Investigating the relationship between glucose homeostasis and torpor in mice

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Background

Blood glucose levels are tightly regulated within a narrow range to avoid hypoglycaemia and hyperglycaemia. Hunger is associated with a reduction in blood glucose and distinct changes in circulating hormones, which trigger arousal and food-seeking behaviour. An alternative strategy that many species employ when facing a limited food supply is energy conservation, which can be achieved by entering torpor. Torpor is characterised by a profound attenuation of physiological functions, wherein body temperature can drop to within a few degrees of ambient temperature [1-3]. Mice are a facultative heterothermic species that readily display torpor bouts in response to food deprivation [4-7], with the propensity for torpor influenced by metabolic and endocrine status, as well as ambient temperature. Fasting-induced torpor in mice is a profound metabolic challenge [6, 8], yet the physiological mechanisms coordinating metabolic flexibility during torpor, and the metabolic costs associated with torpor, are unclear.

Aim

To investigate the link between glucose homeostasis and fasting-induced torpor in mice.

Description of work

Mice routinely employ torpor in response to food deprivation [4, 6]. To define behavioural state, mice will be implanted with EEG and EMG electrodes (established in Vyazovskiy lab). In parallel, we will establish continuous glucose monitoring (CGM) using radiotelemetry modules validated for use in mice. The Peirson lab has expertise with DSI telemetry [9], and the Cantley lab has expertise in assessing glucose homeostasis [10]. To induce torpor, mice will undergo an established fasting protocol. Using remote telemetry, we will continuously record EEG, EMG, movement, temperature and blood glucose preceding, during and following torpor: this has not previously been possible with conventional glucose sampling techniques. Glucose homeostasis and metabolic profiles will be assessed in mice that have undergone torpor, relative to controls. Finally, we will experimentally manipulate blood glucose to investigate the metabolic control of torpor.

Outcome

This study will generate new insights into the metabolic control of torpor and central regulation of energy homeostasis, which may reveal novel mechanisms, targets or strategies that could be translated to humans to control energy homeostasis for therapeutic benefit.

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