Drive to Eat in *homo sapiens* and implications for obesity: energy expenditure drives energy intake

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17 January 2022

DJ

Orientation

- Seminar is about the control of human appetite
- Appetite Regulation
- Influence of biology on behaviour
- Q: to what extent is behaviour (eating) influenced by biology, and by the environment?
- Drive to eat; not about food choice
- Appetite and Nutrition are intimately linked

- Working definition: Appetite can be regarded as a biological drive expressed through behaviour in a social environment

- What causes this drive for food?
- How is this linked to obesity?

Puzzling Issues (at least for me)

Fact: People with obesity carry large amounts of stored energy in their bodies

- Why do people with obesity need to eat periodically?
- Why do people with obesity continue to feel hungry?
- What is the driver of appetite in obese people?
- This large amount of fat does not appear to help people control their appetite. In fact the opposite seems to be the case.

Naive Orientation

No one is trying to overeat

- Overconsumption just seems to happen. It is very difficult to oppose this unwanted and accidental overeating. Why?
- There is no biological impediment to prevent this overeating (energy regulation?)

- No one is trying to get fat
- Obesity just happens to people
- Biology does not prevent this from happening (fat regulation?)

- General statements but do not apply to everyone
- Individual variability is very high

Most salient feature of human feeding is that………..

- We are OMNIVORES (not herbivores or carnivores)
- This means that our food repertoire is huge

- But, what we eat is not heavily pre-programmed biologically (has to be flexible)

- Determined by culture, geography, climate, religion.
- Within a culture large variety of individual eating patterns

- As a species we are MEAL eaters and the meal is a significant feature of human appetite

- Distinguish between the TONIC and EPISODIC influences.

- The omnivorous habit is separate from the Drive to Eat

Classical themes in Appetite Research

- The biological control of the amount of food that we eat has been a central issue in appetite research for over 70 years.
- Origins in experimental animal models characterised by over eating and obesity
- This gave rise to the lipostatic or adipocentric theory of obesity – which has dominated thinking
- The belief that body fat controls the amount of food eaten. This depends on the idea that body fat is itself regulated
- Regulation is commonly invoked in referring to body fat and to appetite.

The fascination of VMN hyperphagia and obesity – a line of research important for appetite

- Hetherington and Ranson 1942
- Anand and Brobeck 1951

HYPOTHALAMIC CONTROL OF FOOD INTAKE IN RATS AND CATS*

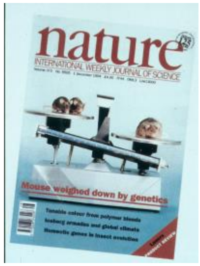
BAL K. ANAND† AND JOHN R. BROBECK

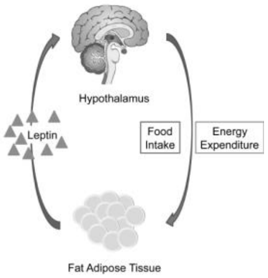
- G C Kennedy 1955
- ‘principle problem is how the normal rat avoids overeating, that is – the mechanism of satiety’ (p578)

Royal Society Publishing
Informing the science of the future

The Role of Depot Fat in the Hypothalamic Control of Food Intake in the Rat
Author(s): G. C. Kennedy
Source: *Proceedings of the Royal Society of London. Series B, Biological Sciences*, Vol. 140, No. 901 (Jan. 15, 1953), pp. 578-592
Published by: The Royal Society
Stable URL: http://www.jstor.org/stable/82630
Accessed: 24/07/2014 06:25

- R Hervey 1965 circulating factor
- J Friedman 1994





- Body adipose tissue regulates food intake – ‘in the absence of leptin…….. animals fail to restrain their food intake’. 1998 pS39

Statements favouring the Adipocentric (Lipostatic) view. Appetite control is linked to the regulation of body fat.

- ‘There is compelling evidence that total body fat is regulated...when it is decreased reflexes restore it to normal.....when it is increased reflexes...elicit weight loss. These processes account for the relatively stable maintenance of body weight over long periods’

- ...’food intake is an effector or response mechanism that can be recruited or turned off in the regulation of body fat’

Editorial Focus

Am J Physiol Regul Integr Comp Physiol 286: R14–R15, 2004;
10.1152/ajpregu.00583.2003.

Regulation of body fat content?

George N. Wade
Center for Neuroendocrine Studies, University of Massachusetts, Amherst, Massachusetts 01003

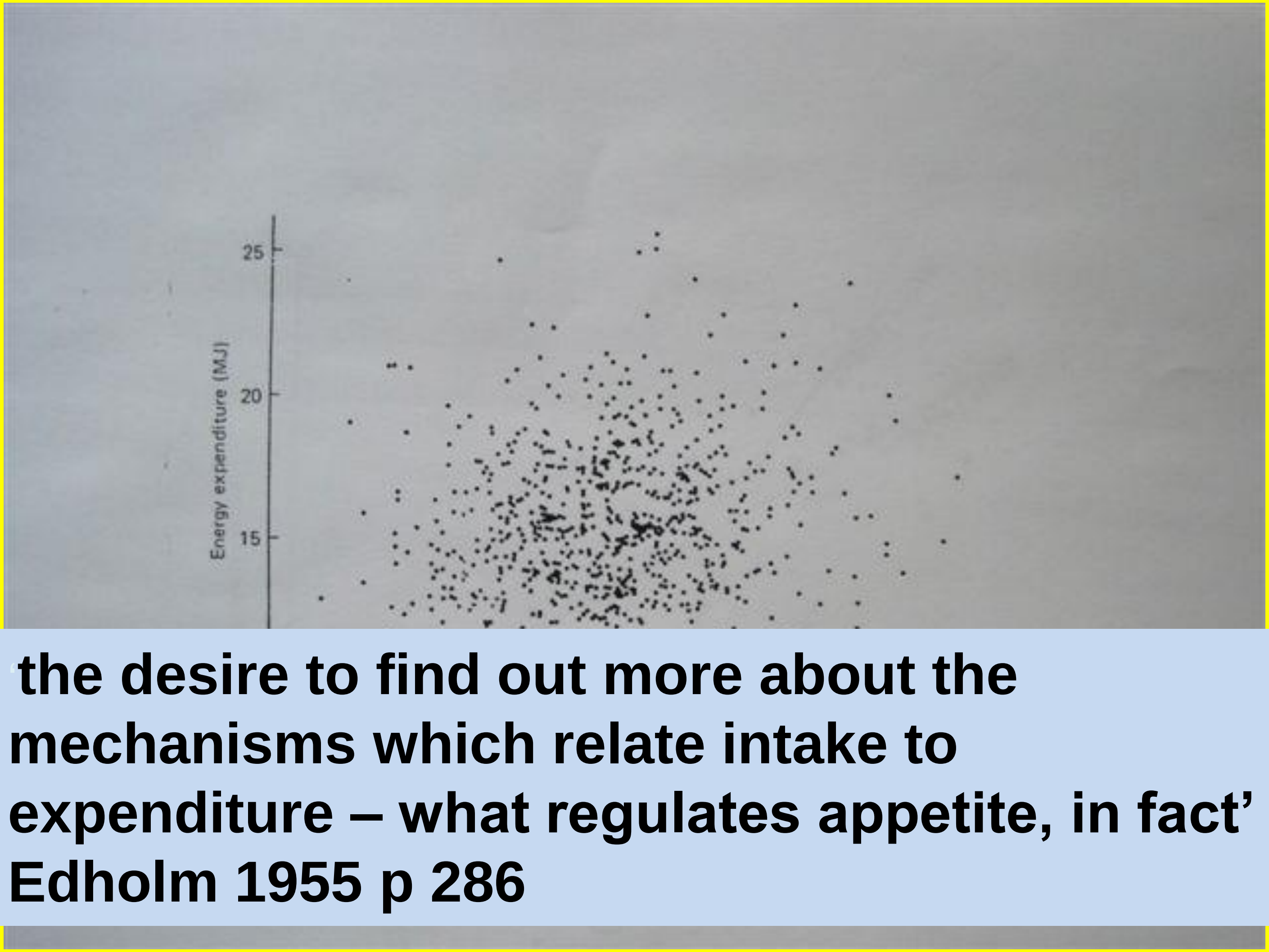
It has been noted that even using the lipostatic set point as a descriptor is not without its hazards (13). Noting the tendency for animals to maintain a constant body weight in this way may give the appearance there is indeed a lipostatic set point and that this explains, rather than describes, the phenomenon. Such a facile explanation has the potential to set back progress in a field by years, because the problem is thought to have been solved (10). A more serious problem is that, for the uncritical, the existence of a lipostatic set point is inherently unfalsifiable, and scientific hypotheses are useful only to the extent that they can be falsified. If an experimental manipulation results in a

An alternative view

- In contrast to the view that energy intake is driven in order to regulate body fat…..
- …..Energy Intake is driven in order to meet the energy requirements of maintaining vital organs (FFM) – Fat Free Mass.
- Introduce a role for ‘lean’ tissue (in addition to adipose tissue) in appetite

An Alternative Approach to Appetite Regulation (not concerned with adipose tissue, or brain mechanisms but with nutrition and physiology):

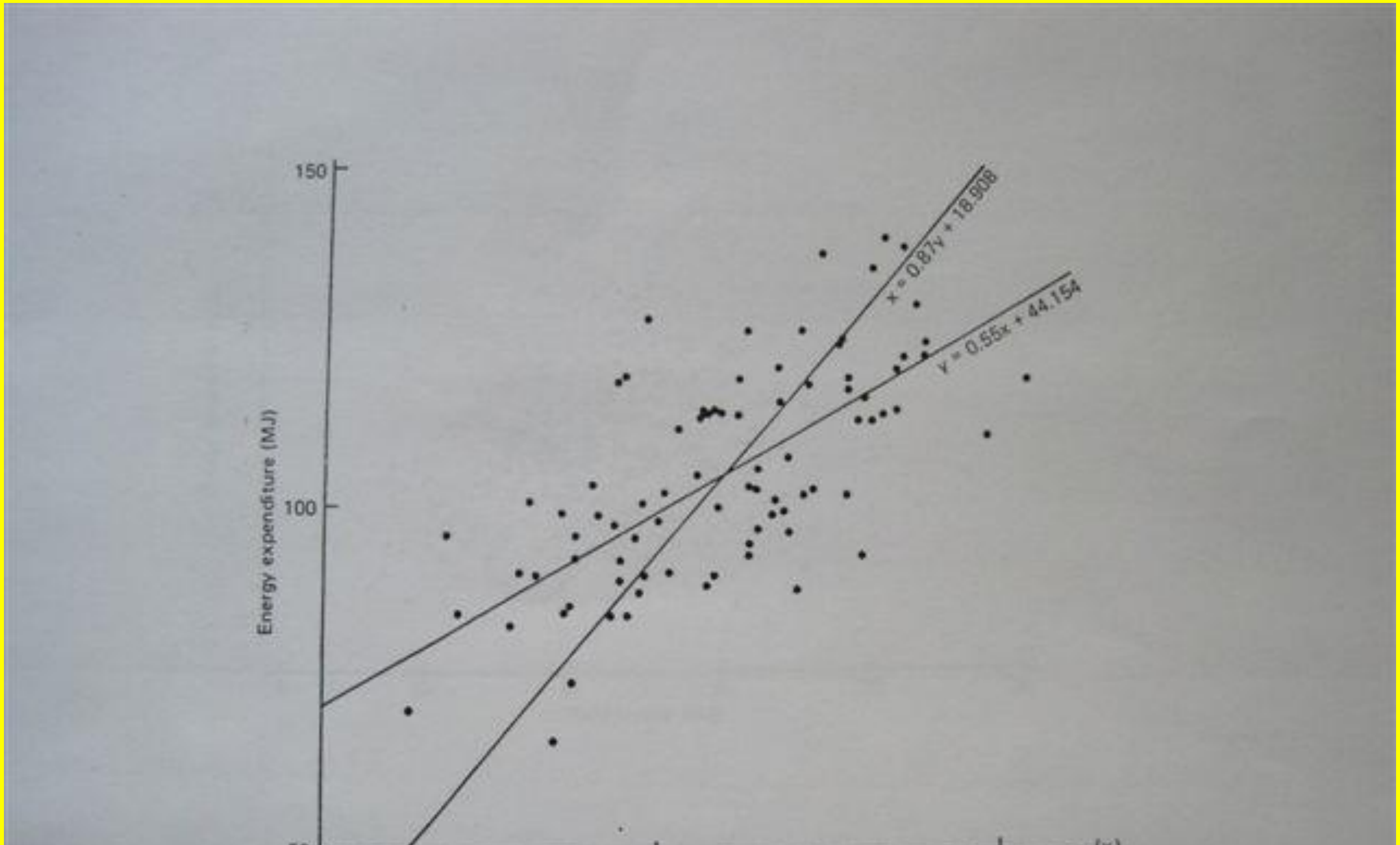
Relating energy expenditure and Energy Intake



