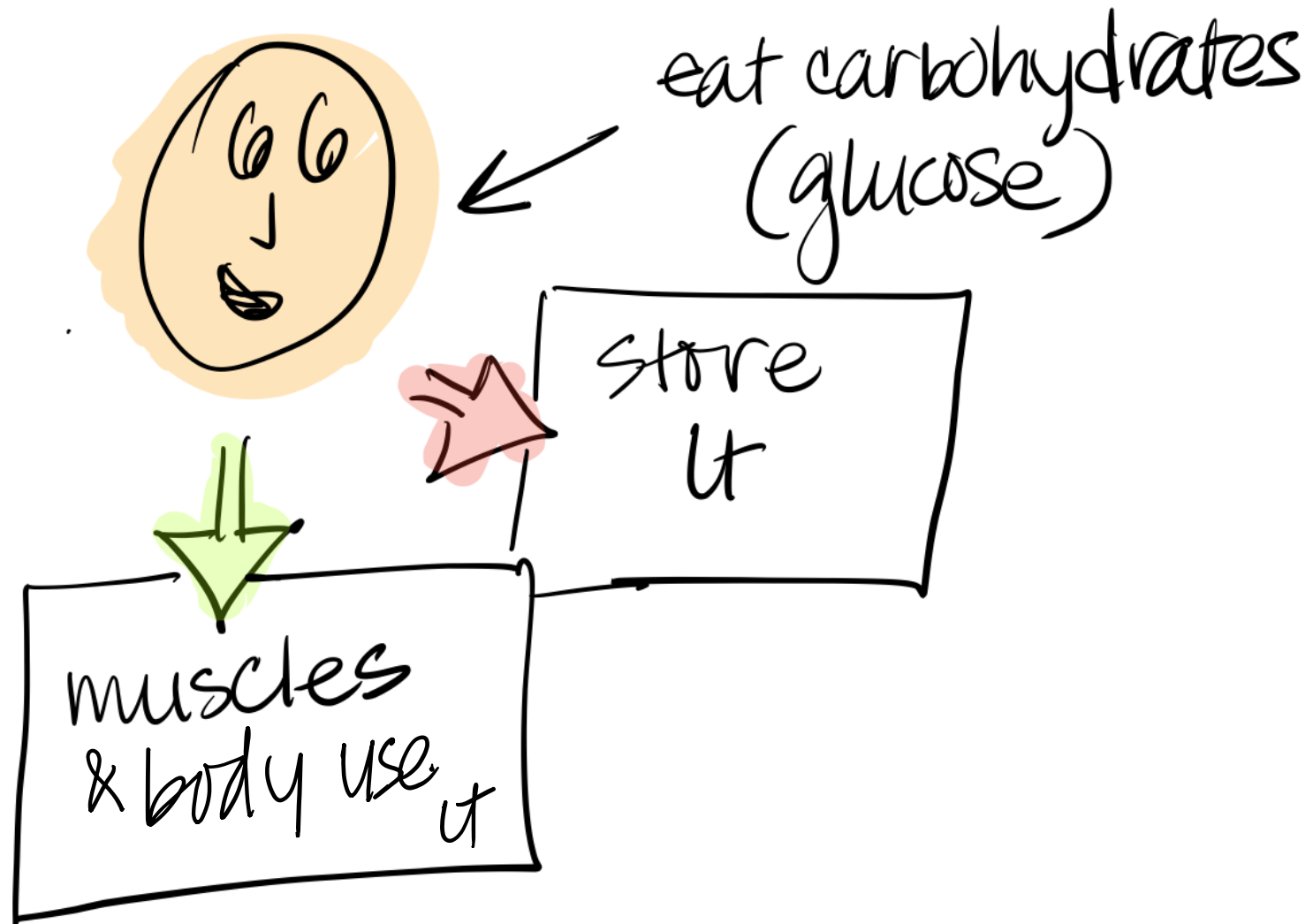
