I'm going to talk today about a paradox of why the fat man is hungry

Why is the fat man hungry?

The paradox of the man who evidently has fuel to burn, but is still getting low energy signals.

it's the paradox of the man who evidently has fuel to burn but is still getting low energy signals

This is a picture of me in 2014 just before I went ketogenic

I was 44 kilograms heavier then and this fella is going to join me on this presentation and we're going to see a lot of him

See the paradox?

1: Hunger is a signal that we are running out of energy

Do you see the paradox?

Hunger is a signal that we're running out of energy

See the paradox?

1: Hunger is a signal that we are running out of energy

2: But the fat man evidently has plenty of energy!

Yet the fat man has evidently got plenty of energy you can see it on his body

Paradoxes are a good thing

I like paradoxes they're a good thing

They let you see that some of your Dogma, some of your underlying assumptions may be incorrect

Paradoxes are a good thing

- Diet heart dogma
  - Saturated fat is associated with increased LDL-cholesterol

I'll give you a good example of one for example

This one's close to our heart.

The diet heart hypothesis goes something like this;

saturated fat is associated with increased LDL cholesterol …

Paradoxes are a good thing

- Diet heart dogma
  - Saturated fat is associated with increased LDL-cholesterol
  - LDL-cholesterol is associated with cardiovascular disease

LDL cholesterol is associated with cardiovascular disease …

Paradoxes are a good thing

- Diet heart dogma
  - Saturated fat is associated with increased LDL-cholesterol
  - LDL-cholesterol is associated with cardiovascular disease
  - Saturated fat intake is associated with cardiovascular disease

So you can see the assumptions. We assume these things are both true.

If we connect the dots we can see that eating saturated fat definitely must cause heart disease

Para

- Diet h
  - Sat
  - LDL
  - Sat

Saturated Fat

Eating foods that contain saturated fats raises the level of cholesterol in your blood. High levels of LDL cholesterol in your blood increase your risk of heart disease and stroke.

https://www.heart.org/en/healthy-living/healthy-eating/eat-smart/fats/saturated-fats

It's not just me saying this this is the American Heart Association.

This is pulled off their website today

https://www.heart.org/en/healthy-living/healthy-eating/eat-smart/fats/saturated-fats

You can see down the bottom that eating foods that contain saturated fat raises the level of cholesterol in your blood high levels of LDL cholesterol in your blood increased your risk of heart disease and stroke

These are the experts

Paradoxes are a good thing

- Diet heart dogma
  - Saturated fat is associated with increased LDL-cholesterol
  - LDL-cholesterol is associated with cardiovascular disease
  - Saturated fat intake is associated with cardiovascular disease
- French paradox
  - The French have very high dietary Saturated fat intake
  - The French have very low incidence of cardiovascular disease

Then there's the French the French paradox.

The French happen to eat a lot of saturated fat because they eat a lot of butter and cream with everything and the French have some of the lowest cardiovascular disease rates in Europe

There's the paradox. How is it possible that the first three statements are correct and the second two statements are also correct?

Paradoxes are a good thing

- Diet heart dogma
  - Saturated fat is associated with increased LDL-cholesterol
  - LDL-cholesterol is associated with cardiovascular disease
  - Saturated fat intake is associated with cardiovascular disease
- French paradox
  - The French have very high dietary Saturated fat intake
  - The French have very low incidence of cardiovascular disease

A paradox means …

maybe some of our underlying assumptions are wrong

A paradox means that some of your underlying assumptions may be wrong.

Paradoxes are a good thing

- They warn us our dogma is wrong
  - Maybe the French are just different
  - Or maybe it's something in the wine
  - Or maybe, LDL associated with Saturated fat intake is DIFFERENT from the LDL associated with CVD risk.
- For more on the French paradox see the first chapter of "Why is the fat man hungry" available at fatmanhungry.com/ketofest

They basically warn us that our that something about a Dogma is incorrect

Maybe it's just the French being French or maybe it's something in the wine (like resveratrol) or some other chemical that only the French eat that protects them against cardiovascular disease

Or maybe the LDL associated with saturated fat in the diet is different from the LDL that's associated with cardiovascular disease

I go into this in the first chapter of my book on why the fat man is hungry

That's available online now immediately for everybody at this conference so just go to

https://fatmanhungry.com/Ketofest

You can download the first chapter which is all about these paradoxes and how we can use them to see if our underlying assumptions may be incorrect

Let’s return to our fat man

let's go back to our fat man

Why is the fat man hungry?

1: Hunger is a signal that we are running out of energy

2: But a fat man evidently has plenty of energy

One or more of these assumptions must be wrong.

We know hunger is a signal that we're running out of energy, and we know that a fat man has evidently plenty of energy.

One or more of these assumptions must be wrong

Hunger is a signal that we are running out of energy

- Gluttony?
- Sloth?
- Lack of discipline?
- Hyper-palatability?
- Hyper-processing?
- Not enough nutrients?
- Food deserts?
- Carbs make me “hungry”?

So what are the common assumptions about hunger;

Maybe it’s gluttony, or sloth, or just lack of discipline.
Maybe it’s hyperpalateability – the food’s just too tasty
Maybe it’s hyper processing, where we’re messing with the foods to the pointy where they do us damage
Maybe people just aren’t getting enough nutrients and they just have to keep eeating until they get all the nutrients they need
Maybe they live in food desserts where they only have caloric sources and no nutrients.
Maybe it’s just carbs or something in our food that make me hungry

Hunger is a signal that we are running out of energy

~~• Gluttony?~~
~~• Sloth?~~
~~• Lack of discipline?~~

Moral Crisis

- Hyper-palatability?
- Hyper-processing?
- Not enough nutrients?
- Food deserts?
- Carbs make me "hungry"?

The first three are about a moral crisis.

I've never liked the explanation of moral crisis because that is a supernatural explanation which is not only unsatisfying but also a lazy way of looking at the problem.

It has to be more than that because 88% of Americans are metabolically unhealthy according to the CDC, and 53% have type 2 diabetes.

That's just happened in the past 20-30 years. It's not possible that all of a sudden over half of America has a moral crisis

Hunger is a signal that we are running out of energy

- ~~Gluttony?~~
- ~~Sloth?~~
- ~~Lack of discipline?~~
- ~~Hyper-palatability?~~
- ~~Hyper-processing?~~
- Not enough nutrients?
- Food deserts?
- Carbs make me “hungry”?

Moral Crisis

Naturalistic fallacy

Hyper-palateability and Hyper-processing are a naturalistic fallacy.

You know it’s because we’re modern and we’ve been fiddling with this food in unnatural ways too much and that’s made us really sick

Some of these things may have small impacts, but I doubt if any of them have a major role to play here

Worlds greatest chef had metabolic syndrome

Joël Robuchon dropped 60 pounds after a blood test illuminated problems with high levels of cholesterol, blood pressure and blood sugar. Source: NY Post 10/31/2017

Can it be not enough nutrients?

Do you know Joël Robuchon? The best chefs in the world are awarded a Michelin star. Only a very special chef has 2 Michelin stars, and only the greatest chefs in the world have 3.

Joël Robuchon had 32 by the time he died of cancer. He was known as the greatest chef of the 20th century. There was Joël Robuchon , and the daylight, and then some more daylight, and then everyone else.

https://nypost.com/2017/10/31/how-the-worlds-most-celebrated-chef-lost-60-pounds/

He had metabolic syndrome and this guy had access to the greatest produce on the planet, flown fresh to him every day from all over the world. He did not live in a food dessert, nor did he lack for nutrients.