‘the desire to find out more about the mechanisms which relate intake to expenditure – what regulates appetite, in fact’ Edholm 1955 p 286

Edholm, Widdowson, McCance et al, 1955, 1970 1973

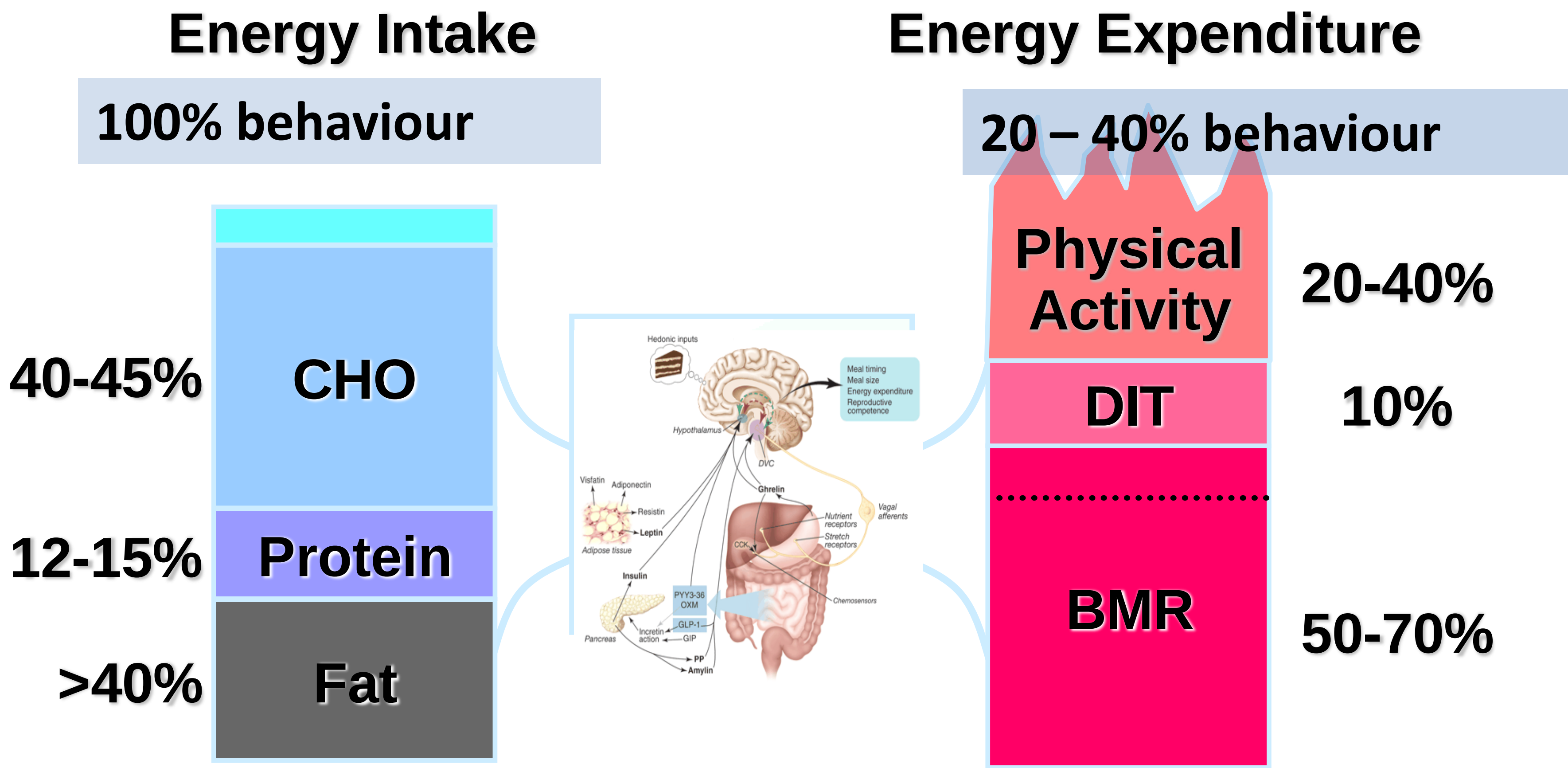
Integrative Biology: relationship between feeding and activity – an energy balance approach



’the differences between the intakes of food (of individuals) must originate in the differences in the expenditure of energy’ (Edholm et al 1955 p 297)

Edholm et al, 1970

energy balance framework for the study of appetite



Leeds multi-level research platform

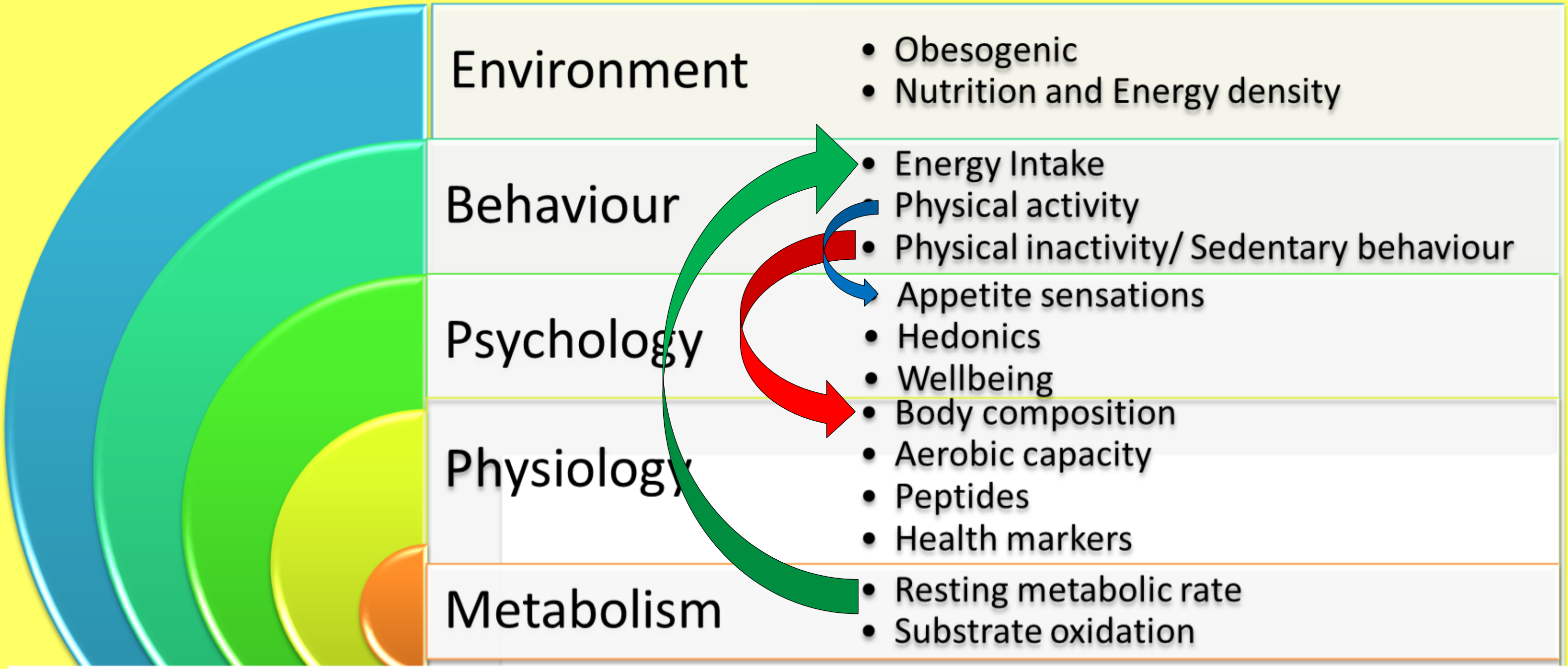


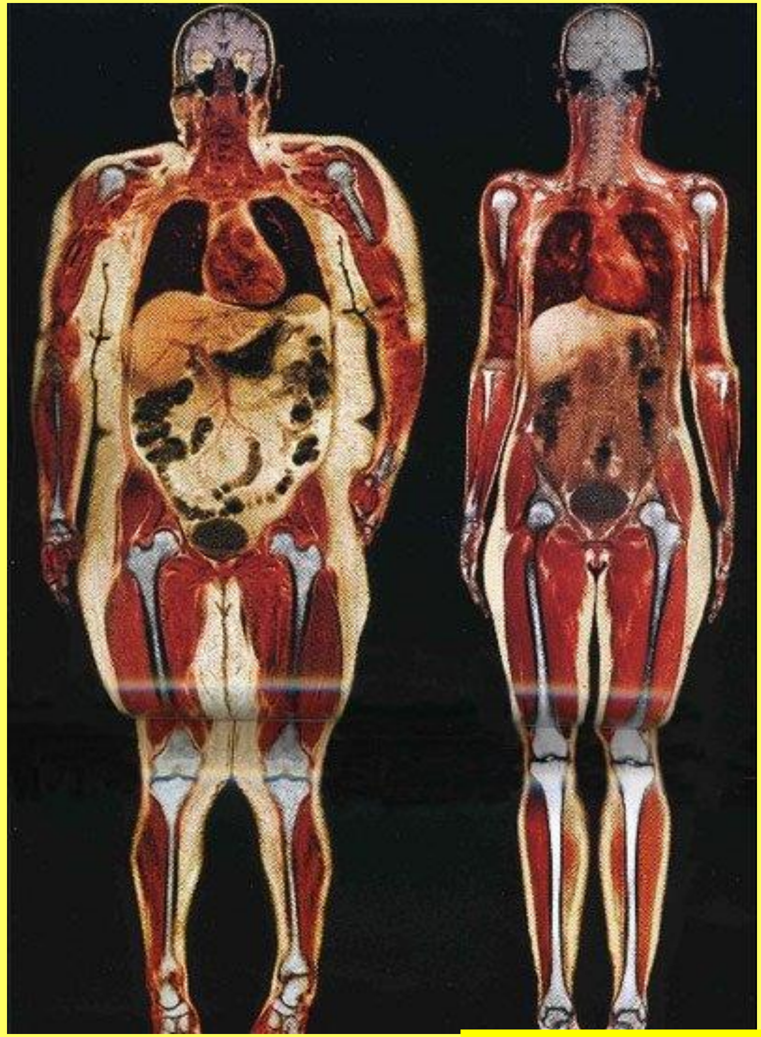
Figure 1. The Leeds multilevel systems approach to the study of appetite control.

