Are all ‘calories’ equal?

Ian Macdonald
University of Nottingham
Outline

• Basic thermodynamics
• Energy balance, substrate oxidation and consequences of overconsumption
• Dietary risk factors for excessive intake – potential for passive overconsumption
• Interaction of macronutrients/foods/meal patterns with appetite / energy intake / metabolism
Are all ‘calories’ equal

• YES

• ‘Calories’ = a unit of measurement of heat – should not be used for Energy in food etc. (Joules should be used)

• The issue is whether dietary macronutrients provide energy which is used in different ways in human metabolism?
So need to consider the fate of the individual nutrients, as well as total energy.

What happens when consume excess amounts of energy?
Excess intake

- If consume extra CHO, it will be used as an oxidative substrate before the dietary fat. If this (together with de-aminated protein) meets metabolic energy requirements, the dietary fat will be stored in AT etc at a low energy cost of storage (approx 2%)

- Similarly with excess intake of dietary fat, it is stored as fat with a low energy cost

- Dietary CHO stored as glycogen has an intermediate energy cost of storage (approx 8%)

- If the CHO intake exceeds energy requirements, it will be used for fat synthesis at a much higher energy cost (approx 25%)
Risk factors for increased energy intake

• Factors which promote ‘passive’ overconsumption
  – Energy dense foods – particularly High fat, but also processed CHO with little water/fibre
  – Drinks containing energy
  – Large portions

• Potential Meal Frequency related factors
  – Eating patterns
  – Breakfast
  – Snacks
Over-eating with high fat, energy dense foods (Stubbs et al)

Subjects unaware of actual dietary fat content, ate similar weights of food on the 3 diets. With the high fat diet they had an excess energy intake and went into positive energy and fat balance.
Meal patterns

• 2 wk of regular eating (3 meals and 3 snacks per day) or 2 wk Chaotic eating (3-9 eating occasions per day)

• Measured fasting blood lipids and insulin sensitivity, postprandial thermogenesis and insulin sensitivity, reported food intake
Chaotic eating in obese women – reduces energy expenditure and insulin sensitivity at a test meal

(Farshchi et al, AJCN, 2005)
Chaotic eating in non-obese women reduces dietary thermogenesis and insulin sensitivity.

Postprandial thermogenic and insulin responses to a high CHO test meal.

Figure 3: Mean (±s.e.m.) AUC (above the baseline) for the serum insulin profiles in nine healthy lean women responding to a high-carbohydrate test meal before and after the regular and irregular meal patterns. There was a significant interaction between pre- and
Reported dietary intake in non-obese women

<table>
<thead>
<tr>
<th></th>
<th>Regular meal pattern</th>
<th>Irregular meal pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>Energy (MJ)</td>
<td>8.18 ± 0.98</td>
<td>7.88 ± 0.47</td>
</tr>
<tr>
<td>Mean EI</td>
<td>8.01</td>
<td></td>
</tr>
<tr>
<td>Protein(%)</td>
<td>15.0 ± 5.6</td>
<td>14.2 ± 4.0</td>
</tr>
<tr>
<td>Fat(%)</td>
<td>42.4 ± 7.1</td>
<td>37.6 ± 7.5</td>
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<tr>
<td>CHO(%)</td>
<td>42.6 ± 8.3</td>
<td>45.5 ± 7.4</td>
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</tbody>
</table>

Overeating with erratic pattern
Breakfast

2 weeks of normal breakfast consumption or delaying the cereal and milk until 12-00. Mid-morning snack at 10-30 on both periods.

Mean daily nutrient intake and macronutrient composition (as % of energy) during the intervention periods:

<table>
<thead>
<tr>
<th></th>
<th>Eating breakfast period</th>
<th>Omitting breakfast period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (MJ)</td>
<td>6.97 ± 0.59</td>
<td>7.35 ± 0.65²</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>14.5 ± 2.2</td>
<td>15.1 ± 2.3</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>34.5 ± 4.4</td>
<td>34.5 ± 2.3</td>
</tr>
<tr>
<td>Carbohydrate (% of energy)</td>
<td>50.4 ± 5.1</td>
<td>48.5 ± 3.8</td>
</tr>
</tbody>
</table>

1 All values are $\bar{x} \pm SD; n = 10$. There were no significant differences in macronutrient composition over the course of the experiment.
2 Significantly different from the eating breakfast period, $P = 0.001$ (paired $t$ test).