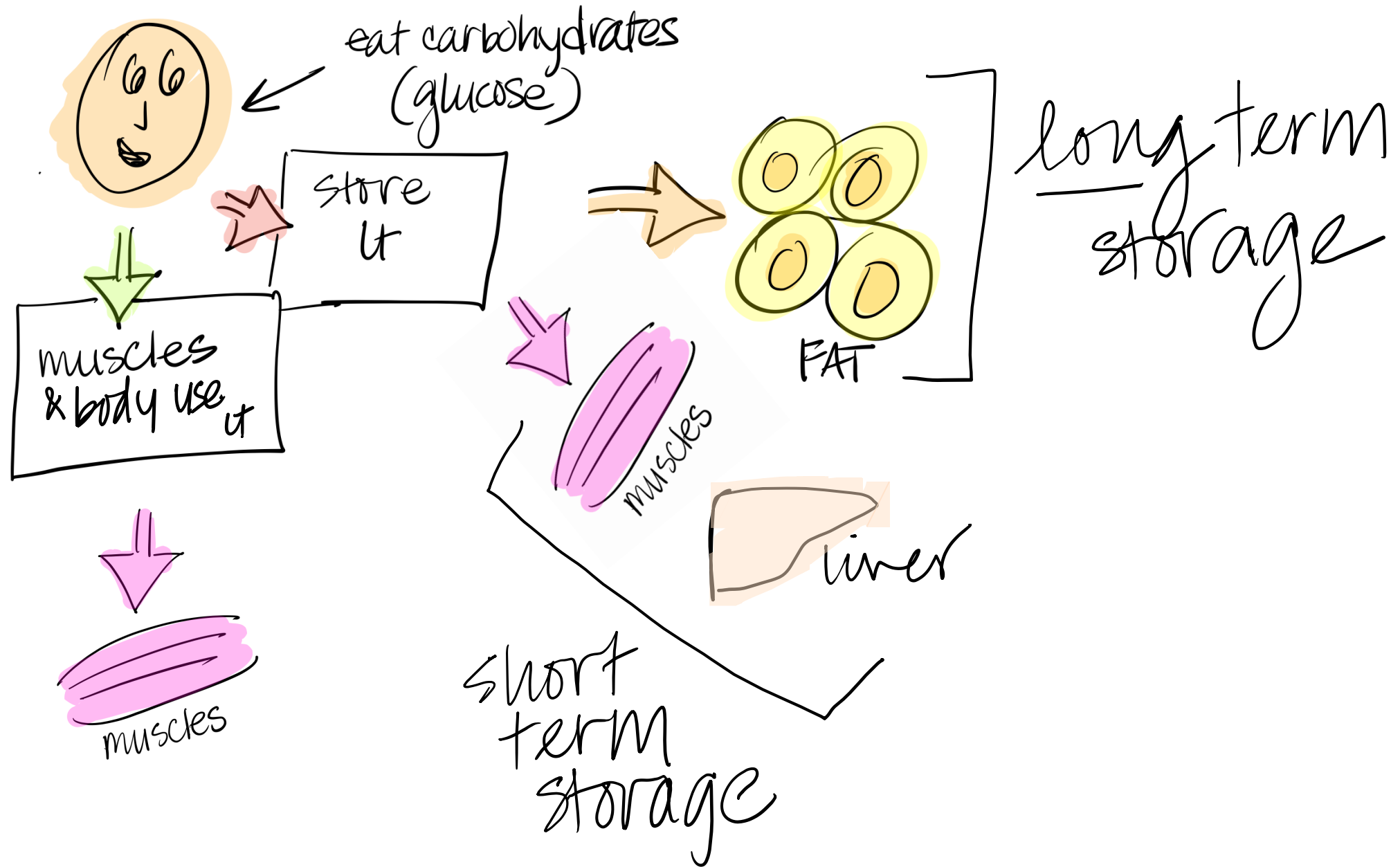


