or listen to music etc.

Throughout the study, we will be monitoring your body temperature continuously. Body temperature will be measured using two devices: (1) a rectal thermometer and; (2) a tiny capsule (which contains a temperature sensor) that you will be asked to swallow (about the size of a multi-vitamin). The capsule transmits a signal to a small monitor pack that will be worn around the waist. At all times, you will have one capsule traveling through your digestive system. The capsules take approximately two days to pass through your system (although this may vary between individuals) and you will be required to swallow approximately 10 capsules (1-2 capsules every second day depending on your bowel activity) over the course of the study.

All of your meals will be supplied during the study, and you will not be allowed to bring any food with you. If you have any special dietary requirements, please let the staff know so that we can accommodate you. It is important to remember that throughout the study, and in the 24hr prior to the first baseline night, you will be asked to refrain from consuming any alcohol or caffeine.

**Are there any risks?**

The capsule that we are asking you to swallow (to record your body temperature) transmits data via low power radio frequency. This produces a small level of electromagnetic radiation, but it will be at level of exposure that is considered safe. For example, mobile phones also produce electromagnetic radiation, reaching peak levels of ~2000 milliwatts. The level produced by the ingestible capsule is approximately 1000 times lower than the level produced by a mobile phone. It is important, however, to notify Research Staff if you have been exposed to radiation in other research projects, or as a part of investigation (X-Rays) or treatment (Radiotherapy) in the past year.

In rare instances, you may experience some gastrointestinal discomfort following ingestion of the temperature capsule, or it may become lodged in the intestines. We will be monitoring you closely at all times during the study, and it is important for you to let Research Staff now if you are experiencing any untoward symptoms so that the appropriate action and treatment can be initiated. You may experience some difficulty when swallowing the capsule, which could result in a potential choking hazard. At all times, the capsules will be administered to you according to the manufacturer's recommendation (i.e. the capsule will always be swallowed with water or other suitable liquid) and you will be instructed not to chew the capsule before swallowing.

You may also experience minor skin irritation from the small electrodes that will be used to monitor your sleep. These are placed on your temples (next to your eyes), your chin, your forehead and your collarbone and are taped to your skin. Attempts will be made to minimize any discomfort by alternating the position of these leads.

**How does my family get in touch with me if there is an emergency?**

An important part of the study protocol is that while you are living in the sleep laboratory, you are unaware of the time of day. This means you will not have access to telephones. However, should your family urgently need to get in touch with you at any time during the study, they can contact the sleep laboratory directly on the following number: 08 8378 4538 (Staff will be available 24hr a day for the duration of the study).

**What do I need to bring?**

You will be staying in the sleep laboratory for 13 days, so you will need to bring enough clothes and toiletries to cover this time. We will provide you with all of your linen (sheets, blankets, towels, pillows etc) but you may wish to bring your own pillow from home. You will have your own bedroom, living area, shower and toilet facilities for the duration of the study. Because there will be periods of spare time throughout the study, please feel free to bring along your own music, books or movies.

**What happens at the end of the study?**

Following completion of the study, you will be given a taxi voucher to cover your transport home. You will not be allowed to drive yourself home. We also advise that you avoid the following activities [driving a car, riding a bike, and/or operating heavy machinery] until you have obtained at least one full night's sleep (uninterrupted for 9 hours or more) following completion of the study. In the 24h following completion of the study, or if you have withdrawn from the study early, staff at the Appleton Institute sleep laboratory will contact you via telephone for follow-up. Following completion of the study, should you need to get in contact with study staff, they can be reached on 08 8378 4527.

**What happens to the results?**

All data from this study will be stored on laboratory computers at the Appleton Institute, with backups on external harddrives in lockable filing cabinets. All information collected, as part of the study, will be destroyed at the end of seven years. Summarized results will be stored as hard copies at the Appleton Institute, and may be used in theses, journal publications and conferences. All records containing personal information will remain STRICTLY CONFIDENTIAL. No information that would lead to the identification of any individual will be released.

**What will you get out of the study?**

While you will not directly benefit from this study, you will be compensated for the inconvenience and loss of time associated with your participation. If you complete the study, you will receive \$1500 (\$960 participation payment + \$540 completion payment). If for some reason you do not complete the whole study, you will receive a pro rata participation payment based on the number of hours that you spent in the sleep laboratory. Upon request, you will be provided with a copy of the final research report.

**Voluntary participation - what happens if I say no?**

Before deciding whether or not to take part in this trial, you may wish to discuss the matter with a relative, friend or your local doctor. You should feel free to do this. It is important that you understand that your participation in this trial is voluntary, as is the case with all research projects at the Appleton Institute. If you do not wish to take part you are under no obligation to do so. If you decide to take part but later change your mind, you are free to withdraw from the project at any stage. Your decision to take part, not to take part, or to withdraw, will not affect your routine medical treatment or your relationship with those treating you or your relationship with the Appleton Institute.

**How do I become a participant?**

If you are interested in participating or have any questions, please contact Stas Kosmadopoulos (email: a.kosmadopoulos@cqu.edu.au; or phone: 08 8378 4527). Alternatively, you can contact Xuan Zhou (email: x.zhou@cqu.edu.au).

**Concerns / Complaints**

*Please contact the CQUniversity Office of Research should there be any concerns about the nature and/or conduct of this research project (tel 0749 23 2603, email ethics@cqu.edu.au; Mailing address: Building 361, CQUniversity, Rockhampton, QLD 4702).*

## Study 3

### INFORMATION SHEET

#### **Project Title: Can the recovery value of daytime sleep be optimised to reduce fatigue risk for night workers in safety-critical industries?**

You have been invited to participate in a research study. Before agreeing to participate in the study, it is important that you read and understand the following explanation of the study and the procedures. This form describes the purpose, procedures, benefits, risks, discomforts and alternative procedures that are available to you. If you choose to participate, you have the right to withdraw from the study at any time.

#### **What is the study about?**

The aim of this study is to improve our understanding of the effectiveness of different sleep strategies between consecutive night shifts on sleep and cognitive performance. The results of this study will enable us to recommend optimal sleep strategies to shift worker.

#### **Who can participate and how does the study work?**

Healthy, non-smokers who are aged between 18 to 35 years old, taking no medication and have a regular sleep pattern are eligible to participate in this study. Before commencing the study, potential participants will be required to attend a screening interview where they will complete a general health questionnaire. Participants will also be required to complete a 7-night sleep/wake diary and wear a wrist activity monitor (small device the same size as a wrist watch). These two measures will allow us to assess your sleep pattern.