Research Question: Investigations of the Drivers of eating behaviour

Do long term markers of energy balance (FM, FFM and RMR) influence within-day appetite control?

Multi-level platform Methodology

- Quantitative and objective measurement of self-determined meals and total daily intake
- Body composition using BodPod
- Metabolic Rate by Indirect Calorimetry.
- Profiles of hunger ratings via validated VAS
- Exposure to high and low energy density diets
- Repeated measurements periodically over 12 weeks.



INDIVIDUAL VARIABILITY

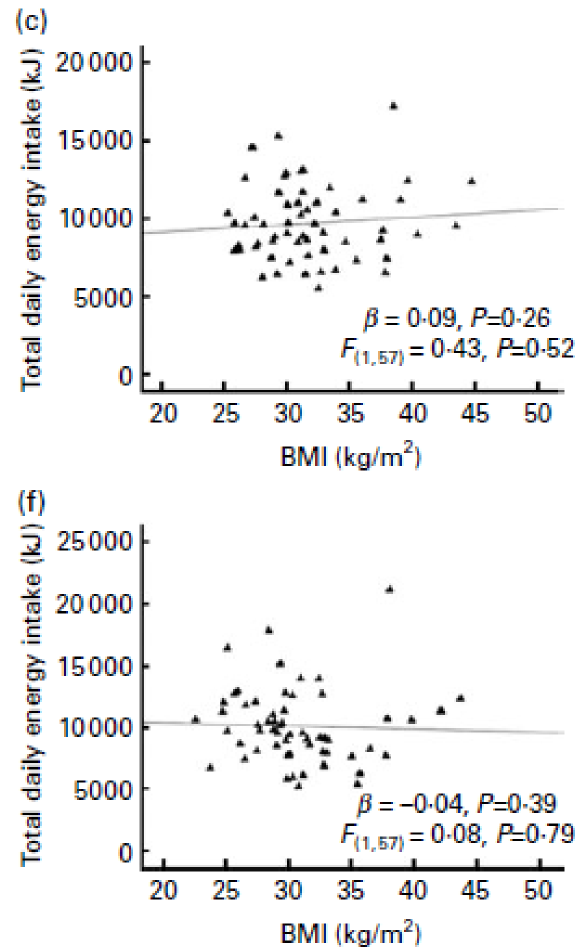
Fat Mass: 19.3 – 58.4kg (22-54%)

F-F Mass: 33.5 – 75.8kg (46-78%)

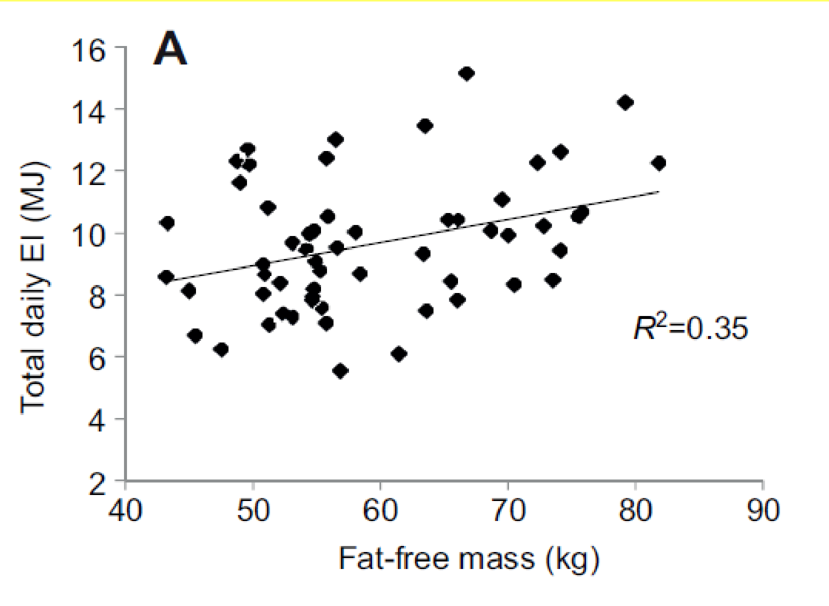
British Journal of Nutrition (2011), page 1 of 6 doi:10.1017/S0007114511003138

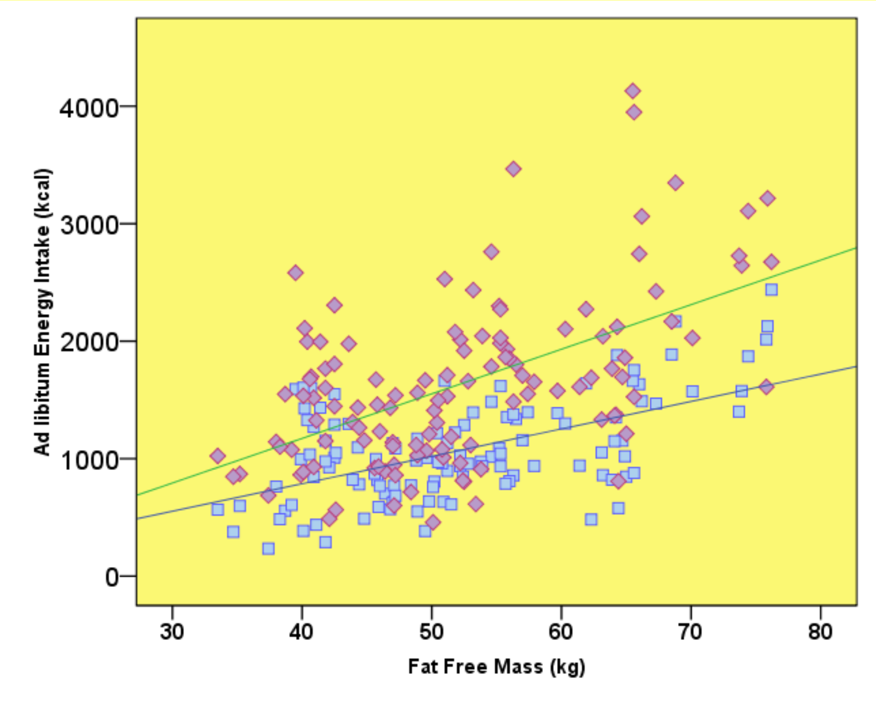
Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans

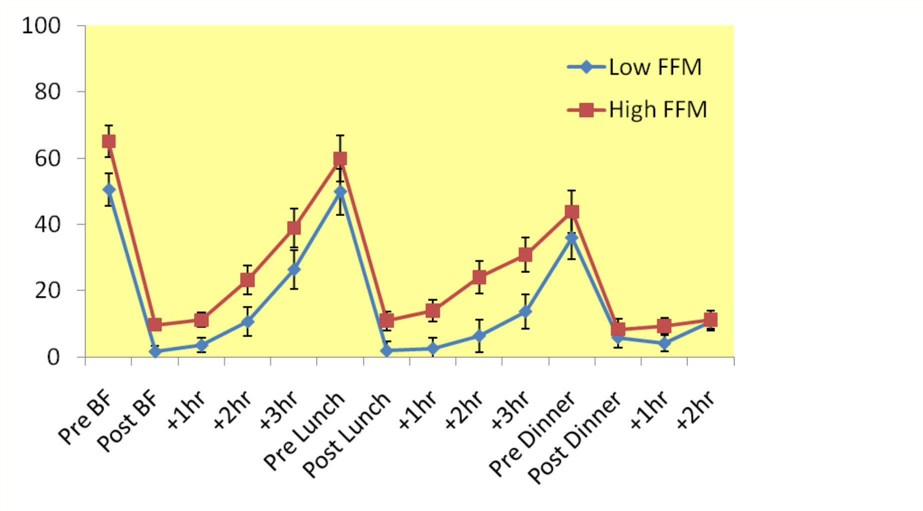
John E. Blundell[1]*, Phillipa Caudwell[1], Catherine Gibbons[1], Mark Hopkins[2], Erik Naslund[3], Neil A. King[4] and Graham Finlayson[1]



Internal confirmation







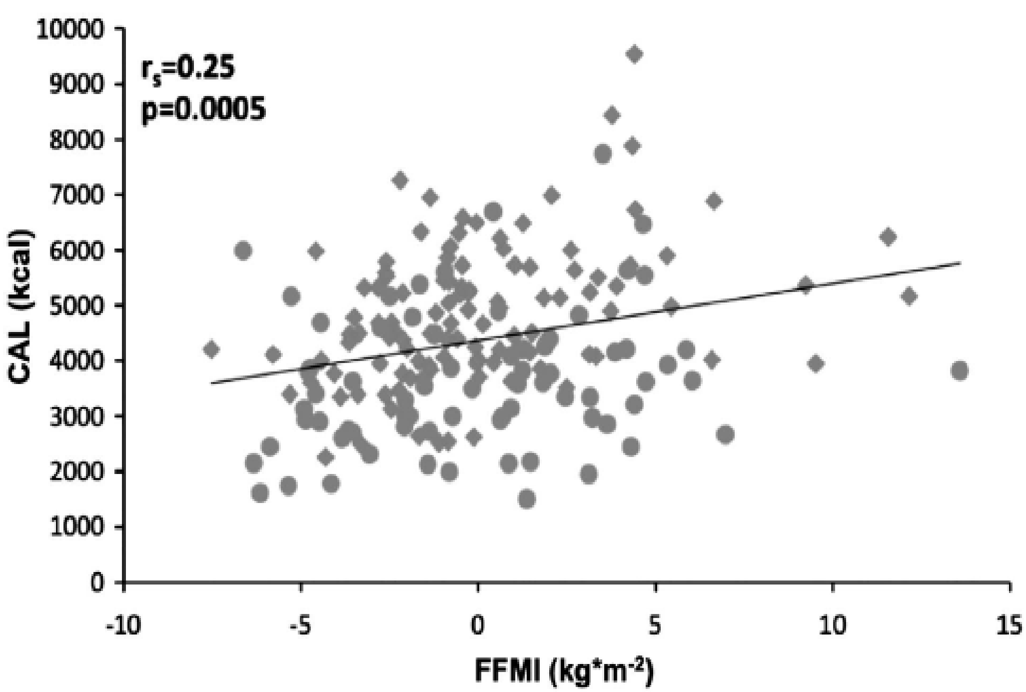
International Journal of Obesity (2013), 1–9

www.nature.com/ijo

ORIGINAL ARTICLE

Body composition and energy expenditure predict *ad-libitum* food and macronutrient intake in humans