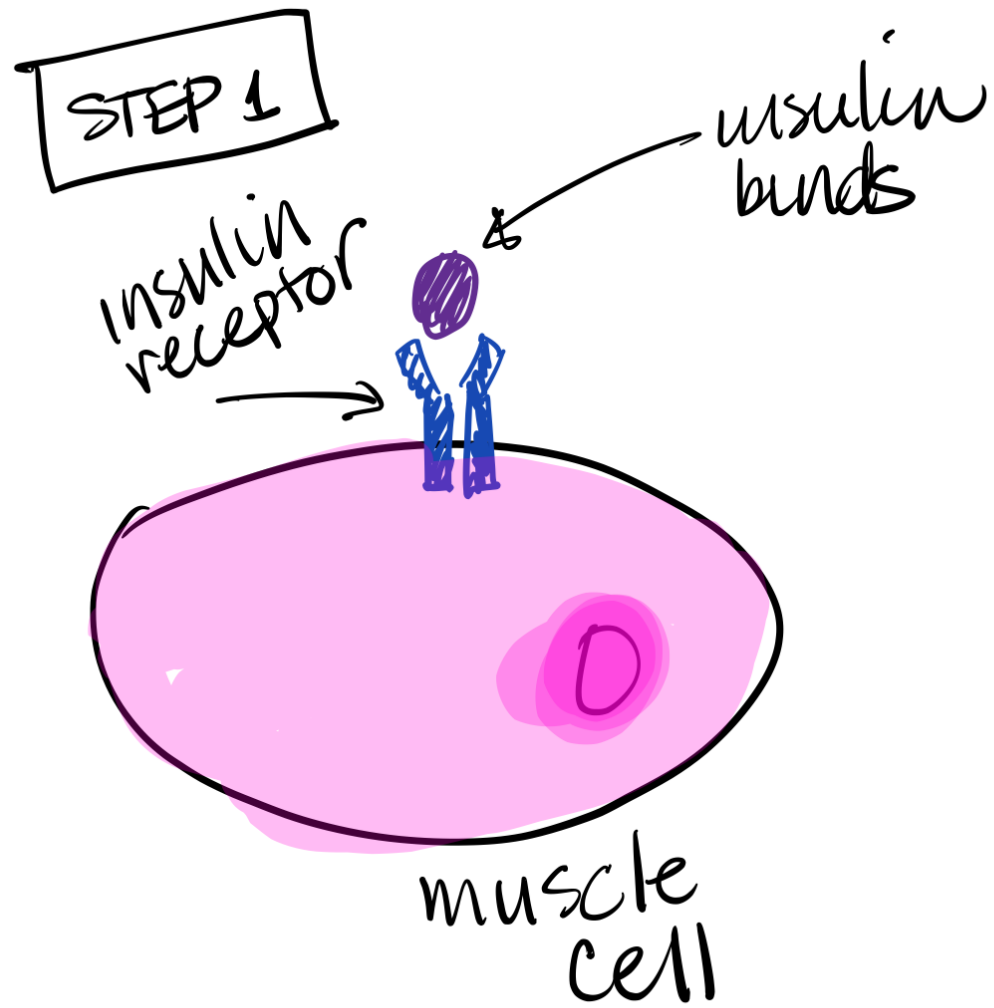
Insulin **resistance**

It starts here...

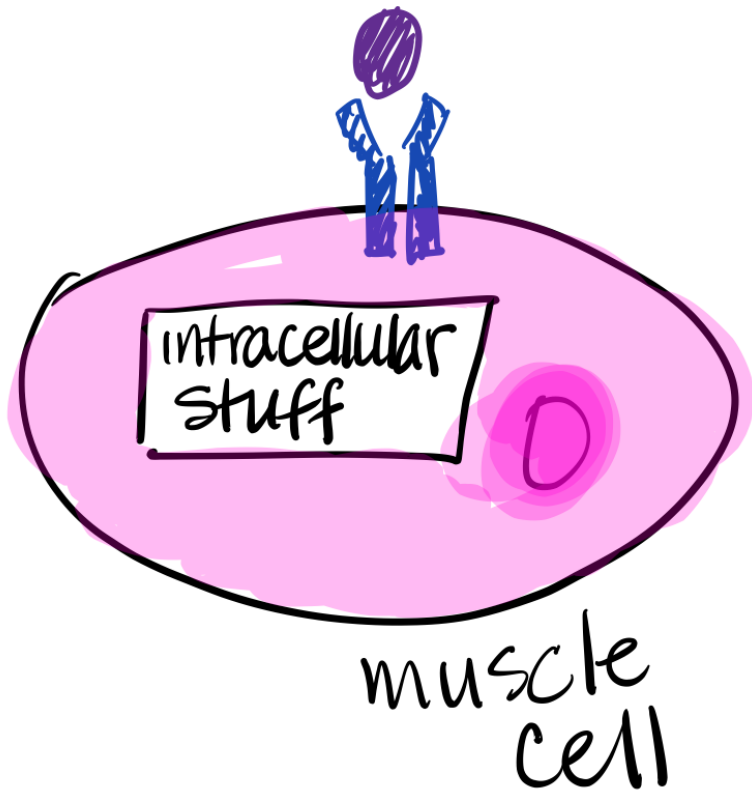
- ▶ How it develops
- ▶ Who is at risk
- ▶ Solutions



