Is obesity a choice?

Giles Yeo

@GilesYeo
Energy balance

Energy Intake
- Food Intake

Energy Expenditure
- Basal Metabolism
- Physical Activity
- Adaptive Thermogenesis
Twin studies

Heritability of BODY WEIGHT ~ 70%
Brain control of food intake

Brain response and translation

Genetic modifiers

Hormonal and nutritional cues

Yeo and Heisler, 2012
Human congenital leptin deficiency

3yr old weighing 42kg

7yr old weighing 32kg

Daily leptin treatment

Farooqi et al, NEJM 1999
Labrador retrievers

Raffan et al, Cell Metabolism 2016
Prevalence

<table>
<thead>
<tr>
<th>All Labradors</th>
<th>Labrador guide assistance dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td>78%</td>
</tr>
<tr>
<td>Hets</td>
<td>20%</td>
</tr>
<tr>
<td>Homs</td>
<td>2%</td>
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</tbody>
</table>

Effect size: Labradors 1.90kg per deletion allele = 0.33 SDs body weight

Raffan et al, Cell Metabolism 2016
A frameshift mutation in *MC4R* associated with dominantly inherited human obesity

Giles S.H. Yeo, I. Sadaf Farooqi, Shiva Aminian, David J. Halsall, Richard G. Stanhope, & Stephen O'Rahilly

Height sds in *MC4R* deficient subjects

p < 0.002
A missense variant of the porcine melanocortin-4 receptor (MC4R) gene is associated with fatness, growth, and feed intake traits

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Melanocortin 4 receptor mutations contribute to the adaptation of cavefish to nutrient-poor conditions

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(a) river (b) Pachón cave (c) Chica cave (d) Subterráneo cave
GWAS and common obesity
Your genes are like a hand of poker

You can’t do anything about the cards you have
But you can choose how to play them
Are we all sinners?
With thanks

Sir Stephen O’Rahilly
Tony Coll

Brian Lam
Marcella Ma
Loraine Tung

Eleanor Raffan

John Tadross
Anna Maria Siegert
Georgina Dowsett
Irene Cimino
Marcella Ma
Maria Chukanova
Kara Rainbow
Debra Rimmington
Dave Withers