Hunger is a signal that we are running out of energy

- ~~Gluttony?~~
- ~~Sloth?~~
- ~~Lack of discipline?~~
- ~~Hyper-palatability?~~
- ~~Hyper-processing?~~
- ~~Not enough nutrients?~~
- ~~Food deserts?~~

Moral Crisis

Naturalistic fallacy

Nutrient deficiency?

- Carbs make me "hungry"?

If micro-nutrient deficiency was responsible for diabetes a multivitamin would cure diabetes.

Let’s table carbs for now

I promise we’ll get back to that in a minute.

Let’s table Carbs make me hungry for now, I promise we’ll get back to that

So that's one part of the picture hunger. Hunger is a fuel signal that we need energy. The other part of the picture is a fat man has clearly plenty of energy

A fat man evidently has plenty of energy

2014 Richard

Body weight:	150 kg ≈ 330 lbs
Fat mass (guesstimate):	70 kg ≈ 154 lbs
"Available" energy:	70 kg x 1000 g/kg x 9 kCal/g
	630,000 kCal

This is 2014 Richard. His body weight was 150 kilograms roughly 330 pounds

I'm guessing my fat mass at that point. My lean mass currently is around about 83 kilograms so it I'm guessing maybe it might have been 70 kilograms.

We will use that as a guesstimate roughly 154 pounds of body fat
Doig the math my available energy was 70 kilograms multiplied by a 1000 grams/kilogram multiplied by the Attwater factor for fat which is 9 kilocalories/gram

Obviously I had 630,000 kilocalories at my disposal

A fat man evidently has plenty of energy

2014 Richard

Body weight:	150 kg ≈ 330 lbs
Fat mass (guesstimate):	70 kg ≈ 154 lbs
"Available" energy:	70 kg x 1000 g/kg x 9 kCal/g
	630,000 kCal

But how much of that potential energy can we access?

But how much of that potential energy can I access

Can we use all of it at once?

Can for example can we use all of that energy at once

A fat man evidently has plenty of energy

2014 Richard = 630,000 kCal

1 stick of Dynamite = 478 kCal

A stick of dynamite is roughly 478 Kilocalories of energy
A stick of dynamite releases all of its energy immediately

A fat man evidently has plenty of energy

2014 Richard = 630,000 kCal

1 stick of Dynamite = 478 kCal

1 x 2014 Richard = 1318 sticks

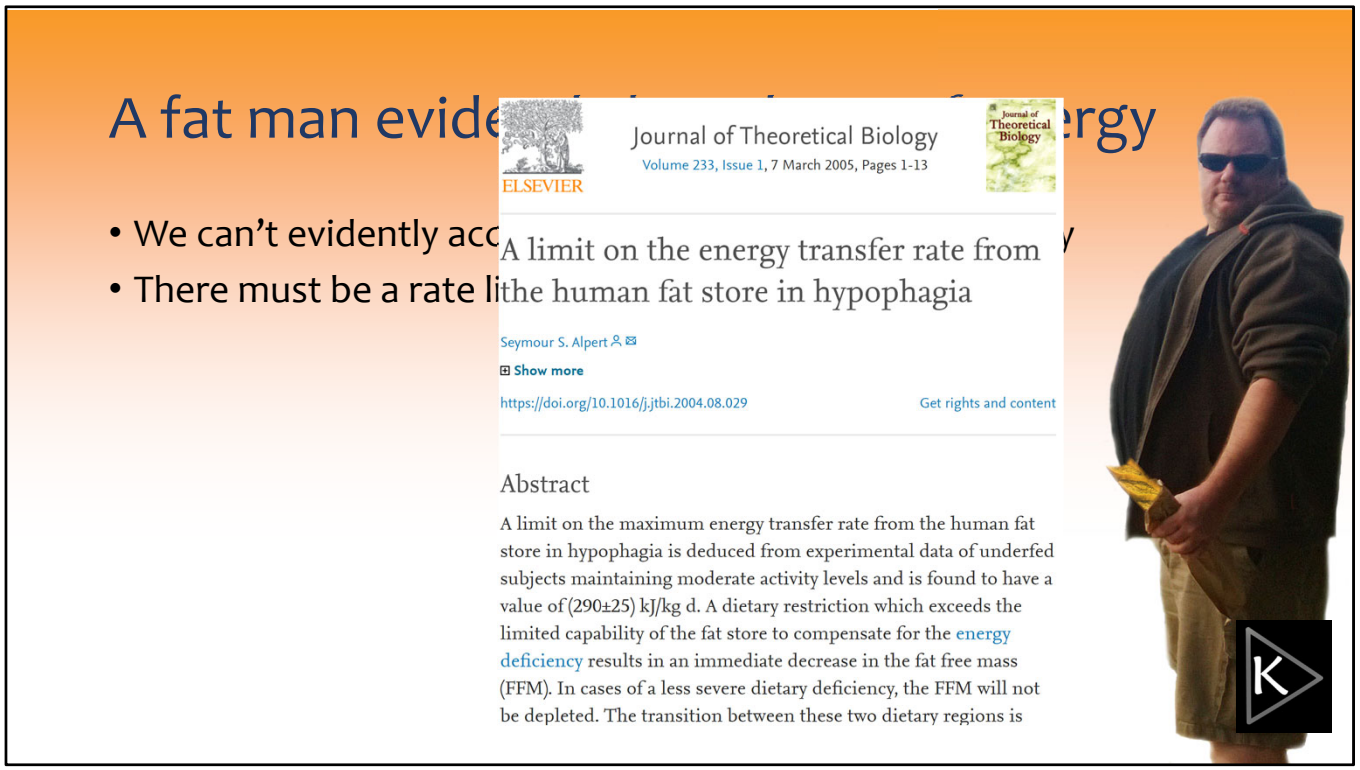
2014 Richard is roughly 1318 sticks of dynamite

A fat man evidently has plenty of energy

- We can’t evidently access an unlimited amount of energy
- There must be some rate limit

Evidently we can't access all of this energy immediately or if a fat man went for a run he might likely self combust so there must be some rate limit involved in how fast we can get energy out of body fat

So just seeing a fat man doesn't necessarily mean he's able to produce adequate calories



Seymore Alpert in 2004 took the data from Ancel Key's Minnesota starvation studies, and determined that the maximum rate that body fat releases energy in a day is 290kj/kg (body fat) 31.5 kCal/lb (body fat)

https://www.ncbi.nlm.nih.gov/pubmed/15615615

The 1944 Minnesota semi-starvation experiment was a 24 week study into men put on a calorie restriction (1500 kCal/day) to reduce their body weight by 25%, followed by a recovery phase.

Alpert re-analysed the weight loss data data looking at how much energy in these subjects was coming from fat mass, and how much was coming from fat-free mass. He determined mathematically the maximal rate at which body fat release energy, beyond which the body would turn to lean tissue.