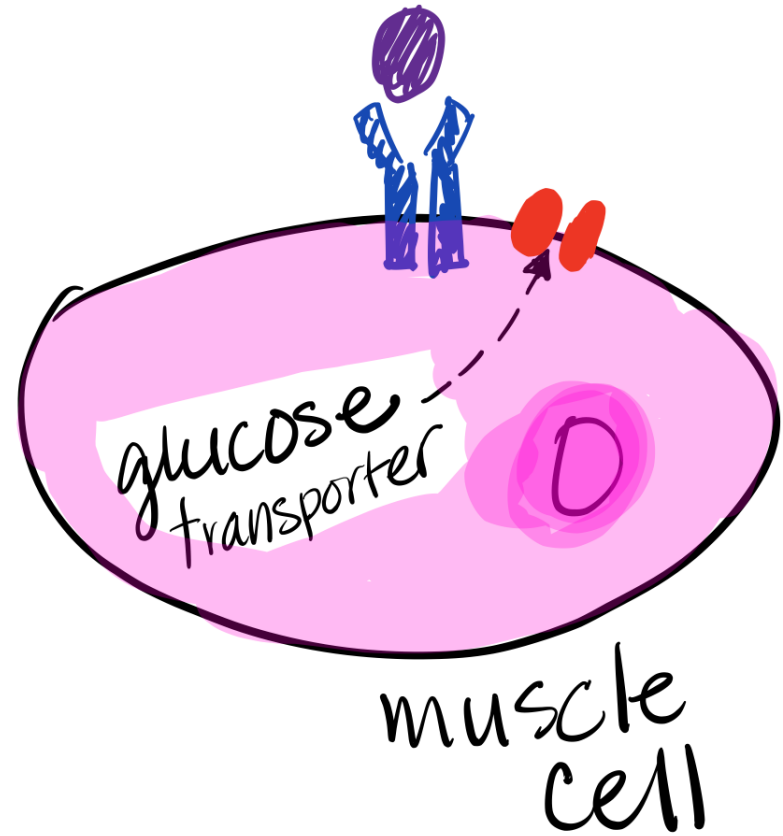




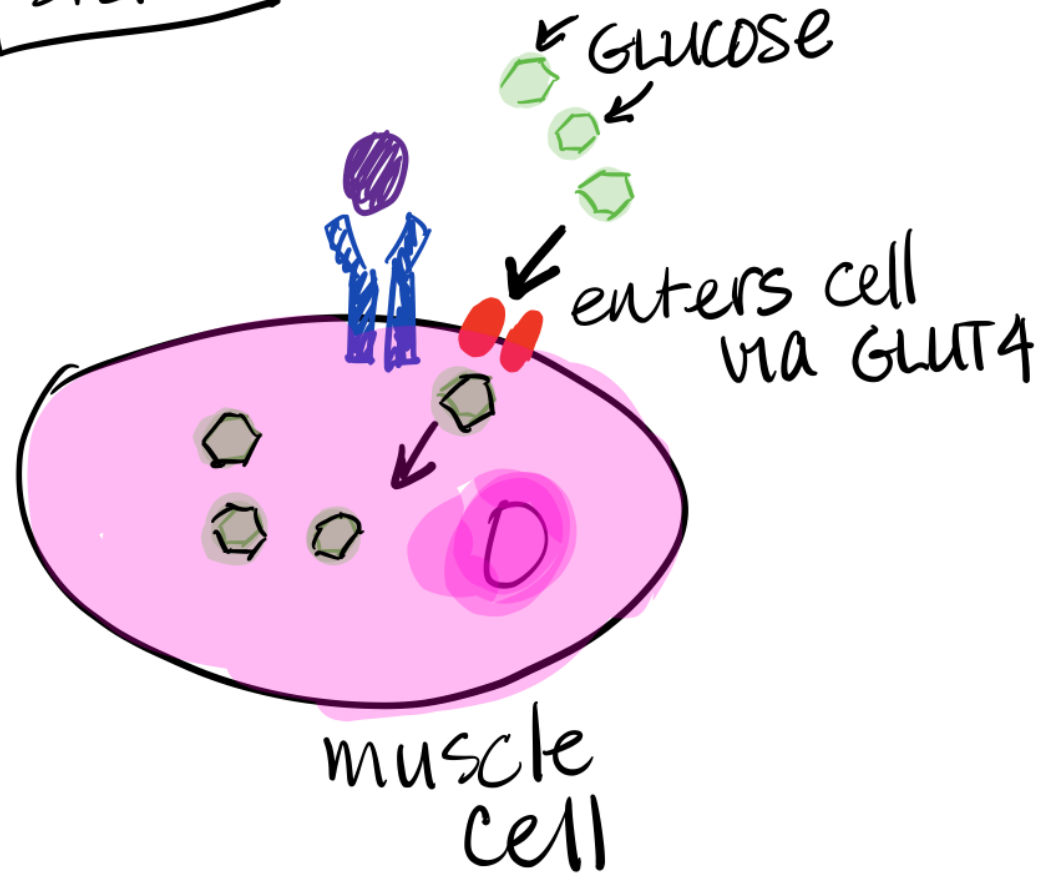
STEP 2



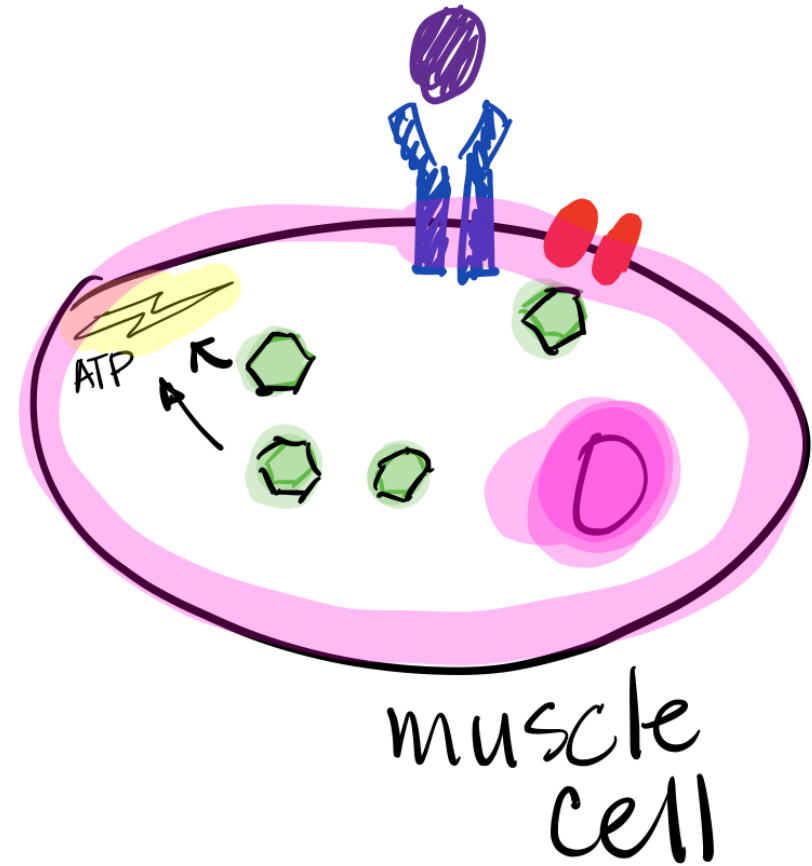
STEP 3

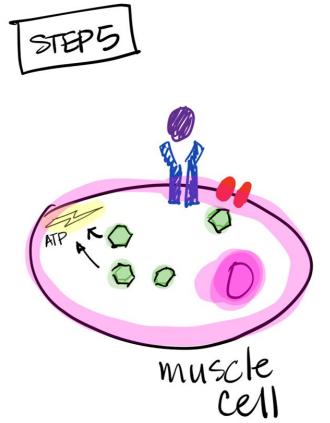
