

# The Case for a Chronobiological Approach to Neonatal Care

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## Description

Chronobiology is the study of biological rhythms that examine cyclic, or periodic, phenomena in living organisms and their adaptation to solar and lunar related rhythms [1]. Chronobiological studies can include comparative anatomy, physiology, genetics, molecular biology, behavior, development, reproduction and evolution. Chronobiology is an interdisciplinary field of investigation and includes sleep medicine, endocrinology, psychiatry, sports medicine as well as space and travel medicine. Variations in the timing and length of biological activities is apparent with many essential biological processes including, but not limited to, eating, sleeping, mating, hibernating, migration and cellular regeneration.

The most central rhythm in chronobiology is the circadian rhythm: a roughly 24-hour cycle that is demonstrated by rhythmic physiological processes approximating a day [2]. It is regulated by circadian clocks which are endogenous, and characterised by a molecular response, such as gene oscillations, to light. Apart from sleep and endocrine cycles in humans, most is known about blood pressure rhythms in humans. Recent work has implicated the circadian clock genes in the regulation of processes in the heart, kidney, vasculature, and the metabolic organs, which are all critical in the regulation of blood pressure [3]. There is some evidence that suggests that disruption to circadian rhythms during pregnancy can increase the risk of hypertensive pregnancy complications.

It is important to consider that time of day does not only affect patients, but also substantially influences human factors relating to the surgeon, anaesthetist, and other healthcare workers caring for patients. Providing round-the-clock clinical care poses unique physiological challenges for healthcare workers that can impact patient outcomes. During a night shift, staff must perform tasks during the circadian phase when they are hard-wired for sleeping. This period of time coincides with the lowest levels of alertness, cognitive function, psychomotor coordination, and mood, which reach a nadir between 3 and 5 AM.<sup>16</sup> Performance is impaired despite increased effort, and the impairment is greater than the individual's subjective awareness of sleepiness, further increasing the risk of errors and harm. After a night shift, the rest period is shifted to the circadian phase least conducive to sleeping, leading to sleep loss and the many documented adverse effects of fatigue.<sup>17</sup> Reducing the length of shifts and overall weekly number of hours worked by trainee critical care doctors increased their total sleep hours and dramatically reduced the number of

attentional failures during night duties.<sup>18</sup> Even after a single night shift, when compared with a night of sleep, trainee anaesthetists demonstrate impaired non-technical skills in a simulated crisis management scenario.<sup>19</sup> In the future, it would perhaps be beneficial to include recognition of fatigue into the training programmes for healthcare professionals.<sup>20</sup> Perhaps the ultimate clock desynchroniser is space travel, during which time there is complete loss of a natural 24-h day. For those astronauts orbiting the earth in the international space station, a sunrise was experienced every 90 min. Studies from space shuttle missions concluded that astronauts experience circadian rhythm disturbances, diminished sleep duration, decrements in neurobehavioural performance, and alterations in rapid eye movement sleep homeostasis.<sup>21</sup> Simulation work looking into the effect of 520 days of isolation and loss of normal external cues that would be experienced in a mission to Mars suggested similar circadian disturbances.<sup>(2)</sup>

## Polysomnography

Time of day is a critical factor for most biological functions, but concepts from the field of chronobiology have yet to be fully translated to clinical practice. Circadian rhythms, generated internally and synchronised to the external environment, promote function and support survival in almost every living species. Fetal circadian rhythms can be observed in utero from 30 weeks gestation, coupled to the maternal rhythm, but synchronise to the external environment only after birth. Important cues for synchronisation include the light/dark cycle, the timing of feeding, and exposure to melatonin in breast milk. Disruption to these cues may occur during admission to the neonatal intensive care unit. This can impair the development of circadian rhythms, and influence survival and function in the neonatal period, with a potential to impact health and well-being throughout adult life. Here we outline the rationale and evidence to support a chronobiological approach to neonatal care [4].

Sleep disturbances are the main health complaints from personnel deployed in Antarctica. The current paper presents a systematic review of research findings on sleep disturbances in Antarctica. The available sources were divided in three categories: results based on questionnaire surveys or sleep logs, studies using actigraphy, and data from polysomnography results. Other areas relevant to the issue were also examined. These included chronobiology, since the changes in photoperiod have been known to affect circadian rhythms, mood

disturbances, exercise, sleep and hypoxia, countermeasure investigations in Antarctica, and other locations lacking a normal photoperiod. Based on the combination of our reviewed sources and data outside the field of sleep studies, or from other geographical locations, we defined hypotheses to be confirmed or infirmed, which allowed to summarize a research agenda. Despite the scarcity of sleep research on the Antarctic continent, the present review pinpointed some consistent changes in sleep during the Antarctic winter, the common denominators being a circadian phase delay, poor subjective sleep quality, an increased sleep fragmentation, as well as a decrease in slow wave sleep. Similar changes, albeit less pronounced, were observed during summer [5]. Additional multidisciplinary research is needed to elucidate the mechanisms behind these changes in sleep architecture, and to investigate interventions to improve the sleep quality of the men and women deployed in the Antarctic. Entrainment of circadian rhythms (CR) to the light dark cycle has been well described under controlled, experimental conditions. However, studies in rodents have reported that rhythms in the laboratory are not always reproduced under field conditions. The aim of this study was to characterise the CR of sheep maintained under conditions of standard UK farm animal husbandry and to investigate the effects of environmental challenges presented by season, weaning and changes in housing on CR. Male sheep (n=9) were kept at pasture, or group housed in barns, under natural photoperiod for one year. CR in locomotor activity were monitored using accelerometry, and 24 h patterns in plasma cortisol and melatonin were measured every 4 h by ELISA. CR was measured before and after weaning, in summer and winter, and at pasture and by barn housing. Cosinor analysis revealed high amplitude, diurnal

rhythms in locomotor activity that were disrupted by weaning and by barn housing. Rhythms in winter showed an interrupted night time activity pattern, but only when the sheep were kept at pasture. Cortisol and melatonin secretion followed typical circadian patterns in winter and summer. The CR of the sheep under the field conditions of this study were strikingly robust under basal conditions, but easily disrupted by environmental challenges. Interrupted patterns of activity during the long nights of wintertime, not previously reported for sheep kept in experimental conditions were recorded. Based on these findings, we propose that animals require exposure to more complex environments than the laboratory in order to exhibit their true circadian phenotype.

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