So the same energy at different times of the day alters the effect on energy intake and metabolism.

Increased food intake

Insulin resistance
Effect of protein preload content on subsequent ad-libitum intake

Standard breakfast, mid-morning liquid preload, ad-libitum lunch

Table 1. Nutrient composition of preloads

<table>
<thead>
<tr>
<th>Preload</th>
<th>Study 1</th>
<th></th>
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<th></th>
<th>Study 2</th>
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<tr>
<td></td>
<td>0</td>
<td>12.5</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>10</td>
<td>20</td>
<td>40</td>
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<tr>
<td>Energy (kJ)</td>
<td>0</td>
<td>1674</td>
<td>1674</td>
<td>1674</td>
<td>0</td>
<td>1046</td>
<td>1046</td>
<td>1046</td>
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<tr>
<td>Protein (g)</td>
<td>0</td>
<td>12.9</td>
<td>25.4</td>
<td>50.4</td>
<td>0</td>
<td>6.8</td>
<td>13.1</td>
<td>25.4</td>
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<tr>
<td>Energy (%)</td>
<td>0</td>
<td>13</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>10</td>
<td>21</td>
<td>41</td>
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<tr>
<td>Carbohydrate (g)</td>
<td>0</td>
<td>63.9</td>
<td>51.6</td>
<td>25.6</td>
<td>0</td>
<td>30.6</td>
<td>24.0</td>
<td>11.2</td>
</tr>
<tr>
<td>Energy (%)</td>
<td>0</td>
<td>64</td>
<td>51</td>
<td>25</td>
<td>0</td>
<td>49</td>
<td>38</td>
<td>18</td>
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<td>Fat (g)</td>
<td>0</td>
<td>10.2</td>
<td>10.5</td>
<td>10.9</td>
<td>0</td>
<td>11.2</td>
<td>11.3</td>
<td>11.3</td>
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<tr>
<td>Energy (%)</td>
<td>0</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>0</td>
<td>41</td>
<td>41</td>
<td>41</td>
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<tr>
<td>Energy density (kJ/ml)</td>
<td>0</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
<td>0</td>
<td>2.6</td>
<td>2.6</td>
<td>2.6</td>
</tr>
</tbody>
</table>
Effects of protein preload content on ad-libitum lunch intake

24 men and women per study

12 men and 12 women per study

Main effect in Men rather than women
Preload/snack composition

- Protein is acutely more satiating than CHO
- Is the effect sustained?
Snack Bars

- **Protein-polydextrose snack**
  Relatively high proportion of energy from whey protein

- **Control snack**
  Similar energy
  Minimal protein
  No added polydextrose
  (Carbohydrate and Fat only)

- **Assigned random code so study could be conducted as a double blind randomized control trial**
Not just an effect of protein, but it does seem to be sustained (at least for 2 weeks)
Longer term aspects of higher protein diets

- A Johnstone (2012): for short-to-medium-term intervention studies (over several months), increasing the energetic contribution of protein does appear effective. Further research is warranted to validate the physiological effects of HP diets over longer periods of time

- Diogenes – 6 months

- Preview – will be 3 years
Diogenes study

Initial 8% weight loss with low energy diet then randomised to 1 of 5 treatments to assess effect on weight maintenance for next 6 months

HP-LGI has best effect on weight maintenance

<table>
<thead>
<tr>
<th>No.</th>
<th>LP-LGI</th>
<th>150</th>
<th>116</th>
<th>121</th>
<th>118</th>
<th>112</th>
<th>104</th>
<th>101</th>
<th>97</th>
<th>106</th>
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<tbody>
<tr>
<td></td>
<td>LP-HGI</td>
<td>155</td>
<td>118</td>
<td>114</td>
<td>118</td>
<td>108</td>
<td>104</td>
<td>95</td>
<td>91</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>HP-LGI</td>
<td>159</td>
<td>132</td>
<td>136</td>
<td>131</td>
<td>125</td>
<td>116</td>
<td>118</td>
<td>114</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>HP-HGI</td>
<td>155</td>
<td>130</td>
<td>124</td>
<td>121</td>
<td>118</td>
<td>114</td>
<td>100</td>
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<td></td>
<td>Control</td>
<td>154</td>
<td>126</td>
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<td>125</td>
<td>131</td>
<td>125</td>
<td>118</td>
<td>110</td>
<td>114</td>
</tr>
</tbody>
</table>
EU FP7 – Preview project

