Neurometabolism in focus

A better understanding of how the brain controls whole-body energy use and storage, as well as eating behaviour, will pave the way for improving therapeutics to fight metabolic diseases. This Focus presents a collection of Reviews, Perspectives and research Articles that integrate the most recent evidence on how the brain controls key aspects of whole-body metabolism.

Whole-body energy homeostasis and weight maintenance are tightly regulated by constant communications between the central nervous system and the peripheral tissues. This complex inter-organ and intercellular dialogue involves the modulation of metabolic processes, such as the storage and use of nutrients, as well as the controlling of eating behaviour, including the neural signals that lead to the opposing sensations of hunger and satiety. In this issue of *Nature Metabolism*, we present a collection of Reviews and Perspectives that integrate the most recent advances in our understanding of how the brain controls energy homeostasis, both from a neurocircuit perspective that leads to the initiation or cessation of eating and from a more granular view of how different cell types in the brain control the use of nutrients and synaptic transmission. We feature these Reviews in a web collection that also includes a selection of research Articles from across the *Nature* Portfolio, which shed light on how the brain controls key aspects of organismal and cellular metabolism.

As a framework for understanding eating behaviour, the Review by Alcantara and colleagues distinguishes between three acts of appetite, dissecting the neural circuits that are involved in food procurement, food consumption and meal termination. While this work mostly focuses on the hypothalamic nuclei governing such behaviours, the Review by Cheng and colleagues instead offers a distinct outlook, where the hindbrain takes centre stage. Here, the authors discuss the circuits within discrete regions of the hindbrain such as the area postrema and the nucleus of the solitary tract, which are relevant for homeostatic feeding and the control of body weight. These two pieces emphasize the importance of understanding how different areas of the brain cooperate to fine-tune different aspects related to feeding behaviour.

Accumulating evidence shows that communication between different cell types in the brain is essential for brain function. As an example of how signals between the brain and peripheral tissues are integrated, the Review by Nampoothiri and colleagues presents glial cells as key players in the regulation of energy homeostasis. Their support to neuronal cells is extended by their modulation of peripheral signals in specific brain regions, notably those devoid of a blood–brain barrier.

Another important aspect to ensure a seamless communication between different cell populations, both within the brain and between the brain and the periphery, is the existence of a complex network of chemical messengers that relay signals from one cell to another, either locally or between different tissues. This concept is nicely illustrated in the piece authored by Busquets-García, Bolaños and Marsicano (which is part of our Metabolic Messenger series), where they present endocannabinoids as an important family of biochemical messengers that participate in a plethora of processes, from coordinating feeding behaviour and body weight to modulating cognitive functions, in part by influencing intracellular metabolism.

In this regard, how intracellular metabolism shapes cellular functions in the brain is an exciting and important research topic. Pekkurnaz and Wang offer an overview of how mitochondrial homeostasis and diversity contribute to meeting cellular demands, diving deeper into the particularities of neuronal metabolism and how mitochondria influence neuronal physiology and survival.

In summary, the complexity of metabolic networks in which the brain is involved, from inter-organ communication to intracellular metabolic fluxes, are instrumental to ensure whole-body energy homeostasis. While this collection furthers our understanding on how the brain controls cellular and organismal energy use, it also highlights the need to uncover new biology to help us deconstruct how central circuits can be influenced by local and systemic metabolism, and how they are impacted in disease states.

With the increasing prevalence of obesity across the globe and the difficulties in maintaining weight loss as a result of lifestyle modifications, the need for more effective and better-targeted therapeutics continues to be a priority for treating and caring for people seeking to lose weight. In order to achieve this goal, our understanding of the central mechanisms governing food consumption and energy expenditure has never been more relevant. Moreover, such research has also evidenced the hardwired circuits that lead us to conserve energy rather than spend it, making it an almost herculean task to lose weight, especially when it has been accumulated over the years. By advancing our understanding of this brain-to-periphery crosstalk, both at the neural and behavioural levels, we will surely be in a better position to tackle the growing rate of metabolic diseases that concern us all. At *Nature Metabolism*, we look forward to the new advances in the field of neurometabolism that will surely contribute to exciting fundamental discoveries in both basic and therapeutic research. ❐

Published online: 25 July 2022
https://doi.org/10.1038/s42255-022-00612-x