Chrono-nutrition and Chrono-pharmacology: Investigating the Impact of Intermittent Fasting and Pharmacological Treatments on Extra-SCN Brain Oscillators for Obesity Management

Supervisory team:
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Project description: Life on Earth is subordinate to periodic alterations in the environment, with most notable changes seen from day to night. To adapt to these cyclic changes, living organisms evolved endogenous 24h timekeeping mechanisms named circadian clocks. In mammals, the suprachiasmatic nuclei (SCN) are conceived as the primary clock, but rhythmic clock gene expression occurs in extra-SCN brain structures and many peripheral tissues, indicating that rhythmic control of homeostasis is devolved to these local clocks. However, the regulation of these rhythms by environmental cues and lifestyle has not been fully understood.

Obesity stands as a formidable public health burden, with about a quarter of the UK adults living with obesity and comorbidities. These include an increased risk of chronic conditions such as diabetes, cardiovascular diseases, and certain cancers, as well as negative impact on mental health. Tackling obesity demands a comprehensive approach, involving public health initiatives, education, and policy changes to promote healthier lifestyles. Recent advances in circadian neuroscience highlight the importance of food and feeding time as a cue synchronising our body clocks. Additionally, restricting food to a narrow window during the day (e.g., intermittent fasting) proves beneficial for general health and well-being, including management of weight, cardiovascular health, and diabetes.

Various pharmacotherapeutic agents, including glucagon-like peptide-1 receptor (GLP-1R) agonists have been investigated for their efficacy in weight reduction. However, challenges persist in terms of long-term sustainability, side-effect profiles, and patient adherence.

This project aims to investigate the effects of intermittent fasting and pharmacological treatments of obesity (e.g., GLP-1R antagonists) on the timekeeping properties extra-SCN oscillators in the mouse brain. It also aims to establish best time of day for obesity drug treatment and potential influence of meal timing on their effectiveness. The student will utilise cutting edge experimental techniques in circadian neuroscience including:

(1) fluorescent in situ hybridisation and confocal microscopy to investigate molecular rhythms in vivo (e.g., clock gene expression);
(2) real-time monitoring of clock gene expression ex vivo using PERIOD2::LUCIFERASE reporter mice;
(3) electrophysiological recordings ex vivo on multi-electrode arrays over 24h;
(4) automated monitoring of feeding, drinking, and wheel running in home cages;
(5) range of molecular methods used for quantitative assessment of gene expression.

This project provides an opportunity to learn basic coding (MatLab, Python, R) and statistical methods (MatLab, GraphPad Prism) used in circadian neuroscience. This set of skills is highly transferable and valuable for further career development in both academic and industrial setup.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.