• Started July 2013 – 2500 IGT/IFG people to be recruited
• Initial 8% weight loss
  – high protein & low GI or normal weight maintenance diet
  – plus moderate or high intensity exercise in physical activity

• Outcome is glucose control/diabetes incidence over next 3 years
Dietary carbohydrate

• Is there a difference between different types of carbohydrates in terms of energy intake, body weight/composition/metabolism?
  – Glycaemic index
  – Sugars

• Is fructose a particular concern?
Glycaemic index/load

• Association between a higher GI/GL diet and increased incidence of type 2 diabetes mellitus (RR 1.03, 95% CI 1.01, 1.06, for each two GI unit increase; p=0.01: RR 1.03, 95% CI 1.00, 1.05, for each 20 GL unit increase; p=0.02)

• Also associations between higher GI and cholesterol, LDL cholesterol and higher GL and lipids, DBP, and CV disease

• What are acute effects of a high GI meal / diet?
Liver and muscle MRS – Lipid and glycogen

**Graph:**
- EMCL CH$_2$
- IMCL CH$_2$
- EMCL CH$_3$
- IMCL CH$_3$

**Frequency (ppm):**
- 2.5

**Image:**
- Normal Volunteer MRI scan showing water, choline, PME, and lipids.
Impact of low v. high GI/GL diets on liver glycogen and lipid (MRS) in healthy young men
(Bawden et al, unpublished)

- Acute effect of a high GI or low GI meal – same CHO content (thus different GL)

- 7 d on High or Low GI diet, fed to meet energy requirements

- Acute response to High or Low GI meal after 7 d on diet
Theoretical aspects

• Sugars Sweetened Beverages (and other energy containing drinks) may be poorly recognised by ‘appetite / satiety’ systems.
  – Could lead to passive overconsumption of energy

• Metabolic effects of fructose (how does it differ from glucose?)
  – Does not stimulate insulin secretion
  – Stimulates hepatic de novo lipogenesis ( Increases liver fat, increases serum TG) – glucose may do the same
  – Depletes hepatic ATP – but at what ‘dose’?
Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies

Lisa Te Morenga research fellow\textsuperscript{1,2}, Simonette Mallard research assistant\textsuperscript{1}, Jim Mann professor\textsuperscript{1,2,3}
Fig 3 Effect of reducing intake of free sugars on measures of body fatness in adults.

Fig 4 Effect of increasing free sugars on measures of body fatness in adults. Po
**Treatments <8 weeks duration**

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bantle 1992</td>
<td>-0.20 (-1.63 to 1.23)</td>
</tr>
<tr>
<td>Bantle 1993</td>
<td>1.00 (-0.43 to 2.43)</td>
</tr>
<tr>
<td>Koivistö 1993</td>
<td>-0.90 (-2.17 to 0.37)</td>
</tr>
<tr>
<td>Malerbi 1996 (1)</td>
<td>0.01 (-0.11 to 0.13)</td>
</tr>
<tr>
<td>Malerbi 1996 (2)</td>
<td>0.70 (0.09 to 1.31)</td>
</tr>
<tr>
<td>Mann 1972b</td>
<td>0.10 (-0.04 to 0.24)</td>
</tr>
<tr>
<td>Mann 1973</td>
<td>0.11 (-0.43 to 0.46)</td>
</tr>
<tr>
<td>Peterson 1986 (3)</td>
<td>0.10 (0.10 to 0.46)</td>
</tr>
<tr>
<td>Peterson 1986 (4)</td>
<td>0.30 (0.13 to 0.73)</td>
</tr>
<tr>
<td>Swanson 1992</td>
<td>0.01 (-0.11 to 0.13)</td>
</tr>
</tbody>
</table>

Subtotal (95% CI)

Test for heterogeneity: $\chi^2=11.50$, df=9, $P=0.24$, $I^2=22%$

Test for overall effect: $z=1.64$, $P=0.10$

**Treatments ≥8 weeks duration**

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grigorescu 1988</td>
<td>-0.10 (-0.24 to 0.04)</td>
</tr>
<tr>
<td>Osei 1989</td>
<td>2.50 (-1.11 to 6.11)</td>
</tr>
<tr>
<td>Santacroce 1990</td>
<td>0.00 (-0.78 to 0.78)</td>
</tr>
</tbody>
</table>

Subtotal (95% CI)