#### **What happens during the study?**

All investigations will be carried out in the Appleton Institute's live-in laboratory. If you are eligible to participate, you will be asked to attend the laboratory on three separate occasions, one week apart from each other. On each occasion, you will stay at the sleep lab for 76 consecutive hours that span over 4 calendar nights/days: one baseline night and day (28h), followed by two study nights and days (48h). During this period, you will not have access to clocks, telephones (mobile phones/internet) or live television/radio. On the baseline day, you will be required to arrive at the lab no later than 12pm. At this time, you will begin training on a number of performance tasks that will be used throughout the study (memory, concentration, alertness, performance tests) until your performance reaches a plateau. For the baseline night, your bedtime will be scheduled at 11:00pm and you will be woken at 8:00am the following morning. You will have a 1-h nap (16:00 – 17:00h) to prepare for the first night shift (18:00h-06:00h). During the shift, you will stay awake and perform the tasks you have practiced previously. You will be given a sleep opportunity on the following day. Sleep laboratory staff will instruct you when it is time to go to sleep and when it is time to wake up. The following night is your second night shift. Once again, you will stay awake all night and perform the required tasks. Following this night shift, you will have a 7-h sleep opportunity (07:00 – 14:00h) before you exit the accommodation suite at 16:30h. Because of these changes to your sleep and wake schedule, you may experience a range of symptoms, including excessive sleepiness and fatigue, irritability, and mild queasiness. During all sleep periods (baseline and study nights) your sleep will be monitored using standard polysomnography, which involves placing electrodes on your face (taped to the skin) and scalp. During the daytime (baseline and study days), you will also be asked to complete a series of performance tasks at set times. When you are not completing these tasks, you may read, watch TV (DVDs/Videos), talk, or listen to music etc. Your movement and activity during wake and sleep periods will be recorded using small, visible cameras that are located in the ceiling of each bedroom and living area. These cameras will not be located in any of the bathrooms. The Research Staff conducting this study will be the only group that will have

access to this data to ensure your confidentiality. All of your meals will be supplied during the study, and you will not be allowed to bring any food with you. If you have any special dietary requirements, please let the staff know so that we can accommodate you.

**Are there any risks?**

You may also experience minor skin irritation from the small electrodes that will be used to monitor your sleep. These are placed on your temples (next to your eyes), your chin, your forehead and your collarbone and are taped to your skin. Attempts will be made to minimize any discomfort by alternating the position of these leads. The tiny sensor that will be used to monitor your blood glucose may also irritate your skin.

**How does my family get in touch with me if there is an emergency?**

An important part of the study protocol is that while you are living in the sleep laboratory, you are unaware of the time of day. This means you will not have access to telephones. Should your family need to get in touch with you at any time, they can contact the sleep laboratory (staff will be present 24hr a day) on the following number: 83784527 or 83784523.

**What do I need to bring?**

You will be staying in the sleep laboratory for four days and nights, so you will need to bring enough clothes and toiletries to cover this time. We will provide you with all of your linen (sheets, blankets, towels, pillows etc) but you may wish to bring your own pillow from home. You will have your own bedroom, living area, shower and toilet facilities for the duration of the study. Because there will be periods of spare time throughout the study, please feel free to bring along your own music, books or movies.

**What happens at the end of the study?**

Following completion of the study, you will be given a taxi voucher to cover your transport home. You will not be allowed to drive yourself home. We also advise that you avoid the following activities [driving a car, riding a bike, and/or operating heavy machinery] until you have obtained at least one full nights sleep (uninterrupted for 9 hours or more) following completion of the study. In the 24h following completion of the study, or if you have withdrawn from the study early, staff at the Appleton Institute will contact you via telephone for follow-up. Following completion of the study, should you need to get in contact with study staff at any time, they can be reached on 83784527.

**What happens to the results?**

All data from this study will be stored on computers at the Appleton Institute, with backups on external hard drives in lockable filing cabinets. All information collected, as part of the study, will be destroyed at the end of seven years. Summarized results will be stored as hard copies at the Appleton Institute, and may be used in theses, journal publications and conferences. All records containing personal information will remain STRICTLY CONFIDENTIAL. No information that would lead to the identification of any individual will be released.

**What will you get out of the study?**

While you will not directly benefit from this study, you will be compensated for the inconvenience and loss of time associated with your participation. If you complete the study, you will receive \$1500. If for some reason you do not complete the whole study, you will receive a pro rata participation payment based on the number of hours that you spent in the sleep laboratory. Upon request, you will be provided with a copy of the final research report.

**Voluntary participation - what happens if I say no?**

Before deciding whether or not to take part in this trial, you may wish to discuss the matter with a relative, friend or your local doctor. You should feel free to do this. It is important that you understand that your participation in this trial is voluntary, as is the case with all research projects at the Appleton Institute. If you do not wish to take part you are under no obligation to do so. If you decide to take part but later change your mind, you are free to withdraw from

the project at any stage. Your decision to take part, not to take part, or to withdraw, will not affect your routine medical treatment or your relationship with those treating you or your relationship with the Appleton Institute.

**How do I become a participant?**

If you are interested in participating or have any questions, please call Stas Kosmadopoulos on 83784527 or email [a.kosmadopoulos@cqu.edu.au](mailto:a.kosmadopoulos@cqu.edu.au).

**Concerns / Complaints**

*Please contact the CQUniversity Office of Research should there be any concerns about the nature and/or conduct of this research project (tel 0749 23 2603, email [ethics@cqu.edu.au](mailto:ethics@cqu.edu.au); Mailing address: Building 361, CQUniversity, Rockhampton, QLD 4702).*



## **Appendix C:    General Health Questionnaire**

---

**GENERAL HEALTH QUESTIONNAIRE****Name:****Section One: General**

Address: _____	Ph (H): _____
Email: _____	Ph (M): _____

DOB: \_\_\_\_\_ Age: \_\_\_\_\_ yr Gender: ☐ male ☐ femaleWeight: \_\_\_\_\_ kg Height: \_\_\_\_\_ cm ☐ Left-handed ☐ Right-handedHighest Level of Education Completed: ☐ Primary ☐ Secondary ☐ Tertiary ☐ Post grad

Occupation: \_\_\_\_\_

Approximate traveling time to work \_\_\_\_\_ minutes

Mode of transportation: \_\_\_\_\_ (bus, train, car, etc)

Are you vegetarian? ☐ Yes ☐ No Is English your first language? ☐ Yes ☐ NoHave you previously participated in a multi-day laboratory study? ☐ Yes ☐ No**If yes**, how long ago? \_\_\_\_\_