CM Weise[1], MG Hohenadel[2], J Krakoff[2] and SB Votruba[2]



Confirmed the association of FFM and EI

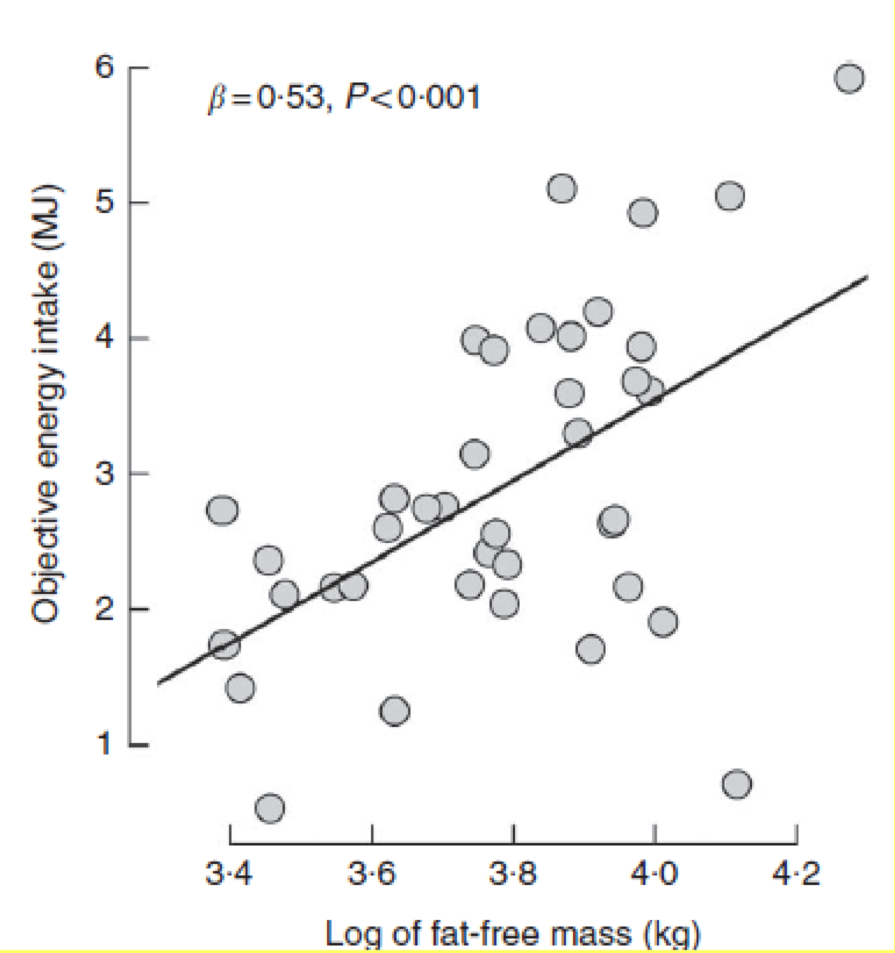
'….FFM and FM may have opposing effects on energy homeostasis…….'

adolescents

British Journal of Nutrition (2016), 116, 1425–1436
doi:10.1017/S0007114516003317

Diet misreporting can be corrected: confirmation of the association between energy intake and fat-free mass in adolescents

Uku Vainik[1,2]*, Kenn Konstabel[1,3], Evelin Lätt[4], Jarek Mäestu[4], Priit Purge[4] and Jaak Jürimäe[4]
[1]Institute of Psychology, University of Tartu, Näituse 2, 50410, Tartu, Estonia
[2]Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, 3801 University St., Montréal, QC, Canada, H3A 2B4
[3]Chronic Diseases Department, National Institute for Health Development, Hiiu 42, 11619, Tallinn, Estonia
[4]Faculty of Exercise and Sport Sciences, University of Tartu, Jakobi 5, 51014, Tartu, Estonia



n = 39

Further confirmation…….

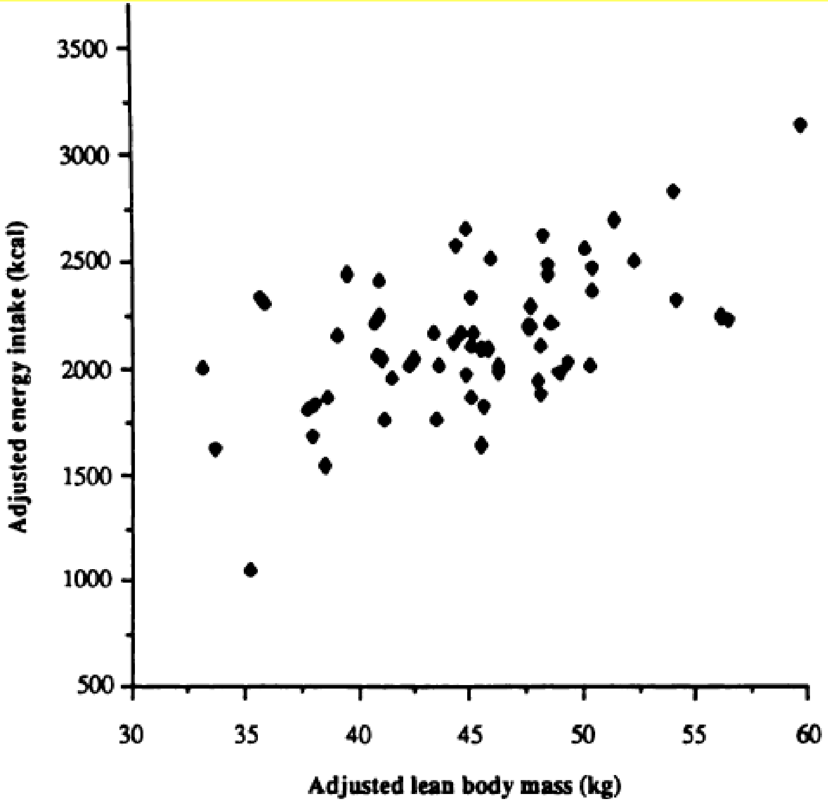


FIG 2. Plot of energy intake (residual kcal + group mean) vs lean body mass (residual kg + group mean) after linear effects of weight change were removed from each axis.

..energy requirement was positively associated with lean mass ($p<0.0001$) whereas fat mass added no predictive value to the model (p 324).

The emphasis of research that focuses on the relationship between EI and obesity is misplaced because EI appears to be a direct function of lean mass rather than adiposity (p 324)

Lissner, Levitsky et al, AJCN 1989

- Interpretation?

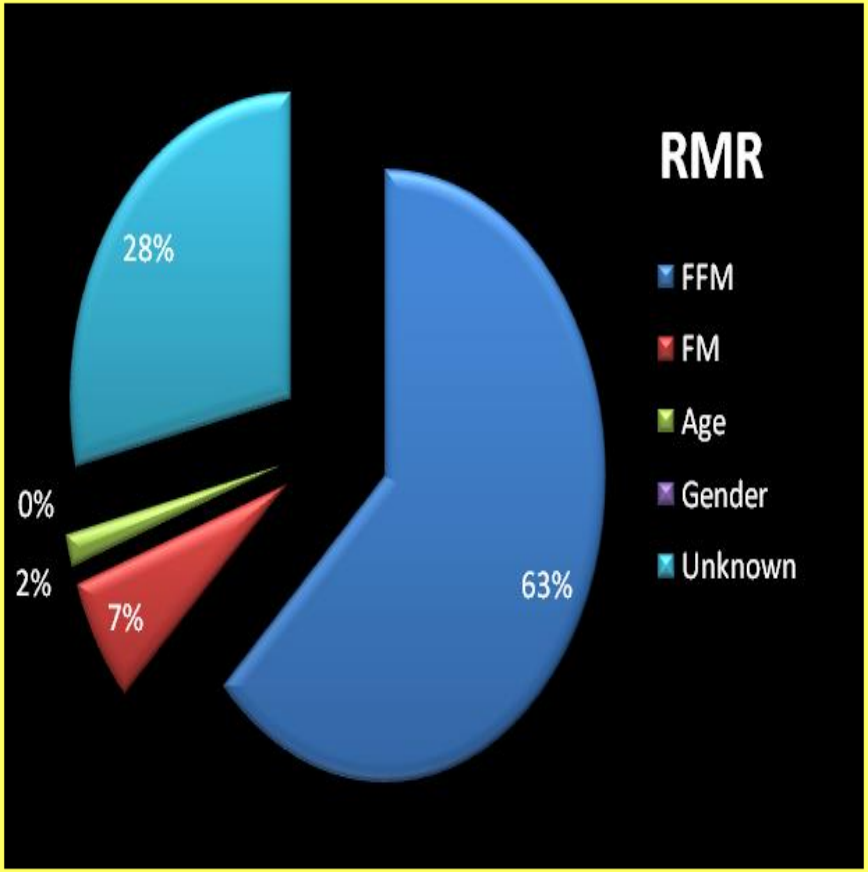
- This outcome suggests that FFM is playing a functional role in the normal control of appetite – influencing the drive to eat (hunger) and the amount of food eaten.

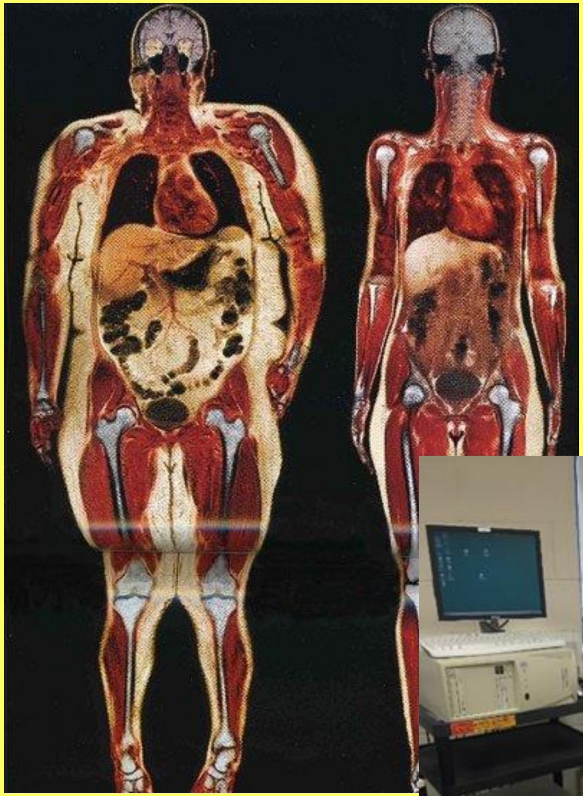
- Mechanism?