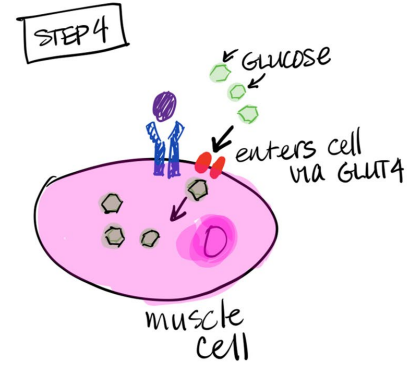
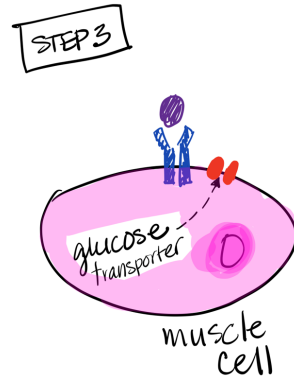
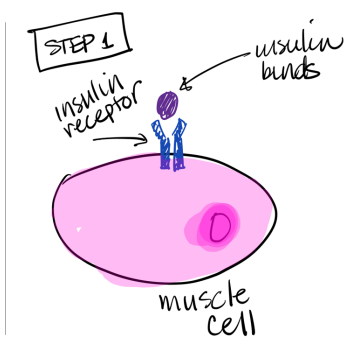
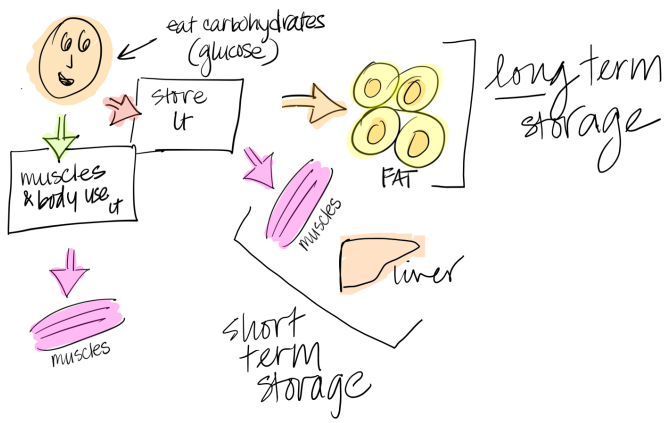