What did it involve? \_\_\_\_\_

1. Have you travelled through time zones in the last 3 months? ☐ YES ☐ NO  
If yes, please provide trip details, including when you arrived here

\_\_\_\_\_

2. Are you, or have you ever been involved in shift work (outside 9am-5pm)? ☐ YES ☐ NO

**If so**: how long ago? \_\_\_\_\_ yr \_\_\_\_\_ months

For how long? \_\_\_\_\_ yr \_\_\_\_\_ months

Please provide details about the shift schedule:

\_\_\_\_\_ (e.g., times, durations)

3. Please list the average amount of caffeine you consume per day (e.g. cups of tea/coffee, cans of caffeinated soft drink and chocolate bars)

\_\_\_\_\_

4. Do you smoke? ☐ YES ☐ NO

**If so**, how many cigarettes/cigars? \_\_\_\_\_ per day

5. Do you take illicit drugs (e.g., Marijuana)? ☐ YES ☐ NO

6. Do you have any children living with you at home? ☐ YES ☐ NO

If so, how many? \_\_\_\_\_

What is your relationship with them? ☐ Parent / Guardian ☐ Sibling ☐ Other \_\_\_\_\_

### Section Two: Sleep

7. What time do you normally wake up? \_\_\_\_\_ week \_\_\_\_\_ weekend

8. What time do you normally go to sleep? \_\_\_\_\_ week \_\_\_\_\_ weekend

9. Do you normally nap during the day? ☐ YES ☐ NO

If so, how often does this occur? \_\_\_\_\_

10. How well do you usually sleep?

Very poorly \_\_\_\_\_ Very well  
1 2 3 4 5

11. On average, how many times per night do you wake up?

☐ never ☐ hardly ever ☐ 1 or 2 ☐ < 5 ☐ 5 – 10  
☐ >10 ☐ don't know

### Section Three: General Health

12. Have you had any serious accidents, head injuries, or concussion? ☐ YES ☐ NO  
**If yes**, please give details:

\_\_\_\_\_

13. Are you currently on any medication? ☐ YES ☐ NO  
**If yes**, please give details:

\_\_\_\_\_

14. Have you been on any medication in the past week? ☐ YES ☐ NO  
**If so**, what medication:

\_\_\_\_\_

15. What exercise do you do?

16. How much exercise do you do, on average per week? \_\_\_\_\_ hours

17. On average, how much alcohol do you drink per week?

\_\_\_\_\_ beer/cider \_\_\_\_\_ wine \_\_\_\_\_ spirits

18. Have you ever experienced any of the following medical conditions, and if so, when?

Don't know = 0      No = 1      Yes in the past = 2      Yes, sometimes = 3  
Yes, at present = 4

- |                                 |       |                               |       |
|---------------------------------|-------|-------------------------------|-------|
| (a) Asthma                      | _____ | (b) Hay fever                 | _____ |
| (c) Eczema                      | _____ | (d) Allergies (Food or other) | _____ |
| (e) Thyroid Problems            | _____ | (f) Undue anxiety             | _____ |
| (g) Sleepwalking                | _____ | (h) Loud snoring              | _____ |
| (i) Nightmares                  | _____ | (j) Bruxism (grinding teeth)  | _____ |
| (k) Difficulty reading/writing  | _____ | (l) Arthritis/Rheumatism      | _____ |
| (m) Clinical depression         | _____ | (n) Heart problems            | _____ |
| (o) Stomach problems            | _____ | (p) Waking with a jolt        | _____ |
| (q) Waking up excessively early | _____ | (r) Difficulty falling asleep | _____ |
| (s) Stress/anxiety at home/work | _____ | (t) Epilepsy                  | _____ |
| (u) Migraine                    | _____ | (v) Colour blindness          | _____ |
| (w) Vision impairment           | _____ | (x) STD / STI                 | _____ |

19. Do you currently have any of the following (yes/no):

- |              |       |                                |       |
|--------------|-------|--------------------------------|-------|
| (a) Bed bugs | _____ | (b) Impetigo                   | _____ |
| (c) Tinea    | _____ | (d) Mite/Tick bites            | _____ |
| (e) Scabies  | _____ | (f) Other contagious condition | _____ |

#### Section Four: Stress and Workload

20. Do you have exams/assignments due/other tests scheduled for one week before, during, or after the study? ☐ YES ☐ NO

Comments: \_\_\_\_\_

21. Are you currently experiencing a greater than your normal amount of stress? (e.g. sick relative, relationship break-up, getting married, moving house?) ☐ YES ☐ NO

Comments: \_\_\_\_\_

**Section 5: Pittsburgh Sleep Quality Index**

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

1. During the past month, when have you usually gone to bed at night?

Usual Bedtime \_\_\_\_\_

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

Number of Minutes \_\_\_\_\_

3. During the past month, when have you usually gotten up in the morning?

Usual getting up time \_\_\_\_\_

4. During the past month, how many hours of actual sleep did you get at night? (This may be different to the number of hours you spend in bed)

Hours of sleep per night \_\_\_\_\_

5. For each of the remaining questions, check the one best response:

**During the past month, how often have you had trouble sleeping because you...**

- (a) Cannot get to sleep within 30 minutes:**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (b) Wake up in the middle of the night or early morning**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (c) Have to get up to use the bathroom**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (d) Cannot breathe comfortably**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (e) Cough or snore loudly**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (f) Feel too cold**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (g) Feel too hot**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (h) Had bad dreams**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (i) Have pain**

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

- (j) Other reason(s), please describe: \_\_\_\_\_**

How often during the past month have you had trouble sleeping because of this?

☐ not during the past month ☐ less than once/week ☐ once or twice/week ☐ 3 or more times/week

6. During the past month, how would you rate your sleep quality overall?

☐ very good    ☐ fairly good    ☐ fairly bad    ☐ very bad

7. During the past month, how often have you taken medicine (prescribed or over the counter) to help you sleep?

☐ not during the past month    ☐ less than once/week    ☐ once or twice/week    ☐ 3 or more times/week

8. During the past month, how often have you had trouble staying awake while driving, eating meals or engaging in social activity?

☐ not during the past month    ☐ less than once/week    ☐ once or twice/week    ☐ 3 or more times/week

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

☐ not a problem at all    ☐ only a very slight problem    ☐ somewhat of a problem    ☐ a very big problem

### Section 6: Epworth Sleepiness Scale

How likely are you to fall asleep or doze off in the following situations, rather than just feeling tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation.