"A dietary restriction which exceeds the limited capability of the fat store to compensate for the energy deficiency results in an immediate decrease in thin the fat free mass"

A fat man evidently has plenty of energy

- We can't evidently access an unlimited amount of energy
- There must be a rate limit

- One pound of body fat can release 31.5 kCal/day

2014 Richard = 70kg x 2.2 kg/lb x 31.5 kCal/lb
= 4,851 kCal/day
from 630,000 kCal

If I'd had 10 lbs of body fat, I could generate 315 kCal per day, if I'd had 20 lbs of body fat I could generate 630 kCal/day. At 70kgs of body fat, or 154 lbs I could generate 4,851 kCal/day from my reserves.

4,851 kCal/day should have been more than adequate for a good day of energy consumption.

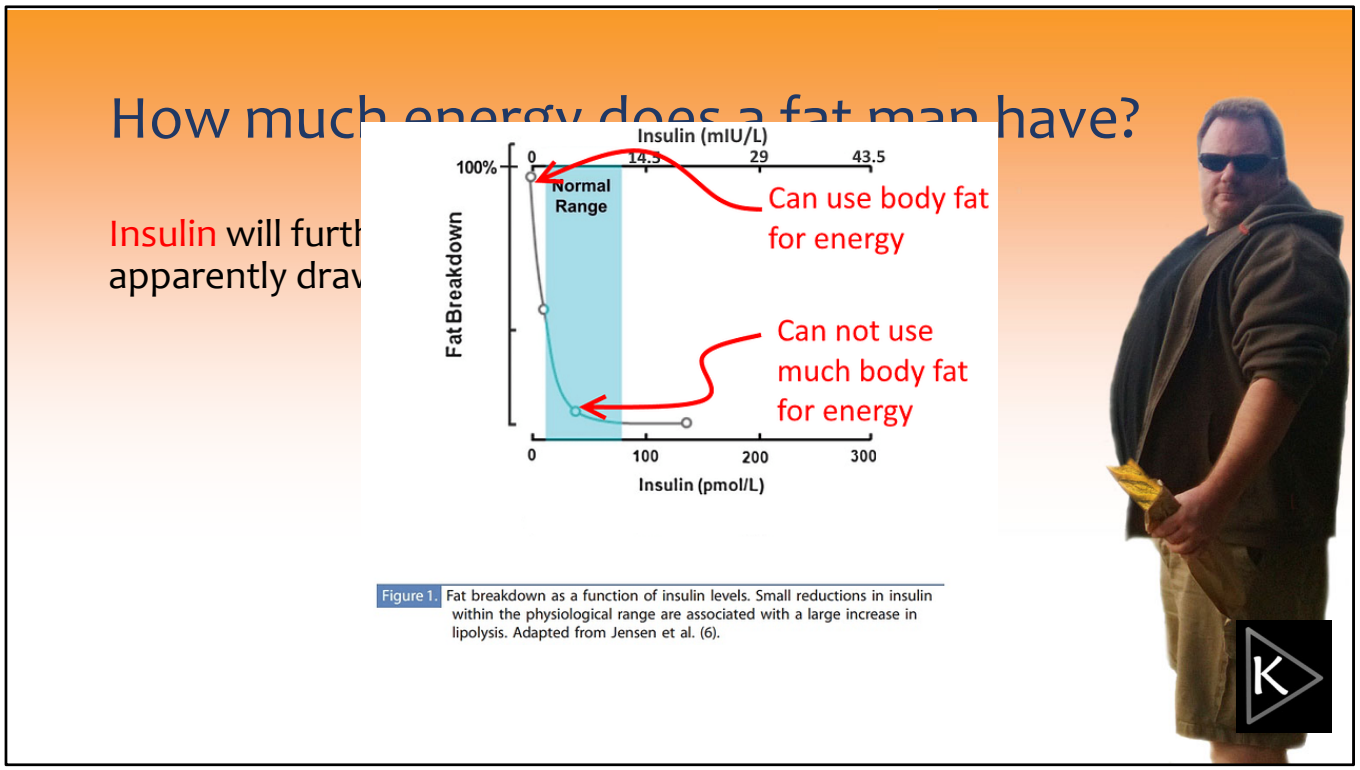
So in theory I should have had enough energy stored in my body fat, that I should have never been hungry.

Why was I hungry ALL THE TIME?

How much energy does a fat man have?

Insulin will further affect how much energy we can apparently draw from body fat

We know that insulin will affect how much energy fat cells are willing to release



This is a meme I created from a chart in a Men's health article by Jeff Volleck showing that as insulin goes up, the free fatty acids released by fat cells for the rest of the body to use for energy drops.

The original chart measure insulin in pmol/L which is a research unit, most of us who have had our fasting insulin measured have been given our result in mIU/L – so I added the extra X-axis along the top to translate the units and pointed out the amount of body fat we can release at low and moderate levels of insulin.

Worth pointing out here the blue band is the NORMAL range of fasting insulin. The first measurement of fasting insulin I ever had was 29 mIU/l (or 200 pMol/l).

How much energy does a fat man have?

Insulin will further aff n
apparently draw fron

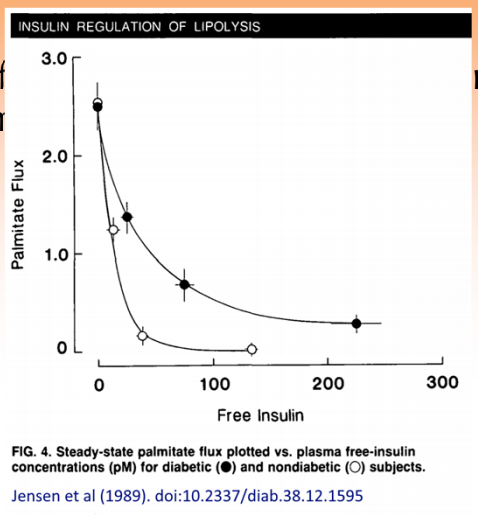


FIG. 4. Steady-state palmitate flux plotted vs. plasma free-insulin concentrations (pM) for diabetic (●) and nondiabetic (○) subjects.

Jensen et al (1989). doi:10.2337/diab.38.12.1595

This is the chart from the original paper Jensen et al 1089

https://www.ncbi.nlm.nih.gov/pubmed/2573554

And you'll see that diabetics (shown here as black dots) get a little more leeway than normal subjects (white dots). Even when insulin is high diabetics can release a little fat from body fat for use by the remainder of the body as energy, where a normal person that would be completely inhibited.

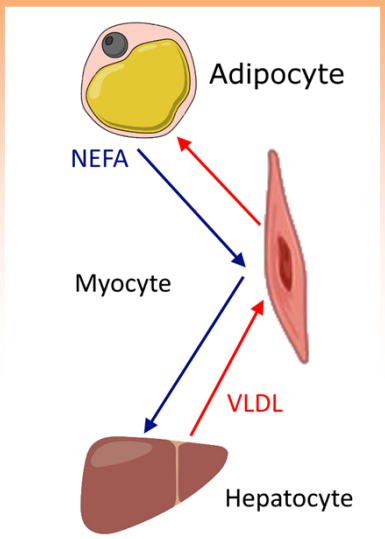
How much energy does a fat man have?

- Insulin regulates availability of fuel from the SOURCE
- Insulin ALSO regulates availability of fuel at the SINK

So we're going to get less fuel released from body fat when insulin is high than the theoretical maximum. But in a fasted person that is just the SOURCE of fuel.

We need to also look at the SINK for that fuel, where is it headed in order to be turned into energy.

How much energy does a fat man have?



This is a simplified look at the source and sink of fuel in a fasted person.