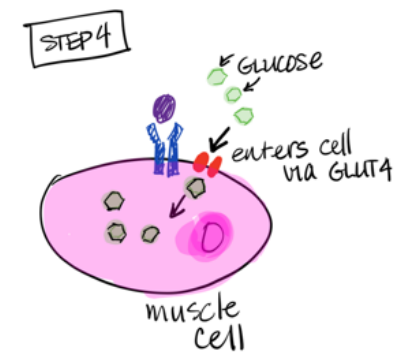
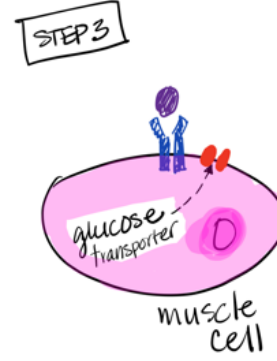
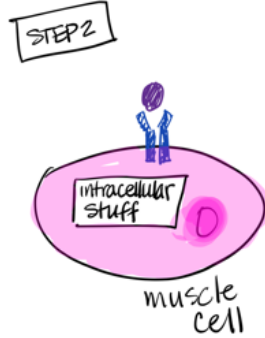
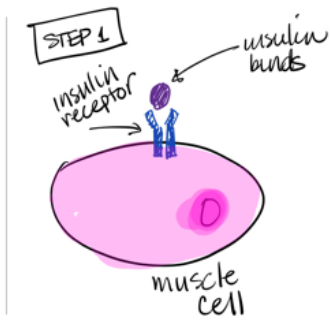
STEP 4