0	=	would never doze
1	=	slight chance of dozing
2	=	moderate chance of dozing
3	=	high chance of dozing

Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g. theatre/meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____
TOTAL	_____

## **Appendix D: Sleep Diary**

---

## **SLEEP DIARY INSTRUCTIONS**

**STEP ONE:** Record the time you go to bed and the time that you get out of bed. Also record the time you that you actually went to sleep and at what time you finally wake up. This should be done for ANY and EVERY sleep period, including short naps.

Also record how many times you woke up during the sleep period, and the TOTAL amount of time you were awake for after you add each of these awakenings together.

**STEP TWO:** The second step involves rating how sleepy/awake you feel just before you go to bed and as soon as you wake up. Do this using the SLEEPINESS SCALE below. Choose the statement which best describes your state of sleepiness immediately BEFORE and AFTER the sleep period.

### **SLEEPINESS SCALE**

- 1 = Feeling active and vital. Alert and wide awake.
- 2 = Functioning at a high level but not at peak. Able to concentrate.
- 3 = Relaxed, awake, responsive, not at full alertness.
- 4 = A little foggy. Not at peak. Let down.
- 5 = Fogginess. Beginning to lose interest in remaining awake. Slowed down.
- 6 = Sleepy. Prefer to be lying down. Fighting sleep. Woozy.
- 7 = Almost in reverie. Sleep onset will be soon. Lost struggle to remain awake.

**STEP THREE:** The third step requires a subjective evaluation to be made about how well you slept. Simply select a number from the following scale, and record it in the column marked "SLEEP QUALITY":

### **HOW YOU SLEPT**

- 1 = Very Well
- 2 = Well
- 3 = Average
- 4 = Poorly
- 5 = Very Poorly

**STEP FOUR:** Finally, first thing after waking, please record how many hours of sleep it felt like you obtained. Accuracy is not important – we are more interested in your subjective estimate.



## SLEEP DIARY

[illegible]

## **Appendix E:     Consent Forms**

---

**Study 1****CONSENT FORM****Validation of Wrist-Actigraphy Technologies Against Gold-Standard Polysmnography**

**I consent to participation in this research project and agree that:**

1. I am aged 18 years or older;
2. An Information Sheet has been provided to me that I have read and understood;
3. I have had any questions I had about the project answered to my satisfaction by the Information Sheet and any further verbal explanation provided;
4. I understand that my participation or non-participation in the research project will not affect my academic standing or my employment;
5. I understand that I have the right to withdraw from the project at any time without penalty;
6. I understand the research findings will be included in the researcher's publication(s) on the project, and these publications may include articles written for conferences, journals as well as other methods of dissemination stated in the Information Sheet;
7. I understand that to preserve anonymity and maintain confidentiality of participants, no personally identifiable information will be used in any publication(s);
8. I am aware that a Plain English statement of results will be available to me on request;
9. I agree that I am providing informed consent to participate in this project.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Name (please print): \_\_\_\_\_

E-mail address: \_\_\_\_\_

I have explained the study to the participant and consider that he/she understands what is involved:

**Researcher:** \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

## Study 2

### CONSENT FORM

**Project Title: Should we go halves? The impact of split work-rest schedules on sleep and cognitive performance**

**I consent to participation in this research project and agree that:**

1. I am aged 18 years or older;
2. An Information Sheet has been provided to me that I have read and understood. Any questions I have had about the project have been answered to my satisfaction by the Information Sheet and any further verbal explanation;
3. I understand that my participation or non-participation in the research project will not affect my academic standing or my employment;
4. I understand that I have the right to withdraw from the project at any time without penalty;
5. I understand the statement concerning compensation for taking part in the study, which is contained in the information sheet.
6. I understand that to preserve anonymity and maintain confidentiality of participants, no personally identifiable information will be used in any publication(s);
7. I understand the research findings will be included in the researcher's publication(s) on the project, and these publications may include articles written for conferences, journals as well as other methods of dissemination;
8. I acknowledge that the results of the sleep study are unknown and that I may suffer a range of symptoms including excessive sleepiness and fatigue, irritability, and mild queasiness. This list of symptoms is not exhaustive;
9. I acknowledge that I have been advised that I should avoid the following activities: driving a car, riding a bike, and/or operating heavy machinery, following the completion of the study, until I have obtained at least one full night's sleep (uninterrupted for 9 hours or more).
10. I release and indemnify the University, its employees, students and agents against liability in respect of all claims, costs and expenses and for all loss, damage, injury or death to persons or property caused or contributed by me in connection with my failure to follow the after study instructions.

**Participant name** (please print): \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Contact e-mail:** \_\_\_\_\_

I have explained the study to the participant and consider that he/she understands what is involved:

**Researcher:** \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

## Study 3

### CONSENT FORM

**Project Title: Can the recovery value of daytime sleep be optimised to reduce fatigue risk for night workers in safety-critical industries?**

**I consent to participation in this research project and agree that:**

1. I am aged 18 years or older;
2. An Information Sheet has been provided to me that I have read and understood. Any questions I have had about the project have been answered to my satisfaction by the Information Sheet and any further verbal explanation;
3. I understand that my participation or non-participation in the research project will not affect my academic standing or my employment;
4. I understand that I have the right to withdraw from the project at any time without penalty;
5. I understand the statement concerning compensation for taking part in the study, which is contained in the information sheet.
6. I understand that to preserve anonymity and maintain confidentiality of participants, no personally identifiable information will be used in any publication(s);
7. I understand the research findings will be included in the researcher's publication(s) on the project, and these publications may include articles written for conferences, journals as well as other methods of dissemination;
8. I acknowledge that the results of the sleep study are unknown and that I may suffer a range of symptoms including excessive sleepiness and fatigue, irritability, and mild queasiness. This list of symptoms is not exhaustive;
9. I acknowledge that I have been advised that I should avoid the following activities: driving a car, riding a bike, and/or operating heavy machinery, following the completion of the study, until I have obtained at least one full night's sleep (uninterrupted for 9 hours or more).
10. I release and indemnify the University, its employees, students and agents against liability in respect of all claims, costs and expenses and for all loss, damage, injury or death to persons or property caused or contributed by me in connection with my failure to follow the after study instructions.

**Participant name** (please print): \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Contact e-mail:** \_\_\_\_\_

I have explained the study to the participant and consider that he/she understands what is involved:

**Researcher:** \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Kosmadopoulos, A.,** Sargent, C., Darwent, D., Zhou, X., & Roach, G. D. (2014). Alternatives to polysomnography (PSG): A validation of wrist actigraphy and a partial-PSG system. *Behavior Research Methods*, 46(4), 1032-1041.  
doi: 10.3758/s13428-013-0438-7.