I like to think of fat at the top of the picture, and it releases fuel as non esterified fatty acids (NEFA).

NEFAs bound to sheets of the lipoprotein albumin deliver that fuel to the peripheral tissue (like a muscle cell -myocyte).

At the bottom of my picture is the liver, which hoovers up all the unused fuel and turns them back into triglycerides and packs those into a different lipoprotein called a vLDL particle.

vLDL then transports the unused fuel back past the peripheral cells which can draw some as they need and eventually the final consumer for fuel is the fat cell which stores it, to begin the cycle again.

We did a keto fest in Australia in Canberra and we tested Carl on a respiratory exchange ratio (RER) machine. He had to put this device in his mouth and breathe through it.

How much energy does a fat man have?

- Insulin regulates availability of fuel from the source
- But insulin ALSO regulates availability of fuel at the SINK

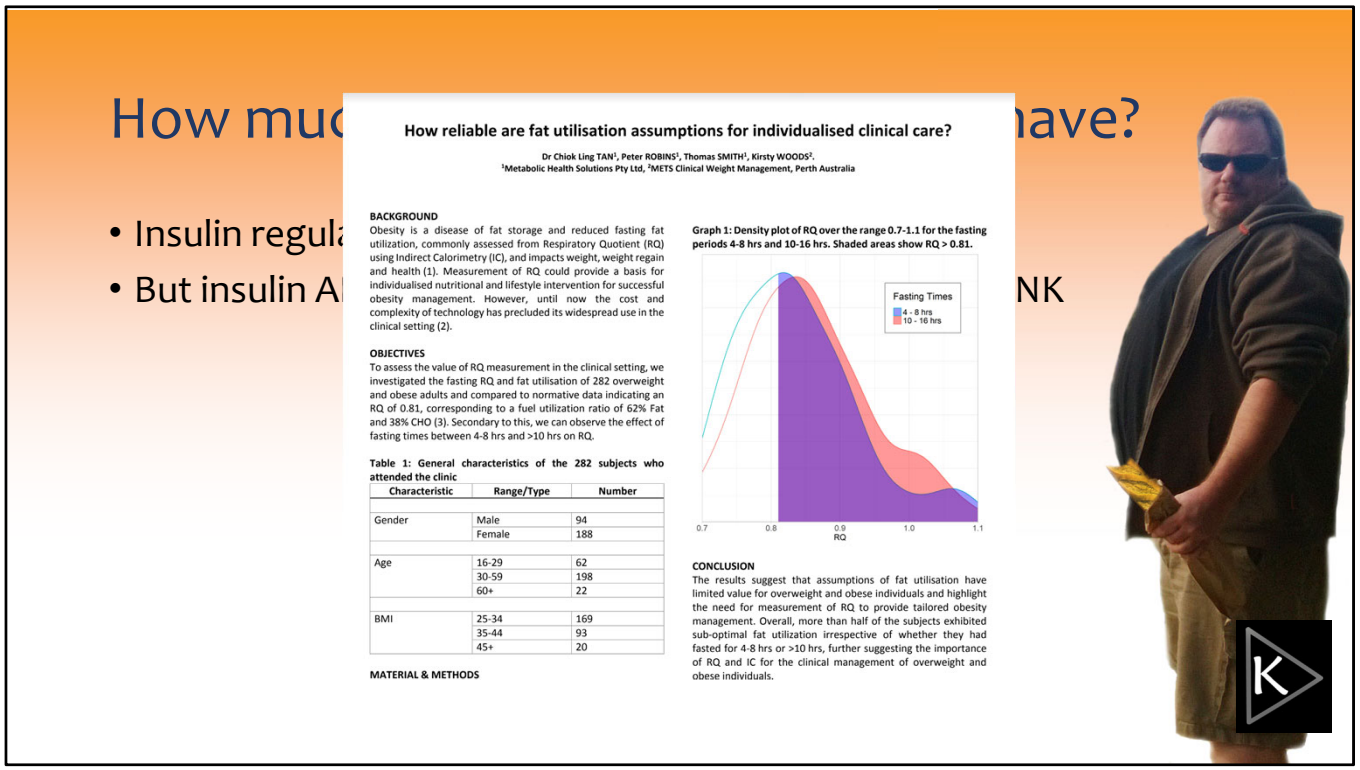
- Respiratory Exchange ratio testing at Metabolic HEALTH SOLUTIONS

This device was from http://metabolichealth.com.au/

It measured the O_2 that Carl breathed in, and the O_2 he breathed out unused as well as the CO_2 he breathed out. This could tell us how much energy he was making, his resting metabolic rate, as well as what he was making that energy from.

If you are burning glucose for energy your respiratory exchange ratio (RER) also knon as a Respiratory quotient (RQ) will be 1.0.

If you are burning fatty acids for energy your RER will be 0.7.



This density plot is from a poster presentation this company did looking at the RER of 282 overweight and obese subjects fasted for 4-8 hours, and 10-16 hours.

Look at the lighter pink area, this is people fasted for at least 4 hours, a few are burning fat (RQ=0.7), some are burning glucose (RQ=1.0) but most are burning a mix of fat+glucose+protein.

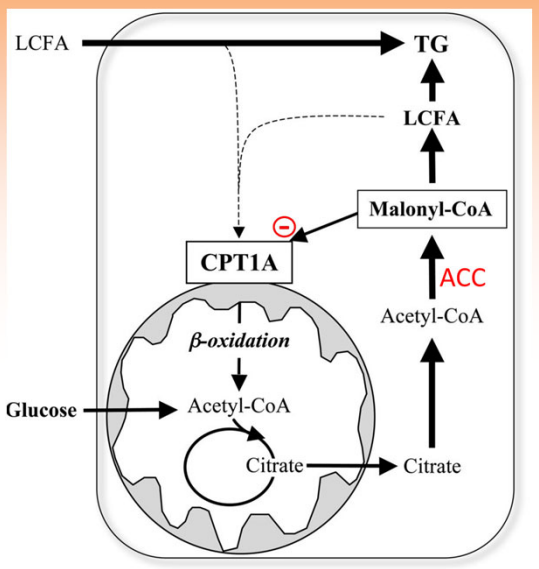
Now look at the darker purple area, this is people fasted for at least 10 hours. Most should be running exclusively from fat, the curve should have shifted right to the left over 0.7 … but most overweight and obese people are still burning mixed fuel. Much fewer are now burning just glucose (1.0) . The majority are around 0.8 burning fat+glucose+a lot more protein.

Fat men just don’t oxidize fatty acids very well

Why is that, then?

This is the secret – Fat men just don’t oxidize fatty acids very well.

Making fat inhibits burning it



When we make fat our liver cells shut off the ability to burn fat and that makes sense because what they're doing is their job is to take excess energy and export it out to cells that are responsible for storing or using excess energy

This liver cell shows a mitrochondria where fuel is converted into energy. Fuel comes in to the liver cells as glucose and long chained fatty acids (LCFA)

Glucose is converted to the universal fuel Acetyl-CoA, and it takes a spin around the citrate (Krebs) cycle and some is made into our energy currency "ATP" and some escapes the mitochondria to be made into Malonyl-CoA using an enzyme called Acetyl-CoA Carboxylase (ACC) and eventually new fat (TG) where it is exported out of the cell to be used or stored.

