

# PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

BIOLOGICAL SCIENCES

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## Causes of obesity: theories, conjectures and evidence

A 2-part theme issue compiled and edited by John R. Speakman, Thorkild I.A. Sørensen, Kevin D. Hall and David B. Allison

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## About this issue

Obesity has been described by the World Health Organisation as the largest health threat facing mankind. Obesity is manifestly an issue of energy balance. Yet, there is surprisingly little consensus about why such energy imbalance develops. This theme issue includes papers by world experts on the plethora of ideas about the mechanisms underlying obesity, and hence how we may tackle it.

This issue is based on a Royal Society Discussion Meeting held in October 2022.

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**Front image:** The regulation of the whole-body energy balance and its diversity among people is complex and incompletely understood. We still know surprisingly little about why and how only some, but now more and more, people get obesity; the specific causes and mechanisms are embedded in a blurred mixture of genetic and environmental influences. The rapidly growing pandemic of obesity with all its accompanying adversities makes it essential that we soon see an enlightening of these processes that hopefully provides the needed tools to mitigate the pandemic. Concept image by Prazis Images/Adobe Stock.

### PART I

**Preface: Causes of obesity, theories, conjectures and evidence**

David B Allison, Thorkild IA Sørensen, Kevin D Hall and John R Speakman

*Breaking down silos: the multifaceted nature of obesity and the future of weight management* Faith Anne N Heeren *et al.*

*Energy homeostasis from Lavoisier to control theory* Nori Geary

*The fructose survival hypothesis for obesity* Richard J Johnson *et al.*

*The evolutionary impact and influence of oestrogens on adipose tissue structure and function* Olgerd Bardhi, Biff F Palmer and Deborah J Clegg

*Is there a role for higher cognitive processes in the development of obesity in humans?* Suzanne Higgs

*Reactive oxygen species: role in obesity and mitochondrial energy efficiency* Barbara E Corkey

*From dearth to excess: the rise of obesity in an ultra-processed food system* Kevin D Hall

*Fat-free mass and resting metabolic rate are determinants of energy intake: implications for a theory of appetite control* Mark Hopkins, Catherine Gibbons and John Blundell

*Does eating less or exercising more to reduce energy availability produce distinct metabolic responses?* Lewis G Halsey, José L Areta and Karsten Koehler

*Early life impacts of maternal obesity: a window of opportunity to improve the health of two generations* Laura Dearden and Susan E Ozanne

*Behavioural susceptibility theory: the role of appetite in genetic susceptibility to obesity in early life* Clare H Llewellyn *et al.*

*Natural selection and human adiposity: crafty genotype, thrifty phenotype* Jonathan CK Wells

*Obesity and environments external to the body* Stanley Ulijaszek

*Physiological protection against weight gain: evidence from overfeeding studies and future directions* Jens Lund and Christoffer Clemmensen

*An adiposity force induces obesity in humans independently of a normal energy balance system—a thought experiment* Thorkild IA Sørensen

### PART II

*Obesity and thinness: insights from genetics* Sadaf Farooqi

*Implication of lipid turnover for the control of energy balance* Samuel Bernard and Kirsty L Spalding

*Carbohydrate-insulin model: does the conventional view of obesity reverse cause and effect?* David S Ludwig

*Protein appetite as an integrator in the obesity system: the protein leverage hypothesis* David Raubenheimer and Stephen J Simpson

*Diet composition and energy intake in humans* R James Stubbs *et al.*

*The provisioned primate: patterns of obesity across lemurs, monkeys, apes and humans* Herman Pontzer

*The dual hypothesis of homeostatic body weight regulation, including gravity-dependent and leptin-dependent actions* John-Olov Jansson *et al.*

*Brown adipose tissue: can it keep us slim? A discussion of the evidence for and against the existence of diet-induced thermogenesis in mice and men* Jan Nedergaard, Gabriella von Essen and Barbara Cannon

*Questioning the foundations of the gut microbiota and obesity* Matthew J Dalby

*Food insecurity as a cause of adiposity: evolutionary and mechanistic hypotheses* Melissa Bateson and Gillian V Pepper

*Obesity and psychological distress* Andrew Steptoe and Philipp Frank

*Models of body weight and fatness regulation* John R Speakman and Kevin D Hall

*Causal models and causal modelling in obesity: foundations, methods and evidence* Roger S Zoh *et al.*