# Declaration of Co-authorship and Contribution

## Research Division



## CHAPTER 3

### Full bibliographic reference

Kosmadopoulos, A., Sargent, C., Darwent, D., Zhou, X., & Roach, G. D. (2014). Alternatives to polysomnography (PSG): A validation of wrist actigraphy and a partial-PSG system. *Behavior Research Methods*, 46(4), 1032-1041. doi:10.3758/s13428-013-0438-7

### Status

Published

### Nature of Candidate's Contribution, including percentage of total

In conducting the study, I was responsible for laboratory setup, recruiting participants, ordering and restocking food, and also the collection, management and analysis of electronic data. This publication was written by me. I formed the research question, collated the literature, analysed the data and interpreted the results. (85%)

### Nature of all Co-Authors' Contributions, including percentage of total

My co-author, Professor Roach, won the funding for the study. My co-authors, Professor Roach, A/Professor Sargent, Dr Darwent and Dr Zhou critically reviewed the manuscript with questions, comments and criticism. They assisted also provided guidance in editing and preparing the manuscript for submission. (15%)

Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

I declare that the publication above meets the requirements to be included in the thesis as outlined in the Research Higher Degree Theses Policy and Procedure

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**Kosmadopoulos, A.,** Darwent, D., & Roach, G. D. (2016). Is it on? An algorithm for discerning wrist-accelerometer non-wear times from sleep/wake activity. *Chronobiology International*, 33(6), 599-603. doi: 10.3109/07420528.2016.1167720.

# Declaration of Co-authorship and Contribution

## Research Division



## CHAPTER 4

### Full bibliographic reference

Kosmadopoulos, A., Darwent, D., & Roach, G. D. (2016). Is it on? An algorithm for discerning wrist-accelerometer non-wear times from sleep/wake activity. *Chronobiology International*, 33(6), 599-603. doi:10.3109/07420528.2016.1167720

### Status

Published

### Nature of Candidate's Contribution, including percentage of total

I was responsible for executing the laboratory studies included in this chapter. For each protocol, I was responsible for the preparing and conducting the study – including laboratory setup, recruiting participants, ordering and restocking food and other consumable materials, and the collection, management and analysis of electronic data. This publication was written by me. I formed the research question, collated the literature, analysed the data and interpreted the results. (80%)

### Nature of all Co-Authors' Contributions, including percentage of total

Both of my supervisors, Professor Roach and Dr Darwent critically evaluated the manuscript with questions, comments, and criticisms. They also assisted by providing guidance in preparing and editing the manuscript. (20%)

Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

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**Kosmadopoulos, A.**, Sargent, C., Darwent, D., Zhou, X., Dawson, D. & Roach, G. D. (2014). The effects of a split sleep-wake schedule on neurobehavioral performance and predictions of performance under conditions of forced desynchrony. *Chronobiology International*, 31(10), 1209-1217. doi: 10.3109/07420528.2014.957763.

# Declaration of Co-authorship and Contribution

Research Division



## CHAPTER 5

### Full bibliographic reference

Kosmadopoulos, A., Sargent, C., Darwent, D., Zhou, X., Dawson, D., & Roach, G. D. (2014). The effects of a split sleep-wake schedule on neurobehavioral performance and predictions of performance under conditions of forced desynchrony. *Chronobiology International*, 31(10), 1209-1217. doi:10.3109/07420528.2014.957763

### Status

Published

### Nature of Candidate's Contribution, including percentage of total

I was responsible for executing the laboratory study included in this chapter. I was responsible for laboratory setup, recruiting participants, ordering and restocking food and other consumable materials, and the collection, management and analysis of electronic data. This publication was written by me. I formed the research question, collated the literature, analysed the data and interpreted the results. (80%)

### Nature of all Co-Authors' Contributions, including percentage of total

My co-authors, Professor Roach, Professor Dawson, and Dr Zhou won the funding for the study. Professor Roach and A/Professor Sargent designed the overall laboratory protocol. Each of my co-authors, Professor Dawson, Professor Roach, A/Professor Sargent, and Dr Darwent and Dr Zhou assisted by critically appraising the manuscript with questions, comments and criticisms. They also provided guidance in editing and preparing the manuscript for submission. (20%)

Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

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**Kosmadopoulos, A.**, Sargent, C., Zhou, X., Darwent, D., Matthews, R. W., Dawson, D. & Roach, G. D. (2017). The efficacy of objective and subjective predictors of driving performance during sleep restriction and circadian misalignment. *Accident Analysis & Prevention*, 99(B), 445-451. doi: 10.1016/j.aap.2015.10.014.

# Declaration of Co-authorship and Contribution

Research Division



## CHAPTER 6

### Full bibliographic reference

Kosmadopoulos, A., Sargent, C., Zhou, X., Darwent, D., Matthews, R. W., Dawson, D., & Roach, G. D. (2017). The efficacy of objective and subjective predictors of driving performance during sleep restriction and circadian misalignment. *Accident Analysis and Prevention*, 99(B), 445-451. doi:10.1016/j.aap.2015.10.014

### Status

Published

### Nature of Candidate's Contribution, including percentage of total

I was responsible for executing the laboratory study included in this chapter. I was responsible for laboratory setup, recruiting participants, ordering and restocking food and other consumable materials, and the collection, management and analysis of electronic data. This publication was written by me. I formed the research question, collated the literature, analysed the data and interpreted the results. (80%)

### Nature of all Co-Authors' Contributions, including percentage of total

My co-authors, Professor Roach, Professor Dawson, and Dr Zhou won the funding for the study. Professor Roach and A/Professor Sargent designed the overall laboratory protocol. Each of my co-authors, Professor Dawson, Professor Roach, A/Professor Sargent, Dr Darwent, and Dr Matthews critically appraised the manuscript with questions, comments, and criticisms. They also assisted by providing guidance in editing and preparing the manuscript for submission. (20%)

Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

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(Original signature of Candidate)

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<http://dx.doi.org/10.1016/j.aap.2015.10.014>

**Kosmadopoulos, A.,** Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2015). Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times? In G. A. Kennedy & C. Sargent (Eds.), *The Time of Your Life* (pp. 32-37). Melbourne, Australia: Australasian Chronobiology Society.

# Declaration of Co-authorship and Contribution

Research Division



## CHAPTER 7

### Full bibliographic reference

Kosmadopoulos, A., Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2015). Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times? In G. A. Kennedy & C. Sargent (Eds.), *The Time of Your Life* (pp. 32-37). Melbourne, Australia: Australasian Chronobiology Society.