- Some privileged molecule expressed from lean tissues is acting as a signal to the brain
- The effect may be related to the metabolic activity of FFM

Beyond fat-free mass: Body composition and Energy Balance

- Fat Mass and Fat-Free Mass contribute to Resting Metabolic Rate





INDIVIDUAL VARIABILITY
Fat Mass: 19.3 – 58.4kg (22-54%)
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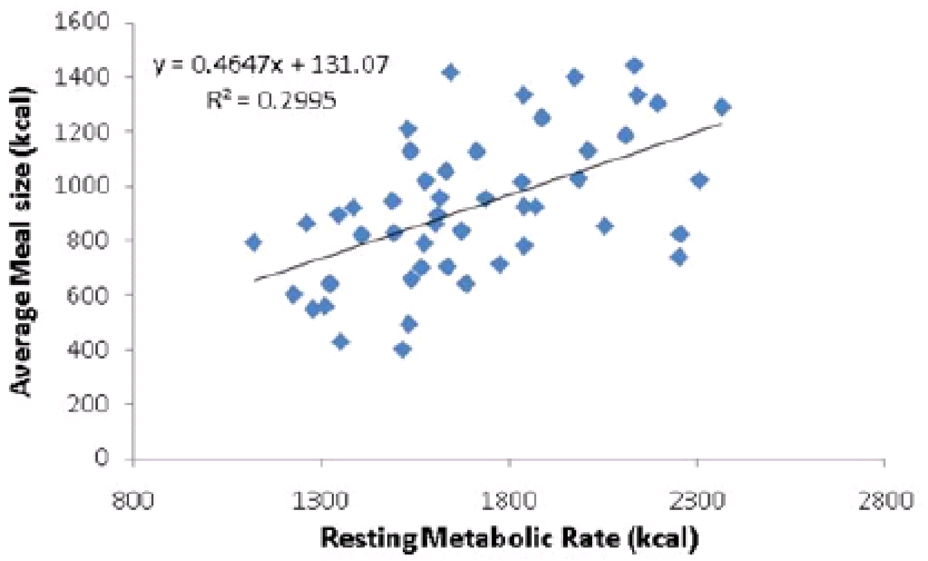
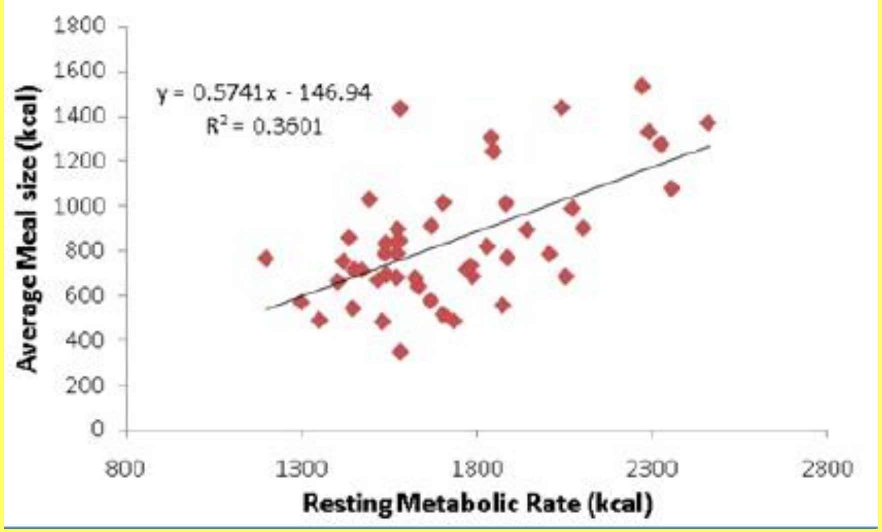
Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite[1–3]

Phillipa Caudwell, Graham Finlayson, Catherine Gibbons, Mark Hopkins, Neil King, Erik Näslund, and John E Blundell



Week 0

Week 12



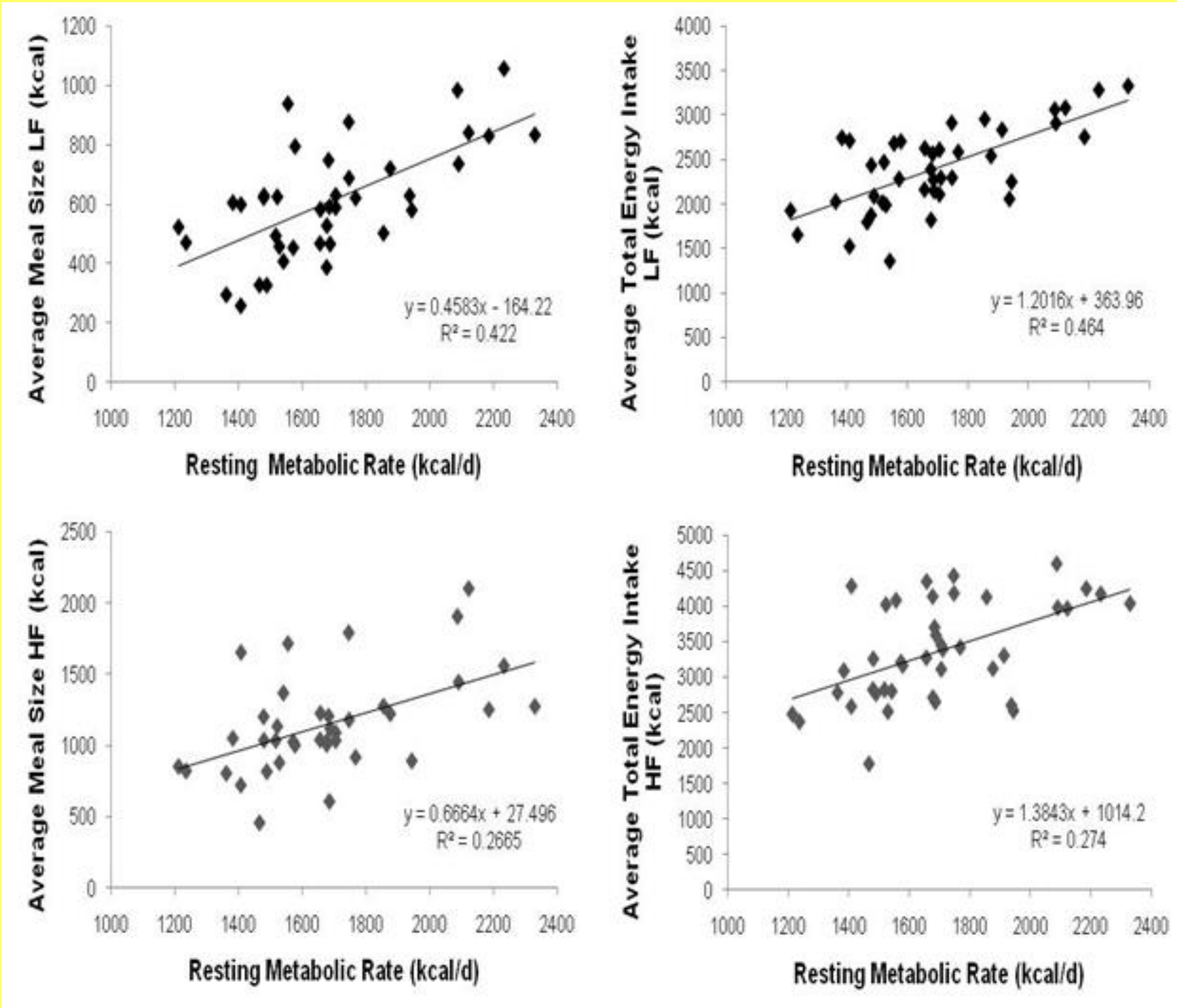
Interpretation: Resting Metabolic Rate is a Driver of Meal Size and Daily Energy Intake

Caudwell et al AJCN 2013

INFLUENCE OF RESTING METABOLIC RATE (RMR)

Meal size

Total Energy Intake



Low energy dense foods

High energy dense foods

All findings replicated in a completely independent data set

British Journal of Nutrition, page 1 of 12
doi:10.1017/S0007114514000154

Measuring the difference between actual and reported food intakes in the context of energy balance under laboratory conditions

R. James Stubbs[1,2]*, Leona M. O'Reilly[1], Stephen Whybrow[3], Zoë Fuller[1], Alexandra M. Johnstone[1], M. Barbara E. Livingstone[4], Patrick Ritz[5] and Graham W. Horgan[6]

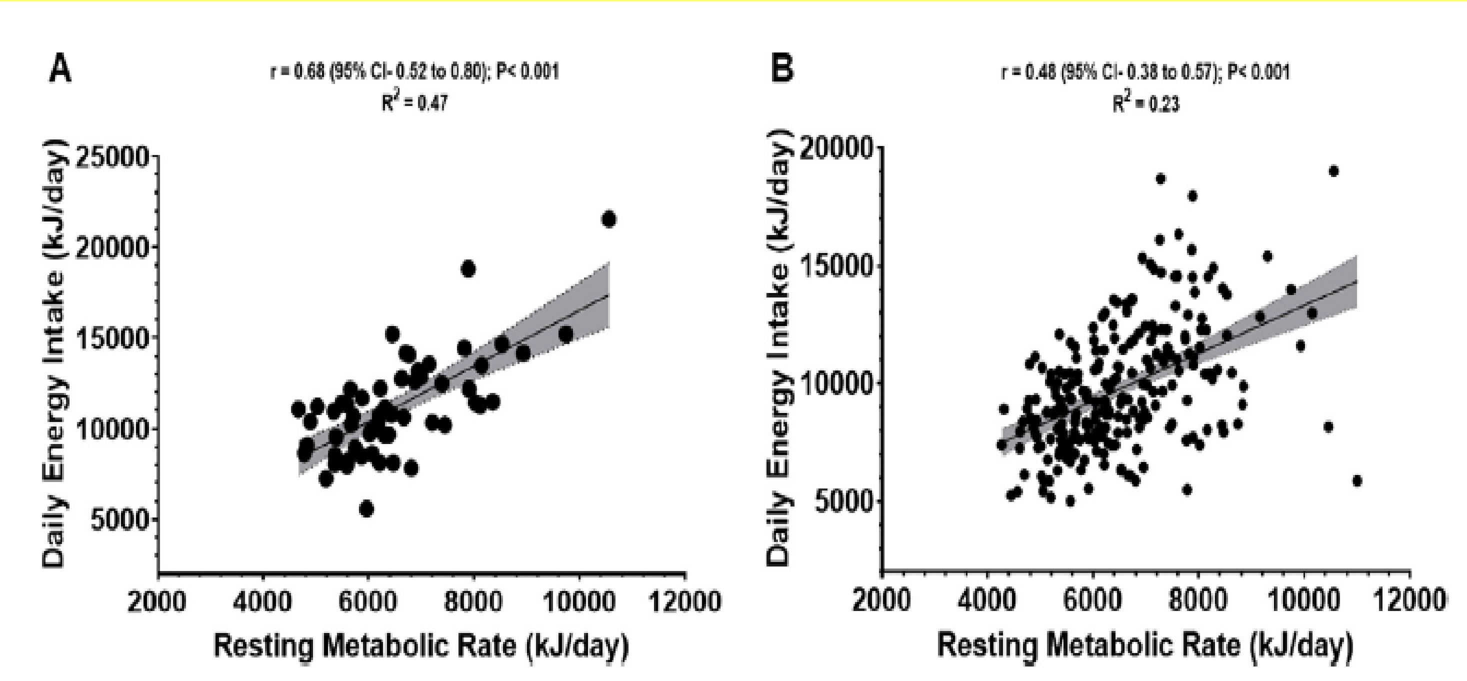
International Journal of Obesity

Biological and psychological mediators of the relationships between fat mass, fat-free mass and energy intake

Mark Hopkins, Graham Finlayson, Cristiana Duarte, Catherine Gibbons, Alexandra M Johnstone, Stephen Whybrow, Graham W Horgan, John E Blundell, R James Stubbs

Objectively quantified daily food intake in research unit
TDEE by DLW; RMR; PAL by HR.