Long chained fatty acids (LCFA) enter the cell and they have to be escorted into the mitochondria by a transport called Carnitine-Palmitoyl-Transferase 1A (CPT 1A)

That shuttle is inhibited by Malonyl-CoA. So the very process of making fat turns off our ability to get fat into our mitochondria to be burned.

Making fat inhibits burning it

Acetyl-CoA carboxylase is the enzyme that when activated switches us from burning fat to making fat

Acetyl-CoA carboxylase is this enzyme that when activated switches us from burning to making fat.

Insulin inhibits burning fat

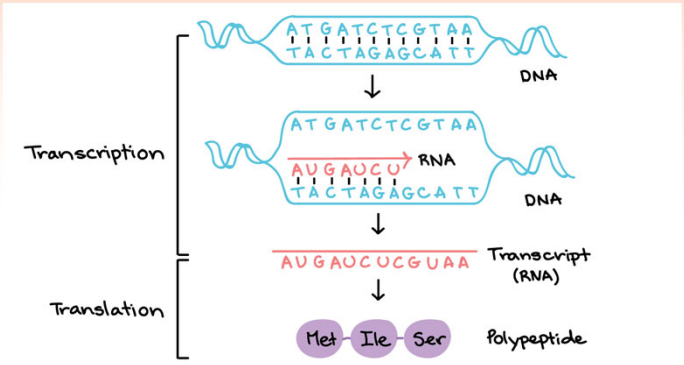
- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase

Insulin promotes the creation of this enzyme 4 fold.

So people who have insulin high make 4 times the amount of this enzyme. And people who have insulin high ALL THE TIME make 4x this enzyme ALL THE TIME.

Insulin inhibits burning fat

- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase



I spent time studying the mechanism of genetics this year. Most people think of protein as a macronutrient or maybe it's something you make your body from. But the reality is that protein is what we make from DNA.

We have a double stranded helix of DNA, containing maybe 30,000 genes.

We transcribe those genes into short segments of RNA

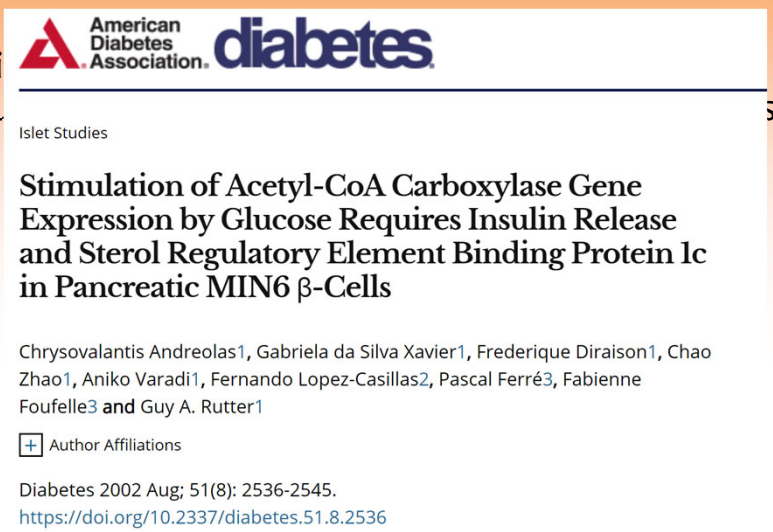
We translate that RNA into proteins.

Enzymes are proteins. This Acetyl-CoA Carboxylase is made from instructions in DNA, and the process that begins the transcription is activated by insulin signalling.

Insulin promotes the transcription of this sequence of DNA to eventually make this enzyme ACC that shifts us from burning fat to making new fat.

Insulin inhibits burning fat

- Insuli
  instru



American Diabetes Association. diabetes

Islet Studies

Stimulation of Acetyl-CoA Carboxylase Gene Expression by Glucose Requires Insulin Release and Sterol Regulatory Element Binding Protein 1c in Pancreatic MIN6 β-Cells

Chrysovalantis Andreolas1, Gabriela da Silva Xavier1, Frederique Diraison1, Chao Zhao1, Aniko Varadi1, Fernando Lopez-Casillas2, Pascal Ferré3, Fabienne Foufelle3 and Guy A. Rutter1

Author Affiliations

Diabetes 2002 Aug; 51(8): 2536-2545.
https://doi.org/10.2337/diabetes.51.8.2536

se

Insulin signalling promotes the expression of Acetyl-CoA carboxylase

http://doi.org/10.2337/diabetes.51.8.2536

In a normal person, that makes sense when glucose is high, so is inulin, and we need to turn some of that glucose into new fat.

In someone who has insulin high all the time, a hyperinsulinaemic (AKA a pre-diabetic), they are making up to 4x more of that enzyme even when glucose is low.

Insulin inhibits burning fat

- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase
- Insulin dephosphorylates Acetyl-CoA carboxylase activating it

Insulin signalling doesn't just mean more of the enzyme.

It activates the enzyme.

Insulin inhibits burning fat

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PNAS
Proceedings of the National Academy of Sciences of the United States of America

Proc Natl Acad Sci U S A. 1988 Aug; 85(15): 5473–5477.
doi: 10.1073/pnas.85.15.5473
PMCID: PMC281779
PMID: 2899891

Insulin stimulates the dephosphorylation and activation of acetyl-CoA carboxylase.

L A Witters, T D Watts, D L Daniels, and J L Evans

Many enzymes have triggers that will turn them on or turn them off. For example some enzymes are activated by the components of the reaction they enable, and deactivated by the products of the reaction. This is how we regulate for example the production of things we need in small amounts.

Insulin signalling activates Acetyl-CoA Carboxylase (ACC) by dephosphorylating it.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC281779/

Someone with chronic high insulin not only could have 4x as much of the enzyme, it's likely all in an active state. Any Acetyl-CoA in the cytosol of the cell will be greedily converted into Malonyl-CoA and eventually new fat while turning off the burning of fatty acids.

Insulin inhibits burning fat

- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase
- Insulin dephosphorylates Acetyl-CoA carboxylase activating it
- Activated Acetyl-CoA carboxylase diverts fuel (Acetyl-CoA) from turning into energy, to make Malonyl-CoA

This switch, triggered by insulin, results in fuel being diverted from making new energy into making malonyl-CoA instead.

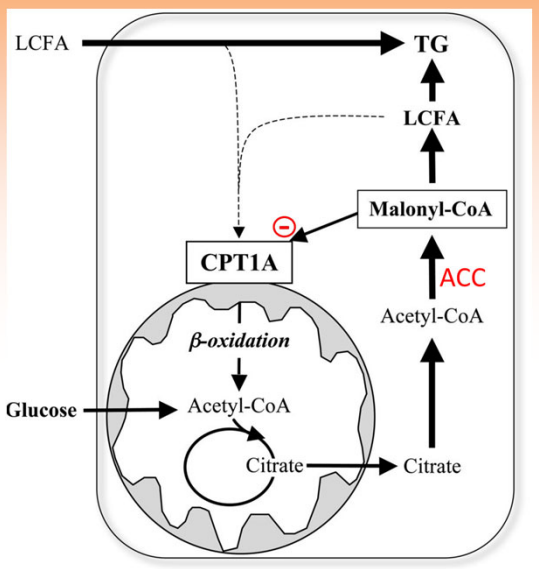
Insulin inhibits burning fat

- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase
- Insulin dephosphorylates Acetyl-CoA carboxylase activating it
- Activated Acetyl-CoA carboxylase diverts fuel (Acetyl-CoA) from turning into energy, to make Malonyl-CoA
- Malonyl-CoA eventually becomes a new fatty acid

Malonyl-CoA inhibits any new long chained fats getting into the mitochondria limiting the available fuel to glucose, amino acids, and short and medium chained fatty acids.

