Project Details	
Project Code	MRCPHS25Br Richmond
Title	Exploring the interplay and mechanisms between sleep, circadian rhythms and physical activity in relation to physical and mental health
Research Theme	Population Health Sciences
Summary	Understanding the interplay between physical activity and sleep is important for improving physical and mental health. A proposed mechanism linking physical activity with improved sleep is through regulation of circadian (24-hour) rhythms in the body. This project will investigate the relationship between physical activity and sleep, and the underlying biological pathways, using both population and experimental research methods.
Description	**Background** Physical activity and sleep are important for both physical and mental health, and therefore understanding the interplay between these behaviours is imperative for reducing risk of disease in the population. In humans, a research suggests that physical activity is beneficial for sleep [1], but the magnitude of the effects varies depending on the activity exposure (acute vs regular, anaerobic vs aerobic, timing of activity) and the type of sleep outcome (sleep timing, quality and quantity). A proposed mechanism linking physical activity with improved sleep is via regulation of circadian (24-hour) rhythms, whereby scheduled exercise may act as a 'zeitgeber' or cue in the regulation of the body clock. Circadian (24-hour) rhythms are largely controlled by molecular clock cells in the brain's suprachiasmatic nuclei (SCN). Time of day effects of daily scheduled voluntary exercise (SVE) have been found to influence behavioural rhythms and SCN molecular and neuronal activities in mice. The Piggins lab have shown that in mice with abnormal circadian timing (Vipr2-/-), timed daily access to SVE stabilises behavioural rhythms [2]. However, this is largely without causing large scale alterations to the SCN transcriptome [3]. This highlights the need to further explore other brain structures and peripheral oscillators, as well as other molecular mechanisms underpinning the effects of physical exercise on the circadian system. **Objectives** As part of this interdisciplinary PhD, the student will investigate the inter-relationships between physical activity and circadian/sleep measures, in order to better understand how they interact to influence physical and mental health. This will be done using both epidemiological (observational and genetic) and experimental (in-vivo and ex-vivo biology) approaches. For the epidemiological aspects of the study, data from two European biobanks (UK Biobank, n~500,000 and the HUNT study, n~125,000) will be used. These studies have obtained self-reported and objective measures of physical activity and sleep, the latter being derived from accelerometers worn by ~90,000 participants in UK Biobank and ~30,000 participants in HUNT. Variables to be assessed will include: intensity, duration, type and timing of physical activity; measures of sleep timing, sleep duration and insomnia; as well as measures of mental and physical health from direct assessment and electronic health records.

	Furthermore, recent genome-wide association studies have identified genetic variants robustly associated with both self-reported and device-measured physical activity [4-6] and sleep [7-9]. These variants can be used in a Mendelian randomization (MR) approach to establish directionality between the physical activity and sleep measures and to estimate causal effects. For the experimental study, the Piggins lab have existing data on scheduled exercise and feeding/drinking rhythms in normal and mutant mice which could be used to develop a model of interactions between these. Another data set has monitored body weight among mice exposed to different light-dark and schedule exercise conditions. Finally, ex-vivo work could be carried out to investigate molecular pathways underlying the effects of SVE on circadian regulation by investigating gene expression in different brain structures and tissues in mouse models. Lab findings will be followed up in the human epidemiological studies and triangulated to better establish the interplay and mechanisms between sleep, circadian rhythms and physical activity. The student will develop ownership of the project by deciding on the optimal split between wet and dry lab research approaches as well as the specific data sets and research questions. Further, the student will decide upon the context in which to evaluate the interplay between sleep and physical activity traits, in terms of the physical and/or mental health trait(s) to be investigated. 1. M. A. Kredlow, et al. (2015). J Behav Med 38(3): 427-49. 2. A. T. L. Hughes, et al. (2021). Commun Biol 4(1): 761. 3. T. Hitrec, et al. (2023). iScience 26(2): 106002. 4. A. Doherty, et al. (2018). Nat Commun 9(1): 5257. 5. Y. C. Klimentidis, et al. (2018). Int J Obes (Lond) 42(6): 1161-76. 6. Y. J. van de Vegte, et al. (2020). Nat Commun 11(1): 1770. 7. H. S. Dashti, et al. (2019). Nat Commun 10(1): 1100. 8. S. E. Jones, et al. (2019). Nat Commun 10(1): 1585. 9. K. Watanabe, et al. (2022). Nat Genet 54(8): 1125-32.
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