RMR emerged as the strongest predictor of daily energy intake



Appetite studied within an energy balance framework: Interesting implications

- RMR influences meal size and daily energy intake
- Can explain why people get periodically hungry throughout the day even when not dieting or deprived of food
- Individual differences in hunger and amount of food eaten
- Why (in general) men eat more than women
- Field athletes and sports people (with very high FFM) have powerful appetites
- Why elderly people with sarcopenia (and reduced EE) suffer from loss of appetite
- Why obese people continue to eat and to feel (very) hungry even with large stores of energy in the body.

Blundell et al, DMM 2012

American Journal of Clinical Nutrition 2013

Original Research Communications

Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite[1–3]

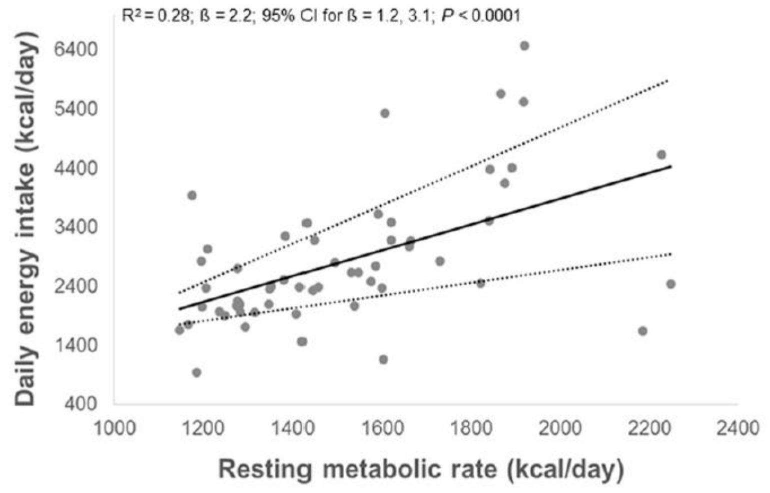
Phillipa Caudwell, Graham Finlayson, Catherine Gibbons, Mark Hopkins, Neil King, Erik Näslund, and John E Blundell

Editorial

Variations in energy intake: it is more complicated than we think

Yan Y Lam[1] and Eric Ravussin[2]

A key finding of this study—that RMR and FFM are the strongest determinants of energy intake—largely confirms the positive correlation between RMR and FFM and energy intake reported



Investigating predictors of eating: is resting metabolic rate really the strongest proxy of energy intake?

Jessica McNeil,[1] Gilles Lamothe,[2] Jameason D Cameron,[4] Marie-Ève Riou,[3] Sébastien Cadieux,[3] Jacynthe Lafrenière,[5] Gary Goldfield,[4] Stephanie Willbond,[3] Denis Prud'homme,[3,6] and Éric Doucet[3]

ORIGINAL ARTICLE

Body composition and energy food and macronutrient intake

CM Weise[1], MG Hohenadel[2], J Krakoff[2] and SB Votruba[2]

ISSN: 1744-6651 (Print) 1744-8417 (Online) Journal homepage: http://www.tandfonline.com/loi/iere20

Mechanisms control: theo implications

British Journal of Nu
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Marl Blun

British Journal of Nutrition (2016), 116, 1425–1436
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doi:10.1017/S0007114516003317

Diet misreporting can be corrected: confirmation of the association between energy intake and fat-free mass in adolescents

Uku Vainik[1,2]*, Kenn Konstabel[1,3], Evelin Lätt[4], Jarek Mäestu[4], Priit Purge[4] and Jaak Jürimäe[4]

Investigating predictors o strongest proxy of energy

Jessica McNeil,[1] Gilles Lamothe,[2] Jameason
Gary Goldfield,[4] Stephanie

Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans

islund[3],

Fat free mass is positively associated with hunger and energy intake at extremes of obesity

Andrew Grannell[a,b,*], Werd Al-Najim[a,b], Aisling Mangan[a], Natasha Kapoor[a], William P. Martin[a], John C. Murphy[b], Neil G. Docherty[a], Carel W. le Roux[a], Colin Davenport[c]

[a] Diabetes Complications Research Centre, Conway Institute, School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland
[b] MedFit Proactive Healthcare, Blackrock, Dublin, Ireland
[c] Department of Endocrinology, St Columcille's Hospital, Dublin, Ireland

COMMENTARY

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Role of resting met expenditure in hunger and appetit a new form

John E. Blundell[1,*], Phi
and Graham Finlayson

Investigating predictors of eating: is resting metabolic rate really the strongest proxy of energy intake?

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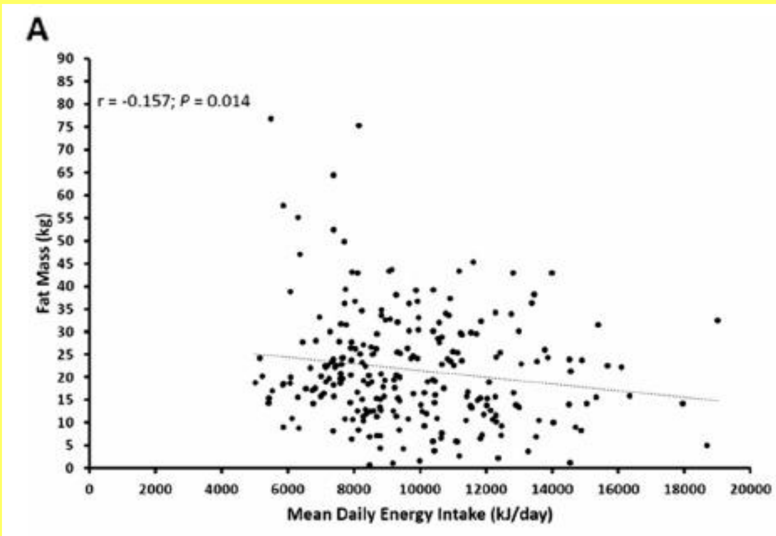
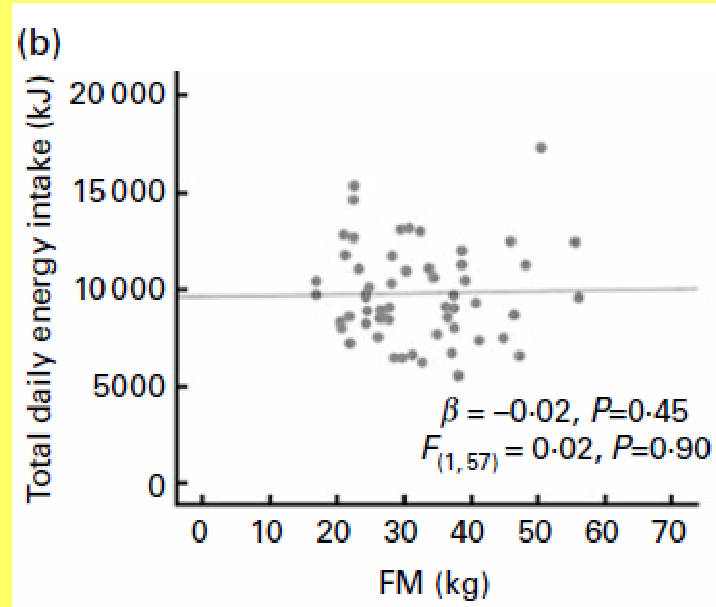
ersity, Sheffield S10 2BP, UK

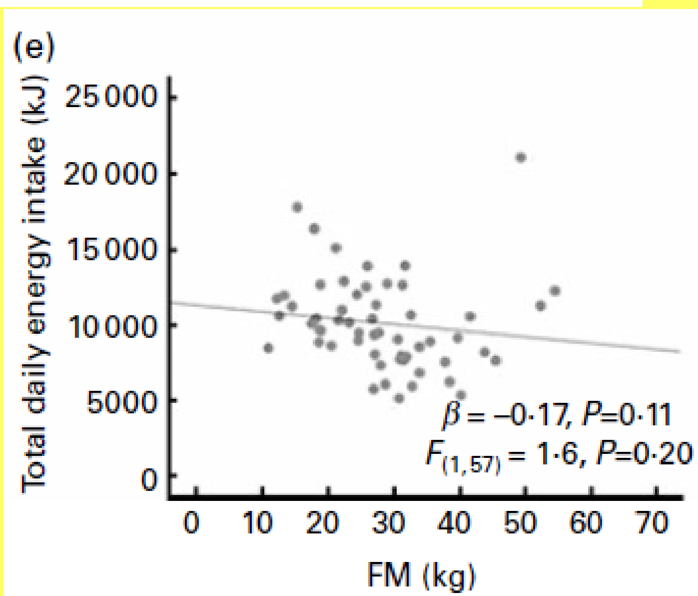
Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite[1–3]

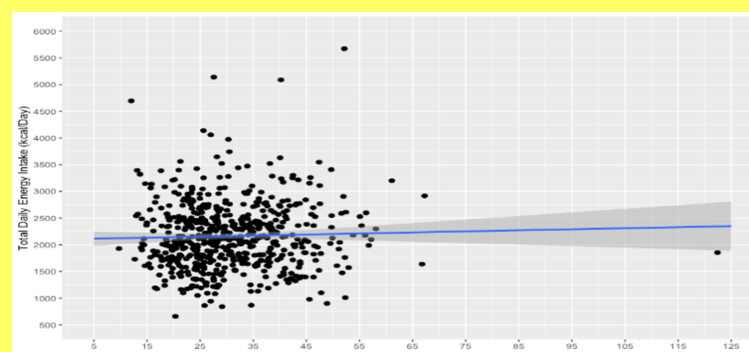
Phillipa Caudwell, Graham Finlayson, Catherine Gibbons, Mark Hopkins, Neil King, Erik Näslund, and John E Blundell