Malonyl-CoA eventually becomes new Palmitic acid (a long chained fatty acid) that is exported to the rest of the body to be stored.

Insulin inhibits burning fat



And you can see ACC making Malonyl-CoA and inhibiting the Carnitine shuttle (CPT1A) preventing long chained fatty acids from being utilized for fuel.

A fat man evidently has plenty of energy

- Insulin promotes the transcription from DNA of the instructions to make 4x more Acetyl-CoA carboxylase
- Insulin dephosphorylates Acetyl-CoA carboxylase activating it
- Activated Acetyl-CoA carboxylase diverts fuel (Acetyl-CoA) from turning into energy, to make Malonyl-CoA
- Malonyl-CoA eventually becomes a new fatty acid
- Malonyl-CoA inhibits shuttling fatty acids into Mitochondria

I wanted to find some studies that gave us an idea of the scale of this.

If it's just a fraction of fuel being diverted into making new fuel then it's just a biochemical mechanistic curiosity.

It turns out that we can become Malonyl-CoA resistant when we have too much of it, just like we can become Insulin resistant. That means that even in people who make a lot of Malonyl-CoA, they might be able to still squeak a little long chained fats into their mitochondria.

Measures of Malonyl-CoA resistance would give us an idea of the scale of hw much new fat diabetics make instead of energy.

A fat man evidently has plenty of energy

- Diabetic Rats have been shown to have 50x increase in malonyl-CoA $K_{inhibition}$ inhibition of CPT-I
- They make 50x more new fatty acids on the same chow

BIOCHEMICAL JOURNAL — PORTLAND PRESS

Biochem J. 1995 Sep 15; 310(Pt 3): 853–858.
doi: 10.1042/bj3100853

PMCID: PMC1135974
PMID: 7575418

Insulin regulates enzyme activity, malonyl-CoA sensitivity and mRNA abundance of hepatic carnitine palmitoyltransferase-I.

E A Park, R L Mynatt, G A Cook, and K Kashfi

Author information · Copyright and License information Disclaimer

This study quantified in diabetic rats the rate constant of inhibition of the carnitine shuttle to Malonyl-CoA.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1135974/

Ki for Malonyl-CoA in these rats was 50x greater than in non-diabetic rats.

In other words the diabetic rats were making 50x the new fat all the time, than non-diabetic rats were – eating the same food.

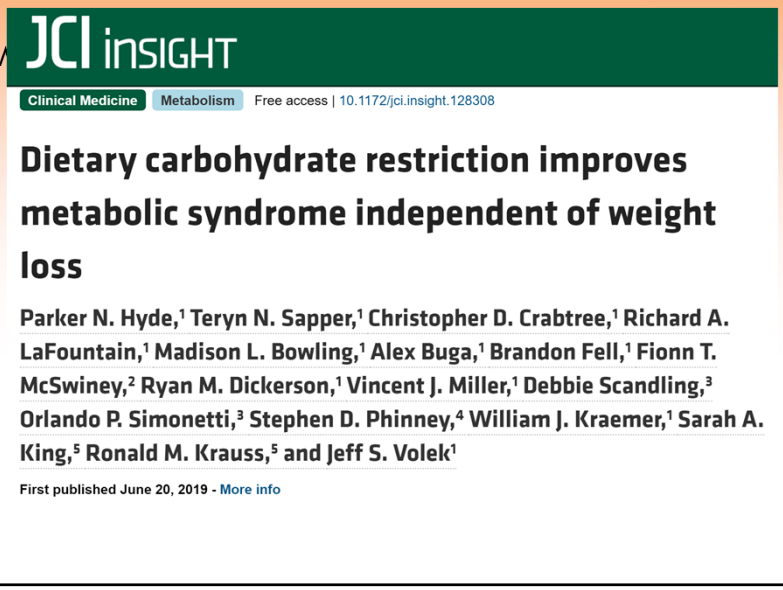
A fat man evidently has plenty of energy

- Humans with Metabolic Syndrome on the latest study from Jeff Volek (Hyde et al)

The latest study from Jeff Volek was published just 3 weeks ago ...

A fat man evidently has plenty of energy

- Humans w
  from Jeff



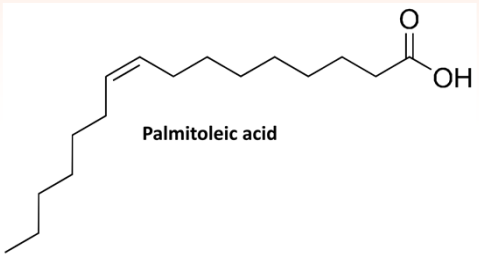
This study was a feeding study in 4 week low, moderate, and high carb arms in subjects with metabolic syndrome. The study was eucaloric so subjects were fed more or fewer calories to keep their weight stable.

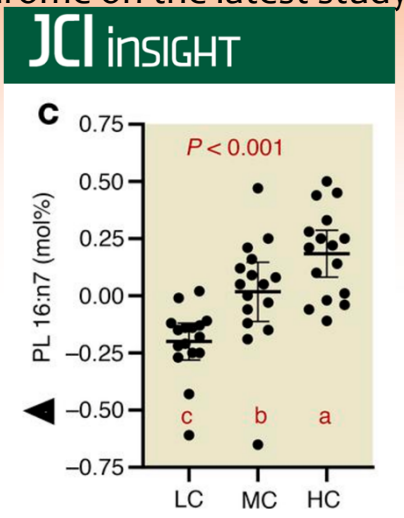
https://www.ncbi.nlm.nih.gov/pubmed/31217353

The results of the study showed that reversal of metabolic syndrome occurs independent of weight loss, and is associated with reduction of dietary carbohydrates.

A fat man evidently has plenty of energy

- Humans with Metabolic Syndrome on the latest study from Jeff Volek (Hyde et al)





What I found interesting in light of our conversation today is that they measure markers of de novo lipogenesis (DNL).

In other words in people who were making new fat, you could measure the amount of palmitoleic acid and extrapolate how much new fat they made.

It probably makes sense that you make more new fat the more carbohydrates (glucose) is in the diet. But remember these people are weight stable. They had no need to store fuel in body fat because they are being given just enough calories in their diet to match their (measured) total daily energy expenditure.

And look at the people on the high fat, low carbohydrate diet – they are still making a lot of new fat … from fat.

A fat man evidently has plenty of energy

Dogma: Fuel = Energy

What if the fat man is not turning fuel into energy
… but instead turning fuel into more fuel?
… and running out of energy
… because his insulin is chronically high

This then is a possible explanation to resolve the paradox

What if the fat man is running out of energy, what if most of that fuel on his body is just being recycled into new fuel, instead of being converted into energy.

Maybe the dogma that Fuel = Energy is not always the case.

Fat men make more insulin

If this is true, it would require that fat men make more insulin to make more ACC, activate it, and turn more fuel into new fuel instead of energy.

T2DM men make more insulin

- Frank Nuttal and Mary Gannon studied Diabetic and non diabetic people challenged with various macronutrients
  - 50g glucose
  - 50g protein
  - 50g glucose + protein

These 2 studies looked into how much glucose and insulin is in circulation in men after eating a 50g protein challenge, a 50g glucose challenge, or a 50g glucose + protein challenge.