Test for heterogeneity: $\chi^2=2.05$, df=2, $P=0.36$, $I^2=2%$

Test for overall effect: $z=0.97$, $P=0.33$

Total (95% CI)

Test for heterogeneity: $\chi^2=17.57$, df=12, $P=0.13$, $I^2=32%$

Test for overall effect: $z=1.03$, $P=0.30$

Test for subgroup differences:

$\chi^2=2.42$, df=1, $P=0.12$, $I^2=58.6%$

(1) Fructose vs starch, (2) Sucrose vs starch, (3) Patients with type 1 diabetes, (4) Patients with type 2 diabetes

**Fig 5** Isoenergetic exchanges of free sugars with other carbohydrates or other m:
Interesting that this figure is described as free sugars intake, but it is a plot of SSB
Te Morenga Review

Abstract: ……In trials of adults with ad libitum diets (that is, with no strict control of food intake), reduced intake of dietary sugars was associated with a decrease in body weight (0.80 kg, 95% confidence interval 0.39 to 1.21; P<0.001); increased sugars intake was associated with a comparable weight increase (0.75 kg, 0.30 to 1.19; P=0.001). Isoenergetic exchange of dietary sugars with other carbohydrates showed no change in body weight (0.04 kg, −0.04 to 0.13).

So the issue is overconsumption of energy not a problem with Sucrose/Fructose

Despite this, there is still a strong view that fructose or sucrose have serious, undesirable metabolic effects that contribute to the development/co-morbidities of obesity
Misconceptions about fructose-containing sugars and their role in the obesity epidemic. (2014) van Buul, Tappy & Brouns. Nutrition Research Reviews

.... fructose, as commonly consumed in mixed carbohydrate sources, does not exert specific metabolic effects that can account for an increase in body weight. Consequently, public health recommendations and policies aiming at reducing fructose consumption only, without additional diet and lifestyle targets, would be disputable and impractical. Although the available evidence indicates that the consumption of sugar-sweetened beverages is associated with body-weight gain, and it may be that fructose is among the main constituents of these beverages, energy overconsumption is much more important to consider in terms of the obesity epidemic.
Johnston et al, 2013, Gastroenterology –
What are the metabolic and BP effects of short term (2 weeks) high levels of consumption of fructose compared to glucose in overweight, insulin resistant men?

a) - energy balance
b) - overfeeding

32 overweight men (mean BMI 30) with large waist (mean 103.8cm) – studied for two separate 2wk periods

1\textsuperscript{st} energy balance
- 75\% from food (all supplied)
- 25\% from glucose / fructose powder added to water

2\textsuperscript{nd} overfed
- 100\% from food (own habitual intake)
- 25\% additional from glucose / fructose powder added to water
STUDY PROTOCOL

Fructose or glucose fed at 25% of energy requirements

Main assessments:
Fasted
MRI + $^1H$ MRS + $^{31}P$ MRS
Bloods + weight
Indirect calorimetry
12/32 Insulin clamp

Mid assessments:
Fasted
Bloods + weight

15 weeks
Fructose energy balance

17 weeks
Glucose energy balance

6 wk washout

2 weeks
Fructose overfeed

2 weeks
Glucose overfeed
At energy balance, Fructose and Glucose had no effect on liver fat content. With overfeeding, Fructose and Glucose both increased liver fat content.
IMCL (soleus muscle triglyceride)
All data

No differences between Fructose and Glucose
No effect on BP or SNS activity with either sugar in either condition, no change in glucose clamp insulin sensitivity

Fructose during ‘isocaloric’ feeding was associated with small increases in uric acid and fasting insulin resistance (HOMA-IR) but neither sugar affected these or any other serum variables (except TAG) during overfeeding

P-MRS showed no effect of fructose on liver ATP (and subsequently found no effect of acute oral fructose on ATP
Fructose v Glucose

• In overweight men with elevated liver fat content, ‘calories’ from fructose and glucose are not substantially different

• The state of energy balance is more important than the type of monosaccharide

• Do not know if similar effects would be seen if fat was overfed in comparison to glucose/fructose
Are all ‘calories’ equal?

• In physical chemistry terms – YES, of course

• In Biological/Nutritional terms, the different macronutrients are handled differently, especially if eaten to excess

• With particular relevance to CHO, there may be differences between high/low GI CHO in terms of the metabolic effects

• Beverages containing energy (predominantly CHO) may also increase the risk of passive overconsumption of energy

• The timing of meals and regularity of meal patterns may also impact on the effect of dietary energy