### Status

Published

### Nature of Candidate's Contribution, including percentage of total

I was responsible for laboratory setup, recruiting participants, ordering and restocking food and other consumable materials, and the collection, management and analysis of electronic data. This publication was written by me. I formed the research question, collated the literature, analysed the data and interpreted the results. (80%)

### Nature of all Co-Authors' Contributions, including percentage of total

My co-authors, A/Professor Sargent and Dr Zhou, were granted funding for the study and developed the overall design of the laboratory protocol. Each of my supervisors, Professor Roach, A/Professor Sargent, and Dr Darwent, as well as Dr Zhou assisted by critically appraising the manuscript with questions, comments and criticisms, and also providing guidance in preparing the manuscript for submission (20%)

Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

I declare that the publication above meets the requirements to be included in the thesis as outlined in the Research Higher Degree Theses Policy and Procedure

A handwritten signature in black ink, appearing to be 'AS', written over a dotted line.

(Original signature of Candidate)

04 / 05 / 2017

Date

## Chapter 6

# Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times?

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**Aims:** Night workers have some flexibility between night shifts to temporally place their sleep episodes in accordance with their preferences. Night workers who are able to obtain sufficient sleep at times of their choosing may perform better and be more alert on shift than those who are not able to sleep at their preferred times due to societal obligations or constraints. The aim of this study was to determine whether neurobehavioural performance and alertness on a 12-h night shift was influenced by the alignment of preferred sleep schedules with actual sleep times. **Methods:** Twelve healthy males ( $M \pm SD$ ; aged  $22.9 \pm 5.2$  years) participated in a repeated-measures laboratory study with three counterbalanced sleep conditions. Conditions differed only in the timing of 7-h sleep opportunities between two consecutive night shifts (1800-to-0600h). Sleep opportunities were either (i) immediate, 0700h-1400h; (ii) delayed, 1000h-1700h; or (iii) split, 0700h-1030h and 1330h-1700h. Psychomotor vigilance tasks were conducted to assess response time performance and visual analogue scales were employed to rate alertness. At the end of the study, participants ranked the sleep conditions in order of preference. **Results:** Repeated measures ANOVA revealed no main effects of ranking (1<sup>st</sup> vs. 2<sup>nd</sup> vs. 3<sup>rd</sup> preference) on response time [ $F(2,20) = .03$ ,  $p = .97$ ] or alertness rating [ $F(2,22) = .11$ ,  $p = .90$ ]. Similarly, there were no significant interactions between scheduled sleep time (immediate vs. delayed vs. split sleep) and the preferred sleep time for response time [ $F(4,16) = 1.96$ ,  $p = .15$ ] or alertness [ $F(4,18) = .42$ ,  $p = .77$ ]. **Discussion:** Results from this study indicate that working at night following a preferred sleep time is no more beneficial to performance and alertness than following less preferred sleep times. Furthermore, performance and alertness following all sleep conditions were not affected by participants' first preference. These findings suggest that if night workers are not able to obtain their daytime sleep episodes at their preferred times, performance on 12-h night shifts may not be adversely affected, at least under laboratory conditions.

**Citation:** Kosmadopoulos A, Zhou X, Roach GD, Darwent D, Sargent C (2015). Is performance and alertness on a night shift influenced by the alignment of preferred sleep times with actual sleep times? In: Kennedy G, Sargent C (Eds). *The Time of Your Life*. Australasian Chronobiology Society, Melbourne, Australia, pp. 32-37.

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In Australia, approximately 16% of employees are shift workers, and 7% usually work at night [1]. Shift work, and

night work in particular, is disruptive because it forces a mismatch between the sleep/wake system and the internal body clock. Night

workers must sleep during the daytime when their body clocks are promoting wake and they must stay awake to work at night when their body clocks are promoting sleep. Combined, the resulting poor sleep quality, longer durations of wake, and increased sleepiness, mean that there is an increased likelihood of making errors, having an accident, or being injured on the night shift [4].

Numerous studies have investigated methods of promoting alertness during night shifts, through the use of caffeine, scheduled naps, bright light, and melatonin [2, 5, 7, 9]. However, there is also research to suggest that the timing of sleep during breaks between consecutive night shifts may also have an effect on night-time neurobehavioural performance and alertness [8]. In spite of this, night workers commonly obtain their daytime sleeps at times broadly covered by three main approaches. For example, some choose to (i) have a single sleep in the morning immediately after work, (ii) others obtain a single sleep in the afternoon/evening prior to work, and (iii) others obtain a nap in the morning and another nap sometime in the evening. The immediate sleep allows recovery from night work to begin as soon as possible, while a delayed sleep reduces the accumulation of prior wake before starting work. A split sleep achieves some of the advantages of both of these, though it may be more difficult to implement.

Taking these factors into consideration, night workers have some flexibility to temporally place their sleep episodes in accordance with their own preferences, with an intention to maintaining performance and alertness on shift. However, due to personal circumstances and having to fulfil social obligations, night workers are not always able to obtain sleep when they would prefer. This may be a concern, as Smith et al. [10] found that shiftwork-specific internality (i.e., the

degree to which individuals believe they can control factors associated with shiftwork, including sleep quality and work performance) can explain 25-31% of the variance in fatigue, and 21% of the variance on night shift drowsiness. It may be the case that night workers who are not able to sleep at their preferred times, possibly having low shiftwork-specific internality, may perform worse on shift than those who are able to obtain sufficient sleep at times of their choosing.

The aim of this study, therefore, was to determine whether neurobehavioural performance and alertness on a 12-h night shift are (i) affected by the order in which sleep times are ranked by preference, or (ii) influenced by the alignment of preferred sleep times with actual sleep times.

## Methods

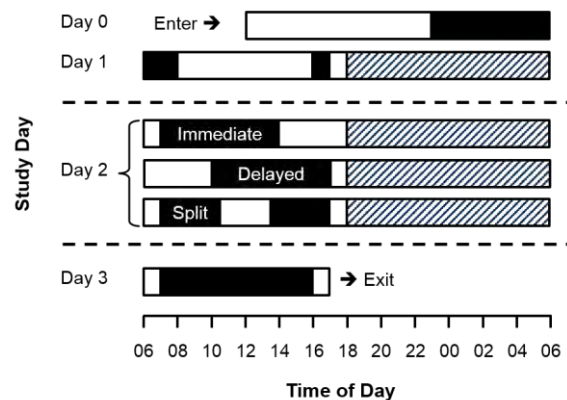
**Participants** Participants were 12 healthy males with a mean ( $\pm$  SD) age of 22.9 ( $\pm$  5.2) years and body mass index of 22.9 ( $\pm$  1.4) kg/m<sup>2</sup> who successfully passed a screening process involving a general health questionnaire, an interview, and a week of wearing wrist activity monitors to measure sleep patterns. Participants did not have any physical or medical disorders, were non-smokers, had not undertaken transmeridian travel or shiftwork in the previous three months, and did not report excessive consumption of caffeine or alcohol. For the week immediately prior to admission, participants were required to maintain consistent night-time sleep schedules of ~8 hours initiated between 2200h–0000h, verified by a week of wrist actigraphy and self-report sleep diaries. Ethical approval for the study was granted by the Central Queensland University Human Research Ethics Committee using guidelines established by the National Health and Medical Research Council of Australia.