You can't really measure the amount of insulin a pancreas secretes, but you can measure how much is in the blood, and the area under the curve of that tells you how much insulin was secreted.

T2DM men mal

- Frank Nuttal and Mary
  diabetic people challe
  - 50g glucose
  - 50g protein
  - 50g glucose + protein

Krezowski, Nuttal, Gannon, Bartosh 1986
"The effect of protein ingestion on the metabolic response to oral glucose in normal individuals"

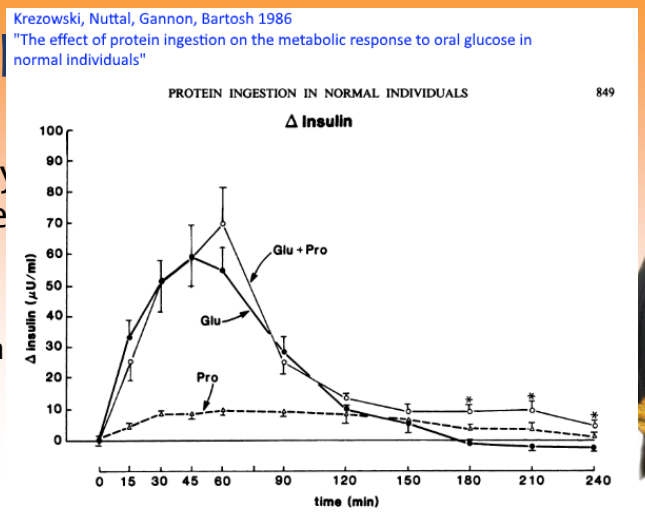


FIG 2. Serum insulin responses to ingestion of 50 g Glu, 50 g Pro, or 50 g Glu + 50 g Pro measured as the change from basal values in eight normal subjects. Basal values were Glu 13 ± 1 μU/mL; Pro 14 ± 2 μU/mL; and Glu + Pro 14 ± 1 μU/mL. * = statistical difference ($p < 0.01$) between the Glu and Glu + Pro curves.

	Net 4-h Area (μU · h/mL)
Glu	78 ± 8
Glu + Pro	99 ± 10
Pro	22 ± 3

This study into normal men

https://www.ncbi.nlm.nih.gov/pubmed/3538843

This is about what you'd expect. From a glucose challenge they saw a lot of insulin 78 units, from a protein challenge they saw a fraction of that; 22 units, and from a combination they saw a combination of both; 99 units.

Notice also the subject's insulin returned back to it's starting position in 3-4 hours

T2DM men make more insulin

- Frank Nutt
  diabetic p
  - 50g gluc
  - 50g prot
  - 50g gluc

Nuttall, Mooradian, Gannon, Billington, Krezowski 1984
"Effect of Protein Ingestion on the Glucose and Insulin Response to a Standardized Oral Glucose Load"

(Glutol, Paddock Laboratories, Minneapolis, Minnesota) or 50 g of protein or a combination of 50 g of glucose with 50 g of protein over 3 consecutive days in a random order. In all studies, protein was given as well-cooked very lean hamburger (236 g raw wt). Blood for glucose and insulin meas-

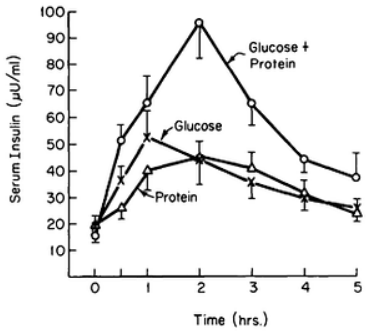


FIG. 2. Serum insulin response to ingestion of 50 g glucose, 50 g protein, or a combination of 50 g glucose and 50 g protein. The subjects are the same as indicated in Figure 1.

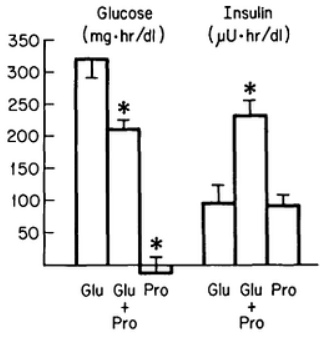


FIG. 3. Areas above baseline for plasma glucose and serum insulin determined over the 5-h period following ingestion of glucose (glu), protein (pro), or a combination of glucose and protein. [*Indicates statistical difference from glucose administration alone for glucose area. For the insulin area glucose + protein is significantly greater than glucose or protein ingestion individually. The glucose and protein area is also significantly greater than the sum of glucose alone plus protein alone ($P < 0.01$). This indicates synergism between oral glucose + oral protein ingestion in the stimulation of insulin secretion.] The subjects are the same as indicated in Figure 1.

Now look at what happened when they looked at type 2 diabetics.

https://www.ncbi.nlm.nih.gov/pubmed/6389060

Firstly at 5 hours when they stopped measuring insulin is still elevated – so they would have under counted the true insulin secretion.

Let's look now at the challenges.

From 50g of glucose they saw roughly 100 units. That's about 25% more than a non diabetic.

From 50g of protein they also saw roughly 100 units. That is 400% more than a non diabetic.

And the kicker is in a combined glucose and protein meal the total secretion until they stopped the experiment was 240 units.

What do we feed Diabetics? Low fat diets. With energy from protein and glucose.

Can this explain the set point?

- Metabolic adaptation
- Rudolph Leibel

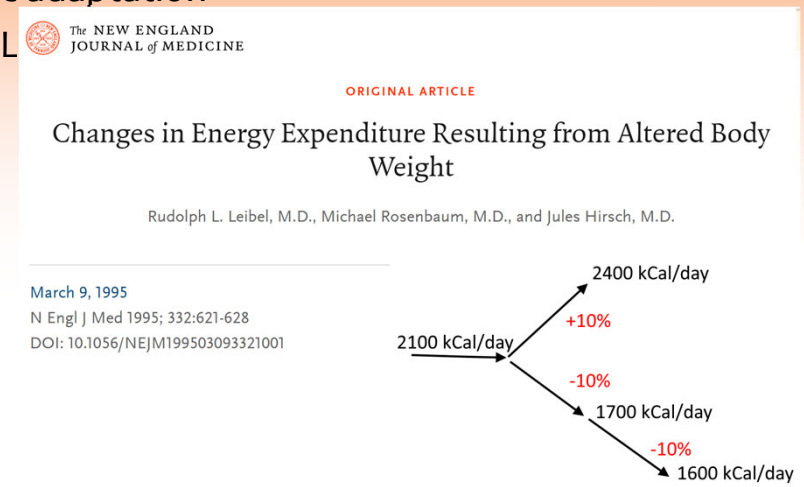
The body set point is known technically as metabolic adaptation.

The seminal study carried out by professor Rudolph Leibel.

https://www.ncbi.nlm.nih.gov/pubmed/7632212

Can this explain the set point?

- Metabolic adaptation
- Rudolph L



He took 18 obese subjects and 23 who had never been obese, measured their resting metabolic rate, then underfed half and overfed the other half until they had respectively lost and gained 10% of their body weight.

Starting at 2100 kCal/day, the people who gained weight increased their metabolic rate to 2400 kCal/day, the people who lost weight reduced their metabolic rate to 1700 kCal/day.