Research platform also throws light on function of body fat





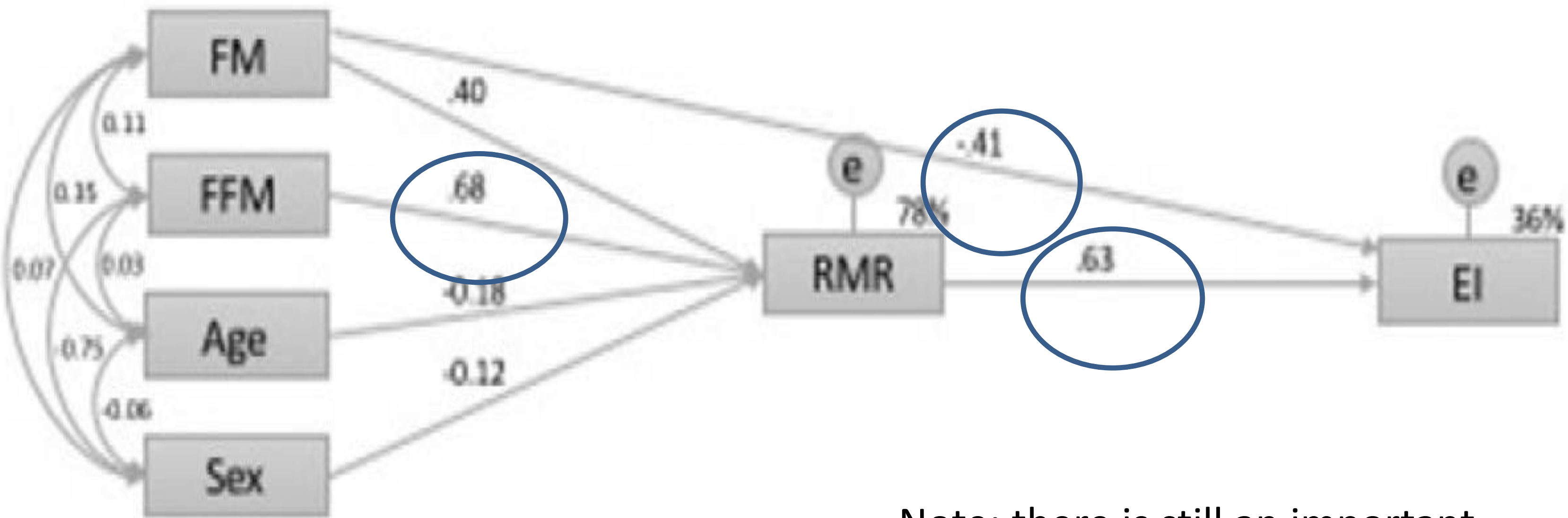




ORIGINAL ARTICLE

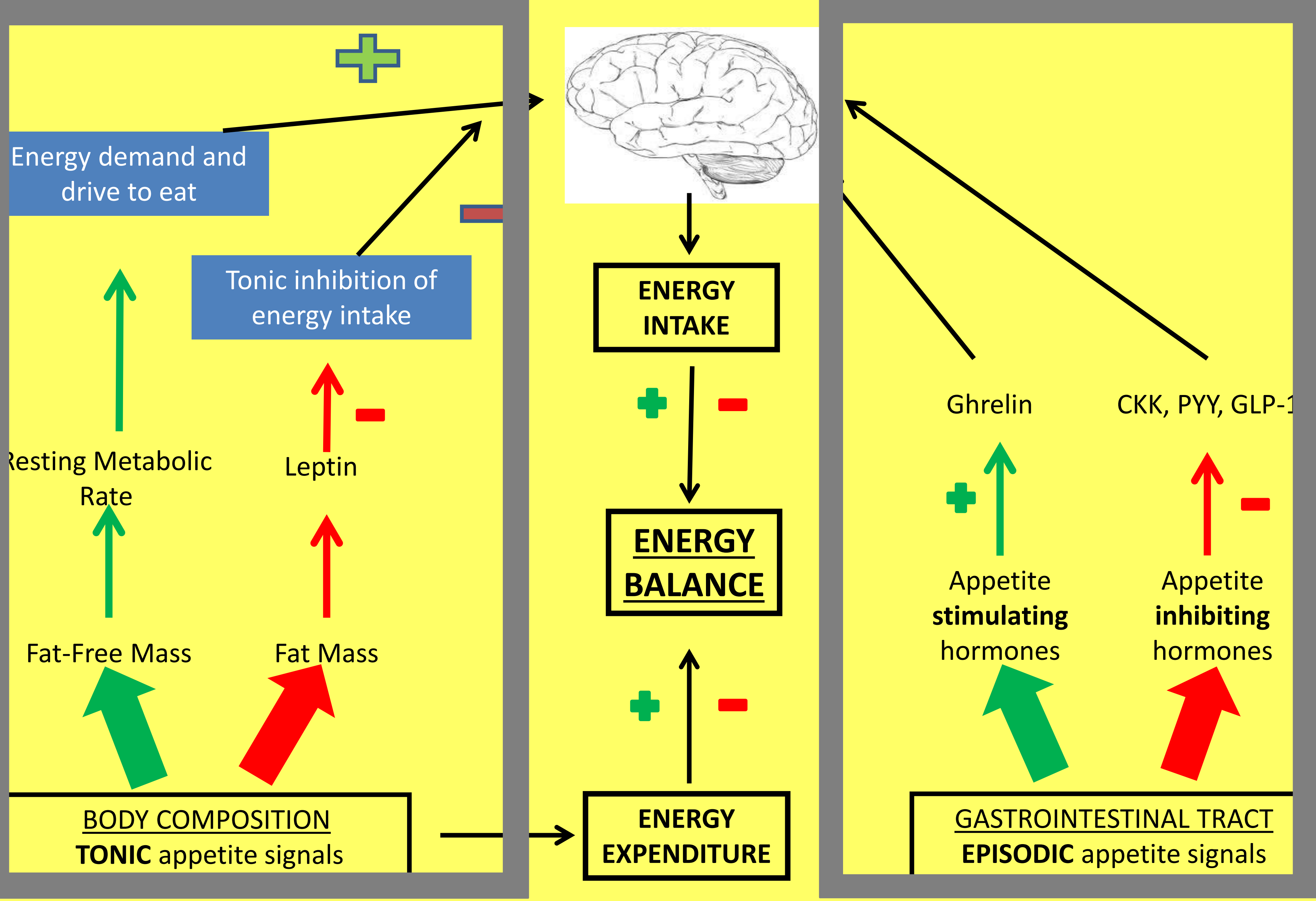
Modelling the associations between fat-free mass, resting metabolic rate and energy intake in the context of total energy balance

M Hopkins[1,2], G Finlayson[2], C Duarte[3], S Whybrow[4], P Ritz[5], GW Horgan[6], JE Blundell[2] and RJ Stubbs[7]



Note: there is still an important role for fat but not within an adipocentric model

n = 242 – 114:128


Energy demand and drive to eat
Tonic inhibition of energy intake
Resting Metabolic Rate
Leptin
Fat-Free Mass
Fat Mass
BODY COMPOSITION
TONIC appetite signals
ENERGY INTAKE
ENERGY BALANCE
ENERGY EXPENDITURE
Ghrelin
CKK, PYY, GLP-1
Appetite stimulating hormones
Appetite inhibiting hormones
GASTROINTESTINAL TRACT
EPISODIC appetite signals

Physiology & Behavior 219 (2020) 112846

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/physbeh

The drive to eat in *homo sapiens*: Energy expenditure drives energy intake

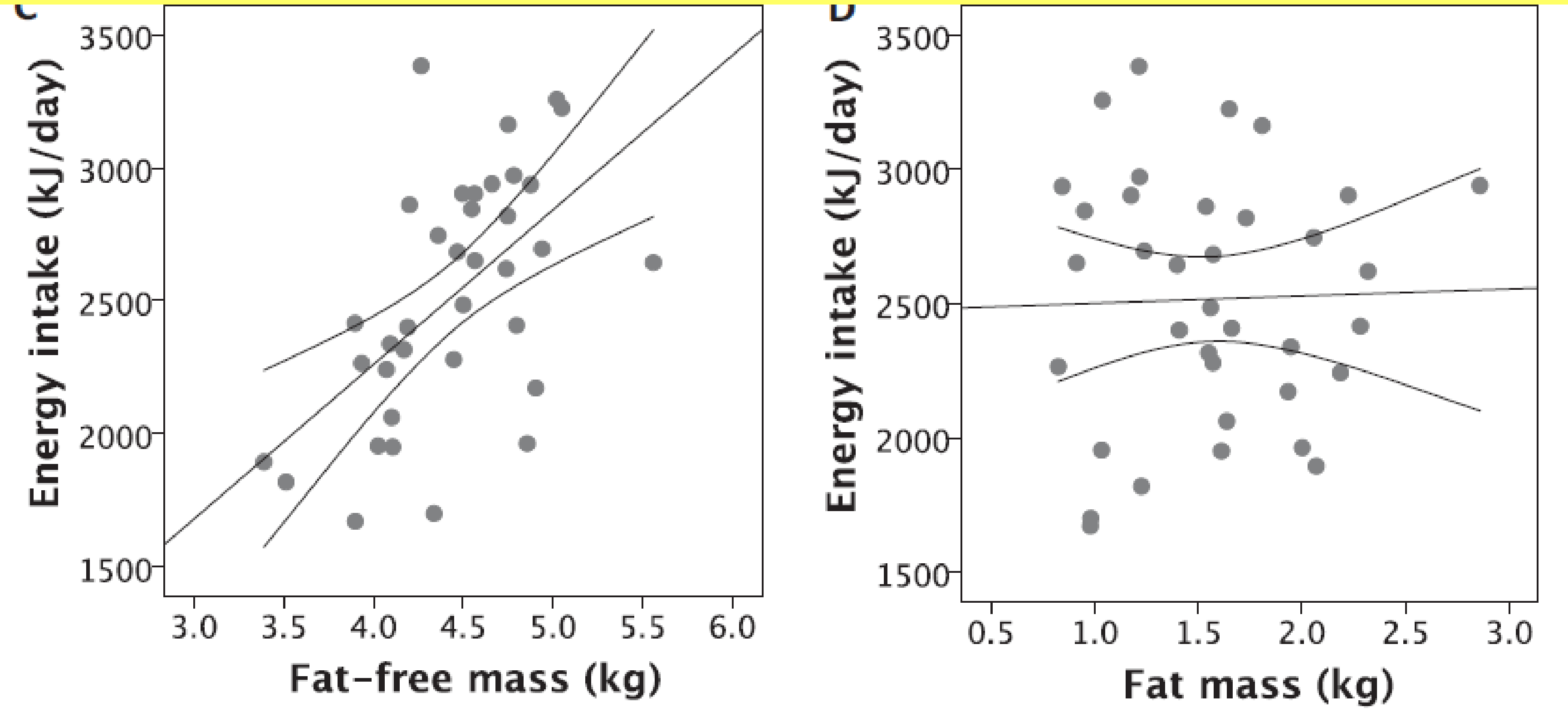
John E Blundell[a,*], Catherine Gibbons[a], Kristine Beaulieu[a], Nuno Casanova[b], Cristiana Duarte[a], Graham Finlayson[a], R James Stubbs[a], Mark Hopkins[b]