**Setting** The protocol was conducted in a sound-attenuated, windowless sleep laboratory at the Appleton Institute, Central Queensland University, Adelaide. The laboratory was configured to accommodate six participants at a time, each with his own bedroom, living room, and bathroom facilities. Participants had access to the time, but were isolated from external environmental cues and were not permitted to leave the laboratory during the protocol. Room temperature was maintained between 21–23°C. During wake periods, ambient light was maintained at normal indoor levels (~300 lux). Lights were extinguished (i.e., <0.03 lux) during sleep periods.

**Protocol** The study employed a repeated-measures design with three randomised, completely counter-balanced, conditions. Participants attended the laboratory on three separate occasions, each covering a four day period, exactly one week apart. Each visit consisted of an adaptation night, two 12-h simulated night shifts separated by a 7-h sleep opportunity, followed by one daytime recovery sleep (Fig. 1). The three conditions differed only in the timing of the 7-h sleep opportunity scheduled between the two night shifts.

The first evening and subsequent morning were used to train participants on the performance tasks. Participants were given 9.5h in bed (2230–0800h) on the first night to familiarise them with the equipment used to monitor sleep and to eliminate any prior sleep debt. On the following afternoon, participants were scheduled a 1-h nap (1600–1700h) to prepare for the first night shift. After completing their first simulated night shift (1800–0600h), participants were provided a 7-h sleep opportunity. The timing of the sleep opportunity reflected one of three common sleep patterns exhibited by shiftworkers between night shifts – i.e., an immediate sleep (0700–1400h), a delayed sleep (1000–1700h), or a split sleep (0700–1030h and 1330–

1700h). These daytime sleeps were followed by a second night shift (1800–0600h) and a 9-hour recovery sleep (0700–1600h) before participants exited the laboratory at 1700h.



**Figure 1.** Protocol diagram. Y-axis represents days in the protocol, and x-axis represents time of day. Black rectangles indicate time in bed (TIB), and shaded rectangles indicate simulated night shifts. The temporal placement of TIB on Day 2 was dependent on whether participants were undergoing the “Immediate”, “Delayed”, or “Split” sleep condition.

During the simulated night shifts, participants completed a 30-minute test battery every two hours (i.e., 6 in total), with the first test battery beginning 30 minutes after the start of the night shift. These test batteries comprised a number of tasks, including measures of neurobehavioural performance and alertness. Participants were kept free from distraction during test batteries by being seated alone in their living rooms in front of a blank wall. Participants had free time between testing bouts during which they could read, listen to music, draw or watch DVDs, but not sleep, exercise or leave their living rooms. Research staff monitored the participants’ compliance with these instructions in person and via a closed-circuit television system. After having completed all three conditions, participants were asked to respond to the question, “If you were working two night shifts in a row,

which type of daytime sleep strategy would you most likely follow?” by ranking them 1 to 3 in order of preference.

**Neurobehavioural Performance and Self-Rated Alertness** Neurobehavioural performance was assessed with a 10-min psychomotor vigilance task (PVT). The PVT, performed on a portable electronic hand-held unit (PVT-192, Ambulatory Monitoring Inc., Ardsley, New York, USA), requires participants to respond to a visual stimulus appearing on a display at random 2-10 second intervals as quickly as possible with a button press. The dependent measure derived from the PVT was mean reciprocal response time (PVT RRT;  $1/\text{ms} \times 1000$ ).

Subjective alertness was assessed using a visual analogue scale (VAS Alert) [3]. This scale required participants to rate their alertness by placing a vertical mark on a 100-mm horizontal line anchored with the statements “struggling to remain awake” on the left and “extremely alert and wide awake” on the right. The dependent variable was the participant’s alertness rating, measured in millimetres from left to right.

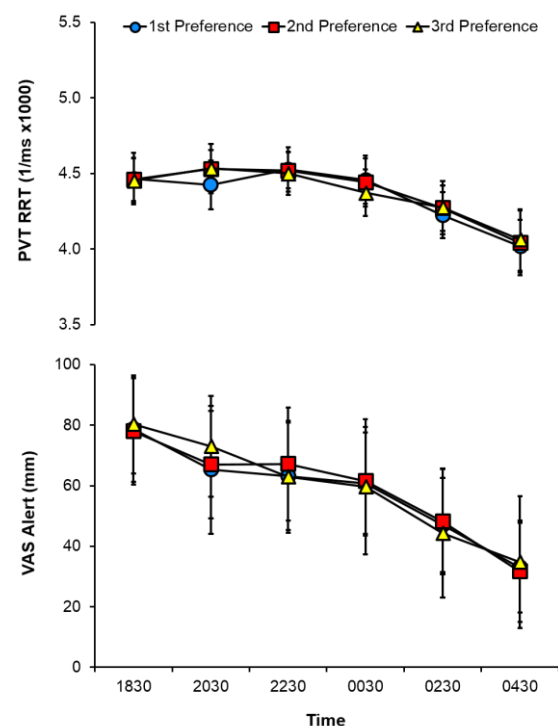
**Sleep** was monitored with standard polysomnography (PSG), using the Grael PSG/EEG System (Compumedics, Melbourne, Australia) and a montage of Grass<sup>TM</sup> gold-cup electrode leads (Astro-Med, Inc., West Warwick, RI). The montage included two EEG channels (C3-M2, C4-M1), right and left EOG, and three channels of chin EMG. Sleep stages were scored in 30-s epochs by a trained technician following standard criteria [6].

**Statistical Analyses** The effect of daytime sleep preferences on night-time performance was examined using repeated measures ANOVAs. For the dependent variables related to neurobehavioural performance (PVT RRT) and subjective alertness (VAS Alert), separate ANOVAs were conducted comprising two within-subject factors – ranking of daytime

sleep conditions by preference (first, second, third) and time of test session. Another set of ANOVAs was subsequently conducted for the same dependent variables to determine whether there was an interaction between daytime sleep condition (immediate, delayed, split) and most preferred condition.