The hypothesis is that metaboiic rate is determined by total lean mass, and our bodies fight efforts to underfeed or overfeed us. Ie: Diets don't work.

Can this explain the set point?

- Metabolic adaptation
- Rudolph Leibel
- Kevin Hall

Dr Kevin Hall from the NiH is a remarkably good scientist who has been building a metabolic model that he fancies can predict metabolic rate given starting lean mass, food intake, and exercise output.

But I think he may have missed a few things …

Can this explain the set point?

- Metabolic adaptation
- Rudolph Leibel
- Kevin Hall – “The Biggest Loser” 6 year followup

Kevin Hall did a study in 2016 into contestants from the TV show “The Biggest Loser” where he measured them at the beginning of the competition, and again after the 13 week series was over, and then again 6 years later.

Can this explain the set point?

- Metabolic adaptation
- Rudolph L
- Kevin Hall

This study

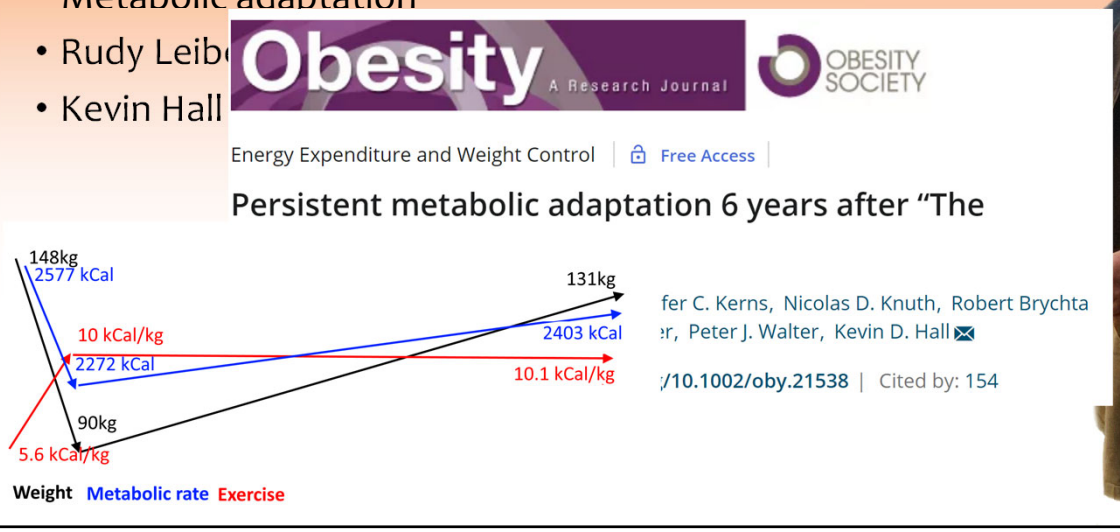
https://www.ncbi.nlm.nih.gov/pubmed/27136388

Showed that contestants lost weight during the 13 weeks of the show, and they gradually gained it all back after 6 years.

That is sad, but probably not a great shock as these people are starving themselves and exercising themselves like mad while there is a prize on the line … you might expect them to not keep all the weight off 6 years later.

Can this explain the set point?

- Metabolic adaptation
- Rudy Leib
- Kevin Hall



Their average starting weight (black line) was 148kgs, dropping to 90kg at the end of the show, and 6 years later it had gone back to 131kg.

Dr Halls metabolic model predicted that their starting metrabolic rate would be 2577 kCal, it would drop with the weight loss to 2272 kCal, and then as they put the weight back on it would go back up to 2403 kCal.

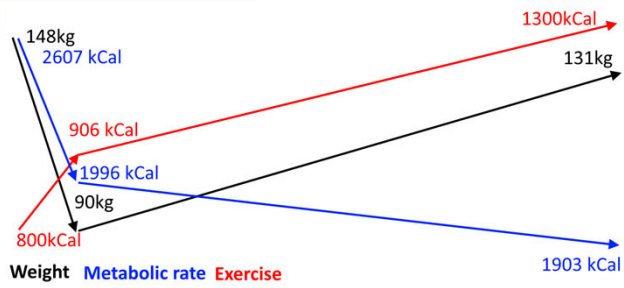
Their exercise went from 5.6 kCal for every kg of weight, to 10 kCal/kg at the end of the show … and 6 years later would it surprise you to know they kept the exercise up?

But do you see what Dr Hall got wrong.

Their body weight was changing, so the ACTUAL exercise 6 years later WENT UP.

Can this explain the set point?

- Metabolic adaptation
- Rudy Leib
- Kevin Hall



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Persistent metabolic adaptation 6 years after "The

nnifer C. Kerns, Nicolas D. Knuth, Robert Brychta alter, Peter J. Walter, Kevin D. Hall

org/10.1002/oby.21538 | Cited by: 154

Look at what these poor people pu themselves through.

Their exercise effort (red line) in kCal went from 800 kCal/day at the beginning of the show, to 906 kCal at the end of the show, to 1300 kCal 6 years later.

They hadn't taken their foot off the accelerator after the prize was awarded – they redoubled their efforts as they were getting slowly fatter over 6 years.

And look at the blue line – thjt is their ACTUAL metabolic rate, not the one predicted by Dr Halls model.

They went from 2607 kCal at the beginning of the competition, to 1996 kCal at the end of the competition. And they lost an additional 100 kCal/day by the 6 year mark.

Can this explain the set point?

- I have an idea … maybe cellular energy constraint is driving metabolic adaptation?
- Prediction: on a low insulinogenic hypocaloric diet RMR would be higher

There may be a better explanation than people with bigger bodies have a higher metabolic rate

Maybe how much energy you body is willing to budget for in the day is determined by how much energy you have available at a cellular level. Your set point then would be determined by how much energy your cell really has … which will be the calories you eat, minus the exercise you do, plus the ability of your body to turn body fat into energy – given all the constraints we have spoken of here.

If so we could test this with a prediction that someone on a low insulinogenic diet eating moderately hypo-caloricly so they lost weight slowly would have a higher resting metabolic rate than someone on an insulinogenic isocaloric diet.

Can this explain the set point?

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Research

Effects of a low carbohydrate diet on energy expenditure during weight loss maintenance: randomized trial

BMJ 2018 ; 363 doi: https://doi.org/10.1136/bmj.k4583 (Published 14 November 2018)
Cite this as: *BMJ* 2018;363:k4583

Cara B Ebbeling, principal investigator, and associate professor [1 2], *Henry A Feldman, principal biostatistician, and associate professor* [2 3], *Gloria L Klein, study director* [1], *Julia M W Wong, associate study director, and instructor* [1 2], *Lisa Bielak, nutrition research manager* [1], *Sarah K Steltz, data and quality manager* [1], *Patricia K Luoto, professor* [4], *Robert R Wolfe, professor* [5], *William W Wong, professor* [6], *David S Ludwig, principal investigator, and professor* [1 2]

This is exactly what David Ludwig observed in Ebberling et al 2018

https://www.bmj.com/content/363/bmj.k4583

After a 12% weight loss, subjects were assigned one of 3 diets; low, moderate, and high carbohydrate.

They observed a difference in energy expenditure of 52 kCal/day for every 10% decrease in carbohydrates.

Fuel ≠ Energy

In summation, we should think of fuel as being something different than energy.

Thank You!

KETOFEST 2019