TABLE 1 Characteristics of the infants and parents in the sample

	n[1]	Mean ± SD	Range
Parental characteristics			
Maternal BMI, kg/m^2	46	23.1 ± 3.3	17.8–30.2
Maternal height, cm	48	162.9 ± 6.2	152–178
Paternal height, cm	46	178.5 ± 6.8	161–190
Infant characteristics			
Breast-fed[2]	24	50	—
Male[2]	22	46	—
Birth weight, kg	48	3.54 ± 0.36	2.70–4.17
Gestational age, weeks	48	40.1 ± 1.3	37.0–42.0
Age at study, weeks	48	12.3 ± 0.7	11.0–14.3
Weight, kg	48	5.97 ± 0.64	4.74–7.52
Length, cm	48	61.1 ± 1.7	57.9–64.2
Fat-free mass, kg	42	4.43 ± 0.44	3.39–5.56
Fat mass, kg	42	1.53 ± 0.50	0.61–2.86
Sleeping metabolic rate, kJ/d	44	1313 ± 156	906–1677
Total energy expenditure, kJ/d	42	1922 ± 363	1289–2825
Milk intake by test-weighing, g/d	42	895 ± 164	562–1244
Supplementary energy intake, kJ/d	48	84 ± 119	0–418
Total energy intake, kJ/d	42	2483 ± 462	1486–3383

The “drive to eat” hypothesis: energy expenditure and fat-free mass but not adiposity are associated with milk intake and energy intake in 12 week infants

Jonathan C Wells,[1] Peter S Davies,[2] Mark Hopkins,[3] and John E Blundell[4]



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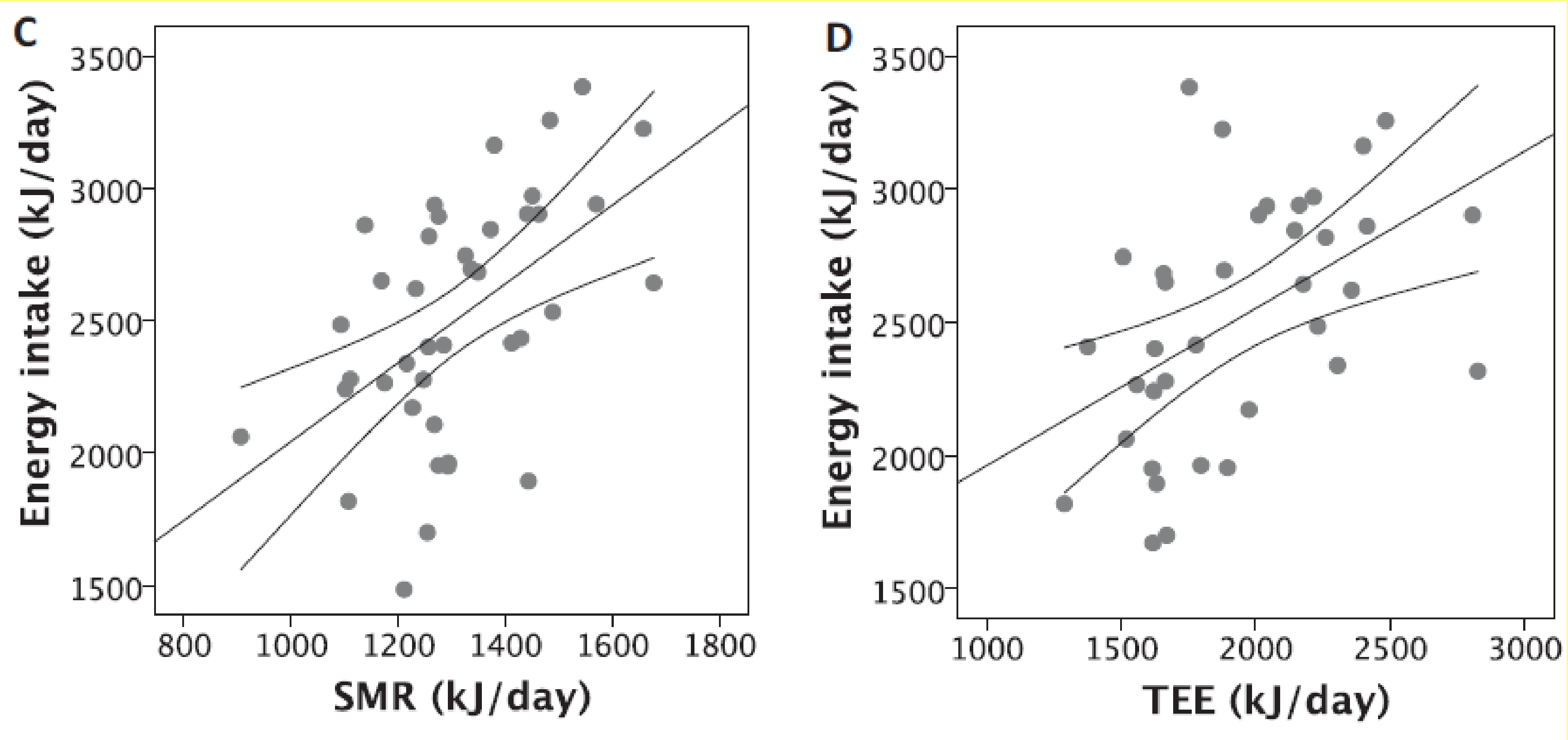
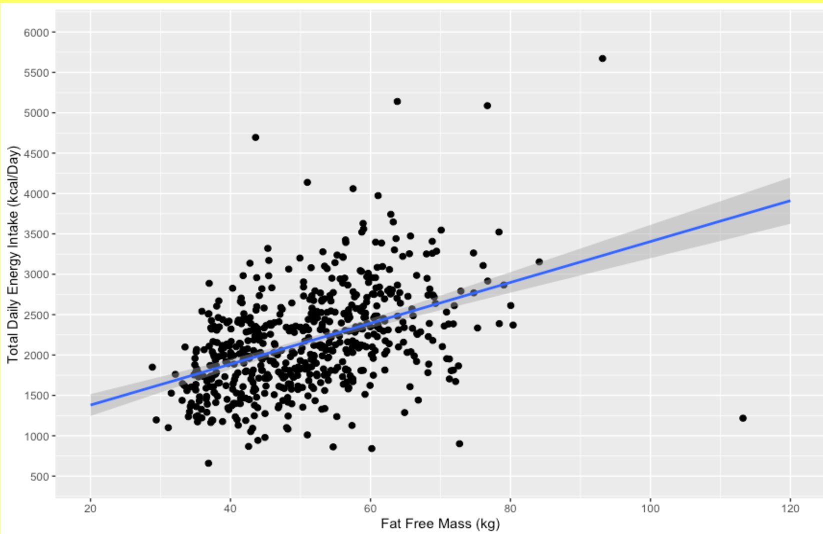


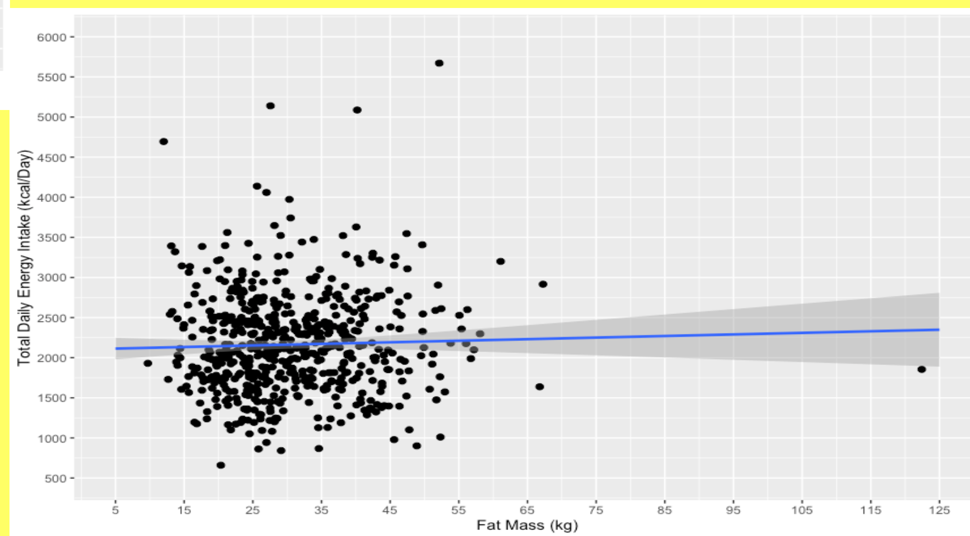
Performance and Feasibility of Recalls Completed Using the Automated Self-Administered 24-Hour Dietary Assessment Tool in Relation to Other Self-Report Tools and Biomarkers in the Interactive Diet and Activity Tracking in AARP (IDATA) Study

Amy F. Subar, PhD, MPH, RD; Nancy Potischman, PhD; Kevin W. Dodd, PhD; Frances E. Thompson, PhD; David J. Baer, PhD; Dale A. Schoeller, PhD; Douglas Midthune, MS; Victor Kipnis, PhD; Sharon I. Kirkpatrick, PhD, RD; Beth Mittl, MA; Thea P. Zimmerman, MS; Deirdre Douglass, MS; Heather R. Bowles, PhD; Yikyung Park, ScD

IDATA in AARP

Hopkins et al, 2022 J Nutrition





Note on Fat-free mass and energy expenditure

- High metabolic rate organs (HMRO) and LMRO

- Skeletal muscle – 14 kcal/kg/day

- Heart, kidney – 440 kcal/kg/day
- Brain – 240 kcal/kg/day
- Liver – 200 kcal/kg/day

- HMRO – 60/70% of REE but <6% weight
- Skeletal muscle – 20/30% of REE but >40% weight

- (Adipose tissue – 4.5 kcal/kg/day)

Javed et al, AJCN, 2010

Formal statement of the hypothesis.
Not complicated – but does <u>not</u> include any claim about <u>regulation</u> of fat or regulation of appetite.

Energy expenditure drives energy intake.

Energy requirements of vital organs such as heart, brain, lungs, liver, GI tract and skeletal muscle generate a drive for energy.

This represents a physiological source of hunger (a NEED state) that drives food intake at a level proportional to basal energy requirement.

This long term (tonic) signal of energy demand helps to 'tune' EI to EE and helps to ensure the maintenance and execution of key biological and behavioural processes.

This is of evolutionary significance.


Clinical Science (2016) **130**, 1615–1628 doi: 10.1042/CS20160006

Review Article

Energy balance, body composition, sedentariness and appetite regulation: pathways to obesity

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Widespread convergence of research outcomes

- Babies
- Adolescents
- Adults – lean
- Adults – obese
- Elderly

- Various ethnic groups
- 9 countries, 3 continents

- Reflects a property of *homo sapiens* ?

Theoretical implications

- Evidence against the adipocentric hypothesis.
- Suggests that appetite is not regulated in order to control body fat
- The Drive to Eat arises from the need to meet the energy demands of vital organs (HMRO) and EE.
- Energy Expenditure drives Energy Intake
- Fat Mass does exert a tonic inhibition via leptin/melanocortin pathway.
- Lean mass and fat mass both play a role but the drive to eat is associated with fat-free mass

IMPLICATIONS FOR OBESITY DEVELOPMENT AND MANAGEMENT

- As FM increases (due to EI+ or EE-, or both), FFM also increases.
- Therefore RMR increases and the drive to eat increases
- The increase in FM induces both leptin and insulin resistance thereby weakening inhibitory control.
- Consequently as people accumulate body fat there is an increase in drive and a weaker resistance (inhibition).
- People are driven more forcefully into the obesogenic environment which tends to promote overconsumption

Thank you

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The drive to eat in *homo sapiens*: Energy expenditure drives energy intake

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