## Results

The immediate sleep was ranked first by most participants (50%), with the delayed and split sleeps ranked first by 33% and 17% of the participants, respectively. The split sleep was ranked last by 58%, followed by the delayed sleep (33%) and the immediate sleep (8%).



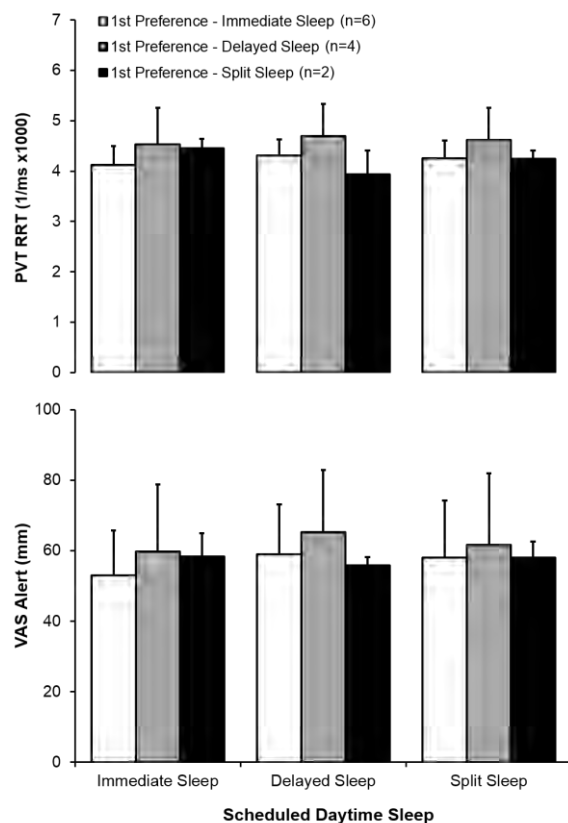
**Figure 2.** Mean RRT and VAS Alert ratings across second simulated night shift by ranking of daytime sleep conditions in order of preference.

The first set of repeated measures ANOVAs revealed there were no main effects of rank order (1<sup>st</sup> vs. 2<sup>nd</sup> vs. 3<sup>rd</sup>) on PVT RRT [ $F(2,20)=.03$ ,  $p=.97$ ] or VAS Alert ratings [ $F(2,22)=.11$ ,  $p=.90$ ]. There were main effects of time such that PVT RRT [ $F(5,50)=18.02$ ,  $p<.001$ ] and VAS Alert ratings [ $F(5,55)=44.5$ ,



$p < .001$ ] progressively declined across the night (Figure 2). However, there were no 2-way interaction effects on PVT RRT [ $F(10,100) = .43$ ,  $p = .75$ ] or VAS Alert rating [ $F(10,110) = .59$ ,  $p = .65$ ].

The second set of analyses revealed no significant interaction between scheduled daytime sleep condition (immediate vs. delayed vs. split sleep) and the preferred sleep condition on either PVT RRT [ $F(4,16) = 1.96$ ,  $p = .15$ ] or VAS Alert ratings [ $F(4,18) = .42$ ,  $p = .77$ ] (Figure 3).



**Figure 3.** Mean RRT and VAS Alert ratings following Immediate, Delayed, and Split conditions by most preferred condition.

## Discussion

The importance of sleep for minimising fatigue-related risks is well-established and some evidence exists to support delayed daytime sleeps for night work [8]. However, this research has limited practical effect in

workforces where employers are constrained in their ability to instruct employees how to behave after outside work. Given that night workers can generally sleep during their breaks at times of their choosing, an aim of this study was to evaluate whether performance and alertness are influenced by the order in which given pre-shift sleep times are preferred. No main effect was found for preference ranking, indicating that participants did not perform significantly better or feel more alert following their most preferred daytime sleep times compared to their least preferred sleep times. Performance and alertness declined as a function of time on shift; however, the absence of an interaction indicated that preference ranking did not have a mediating effect on this decline.

The second aim of this study was to determine whether night-time performance and alertness following a daytime sleep obtained at a given time is better for those who most prefer its timing than for those who do not. As there was no interaction between scheduled sleep times and participants' first preferences, it appears that neurobehavioural performance and alertness are not dependent on the alignment of preferred sleep schedules with actual sleep times. In practice, these findings suggest that neurobehavioural performance and alertness during 12-h night shifts may not be adversely affected if night workers are not able to obtain their daytime sleep episodes at their preferred times.

It is possible the absence of an effect of preferred sleep times on performance and alertness may be due to participants not feeling strongly about the order in which they indicated their preferences. Given that the start and end times for the immediate and delayed sleeps differed by only 3 hours, the 12-h period between the consecutive 12-h night shifts may not have been long enough to substantially differentiate the 7-h sleep



opportunities. This suggests that although performance and alertness may not be affected by daytime sleep preferences for 12-h night shifts, these findings may not apply to 8-h night shifts with longer 16-h breaks. Indeed, breaks that allow workers greater control over their schedule, including flexibility in the choice of sleep times, could see sleep preferences playing a larger role in results.

There are a few limitations to this study. The first is that the protocol simulated only two consecutive night shifts. It is possible that with more consecutive night shifts preferences for any particular sleep time would strengthen and have more of an influence on performance. Another limitation is that preferences for sleep times were assessed by asking participants to rank three broad, pre-determined approaches, rather than allowing participants to choose when they slept. The final main limitation to this study, in terms of generalizability, was that it was conducted in laboratory conditions that facilitated undisturbed sleep. Future research could build on the findings of this study by evaluating performance during 8-h shifts across multiple consecutive nights.

In conclusion, the findings of this study indicate that neurobehavioural performance and alertness during 12-h night shifts may not be associated with preferences regarding the timing of daytime sleeps. Therefore, they suggest that performance on 12-h night shifts may not be adversely affected if night workers are not able to obtain their daytime sleep episodes at their preferred time. It is not clear, however, that these findings would apply to shift lengths of shorter duration.

### Acknowledgements

This study was financially supported by a CQUniversity Merit Grant awarded to Dr Sargent and Dr Zhou.

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**Kosmadopoulos, A.,** Zhou, X., Roach, G. D., Darwent, D., & Sargent, C. (2016). No first night shift effect observed following a nocturnal main sleep and a prophylactic 1-h afternoon nap. *Chronobiology International*, 33(6), 716-720.  
doi: 10.3109/07420528.2016.1167727.

# Declaration of Co-authorship and Contribution

Research Division



## CHAPTER 8

### Full bibliographic reference

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Has this paper been submitted for an award by another research degree candidate (Co-Author), either at CQUniversity or elsewhere? (if yes, give full details)

No.

### Candidate's Declaration

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