

59

Insulin regulates POMC neuronal plasticity to control glucose metabolism

Garron T. Dodd^{1,*}, Natalie J. Michael¹, Robert S. Lee-Young¹, Salvatore P. Mangiafico², Jack T. Pryor¹, Astrid C. Munder¹, Stephanie E. Simonds³, Jens C. Brüning⁴, Zhong-Yin Zhang⁵, Michael A. Cowley³, Sofianos Andrikopoulos², Tamas L. Hovarth⁶, David Spanswick³, Tony Tiganis¹

¹ *Metabolic Disease and Obesity Program, Department of Biochemistry and Molecular Biology, Biomedicine Discovery Institute, Monash University, Clayton, VIC, Australia*

² *Department of Medicine (Austin Hospital), The University of Melbourne, Melbourne, VIC, Australia*

³ *Department of Physiology, Biomedicine Discovery Institute, Monash University, Melbourne, VIC, Australia*

⁴ *Max Plank Institute for Metabolism Research, Cologne, Germany*

⁵ *Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN, USA*

⁶ *Program in Integrative Cell Signaling and Neurobiology of Metabolism, Yale University School of Medicine, New Haven, CT, USA*

Insulin acts on peripheral tissues including liver, muscle and adipose tissue to directly control glucose metabolism, while also acting in the brain to concordantly regulate nutrient fluxes, feeding behaviour and energy homeostasis. Although our understanding of the neural circuitry controlling feeding behaviour and energy expenditure has grown considerably in the last few years, the neural processes by which insulin elicits its effects on glucose metabolism are less clear.

Here we define heterogeneous populations of hypothalamic pro-opiomelanocortin (POMC) neurons that are activated or inhibited by insulin and thereby repress or inhibit hepatic glucose production (HGP). The proportion of POMC neurons activated by insulin was dependent on the regulation of insulin receptor signalling by the phosphatase TCPTP, which is increased by fasting, degraded after feeding and elevated in diet-induced obesity.

TCPTP-deficiency in POMC neurons enhanced neuronal insulin signalling and the proportion of POMC neurons activated by insulin to repress HGP. Elevated TCPTP in POMC neurons in diet-induced obesity and/or after fasting repressed neuronal insulin signalling, the activation of POMC neurons by insulin and the insulin-induced POMC-mediated repression of HGP. Our findings define a molecular mechanism for integrating POMC neural plasticity with feeding to control glucose metabolism.

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60

Dose-responsive benefits of weight loss

Zoltan Pataky

University Hospitals of Geneva, Genève, Genève, Switzerland

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61

Effects of lifestyle changes on non-alcoholic fatty liver disease

Kirsi Pietiläinen

University of Helsinki, Helsinki, Finland

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62

Dose-responsive benefits of exercise

Nathan Johnson

University of Sydney, Lidcombe, NSW, Australia

The consensus data suggest that physical activity benefits weight-related outcomes via its effect on altering energy balance. Therefore analyses of the impact of exercise on weight loss have shown that the extent of weight loss is dependent on the dose of exercise, with relatively small doses associated with little or no weight loss, but large doses capable of delivering significant weight loss provided they are adhered to and sustained. Around 300–420 min per week of moderate to vigorous intensity physical activity appears to be required for meaningful weight loss. The benefits are greater when combined with dietary restriction.

The high exercise volumes recommended for significant weight loss may not be possible, or difficult to achieve for some clientele, and the majority of the population fails to meet these levels. Furthermore, there is large inter-individual variability in weight loss resulting from exercise interventions. Given the benefits of increased physical activity on health, the simplest advice for many people may be that the more activity that is undertaken the better.

Increasing research interest has centred on the benefits of physical activity independent of weight loss, and the usefulness of low levels of exercise for health outcomes. Studies in previously inactive overweight/obese adults suggest that aerobic exercise training at doses below current recommendations is effective for improving fitness and reducing visceral and 'ectopic' adiposity, which are strongly associated with metabolic and cardiovascular disease risk. These benefits can occur independent of changes in body weight. Despite conferring other benefits, the utility of some physical activity approaches (e.g. high intensity interval exercise and resistance exercise) for adiposity management is less clear.

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