STEP 5



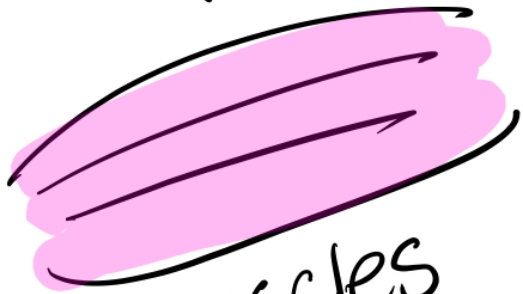




This is equivalent to spending money immediately!

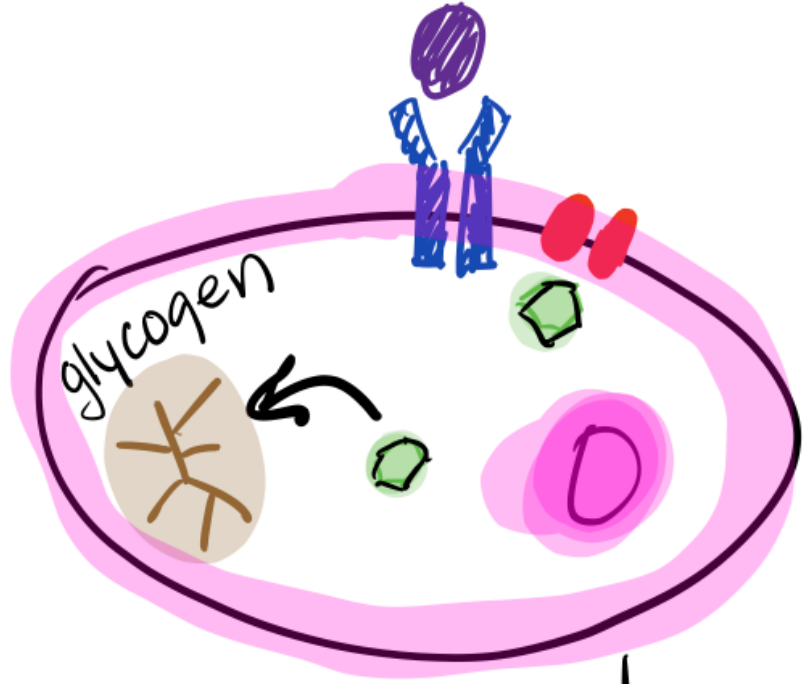


store it
for
later

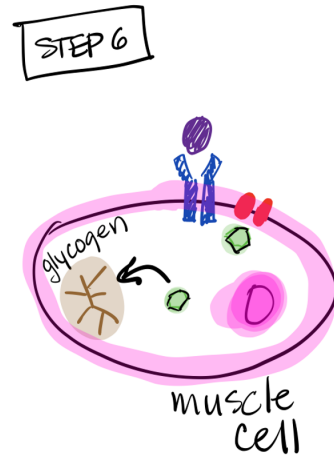
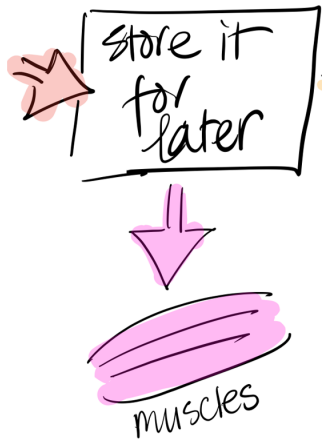


muscles

STEP 6



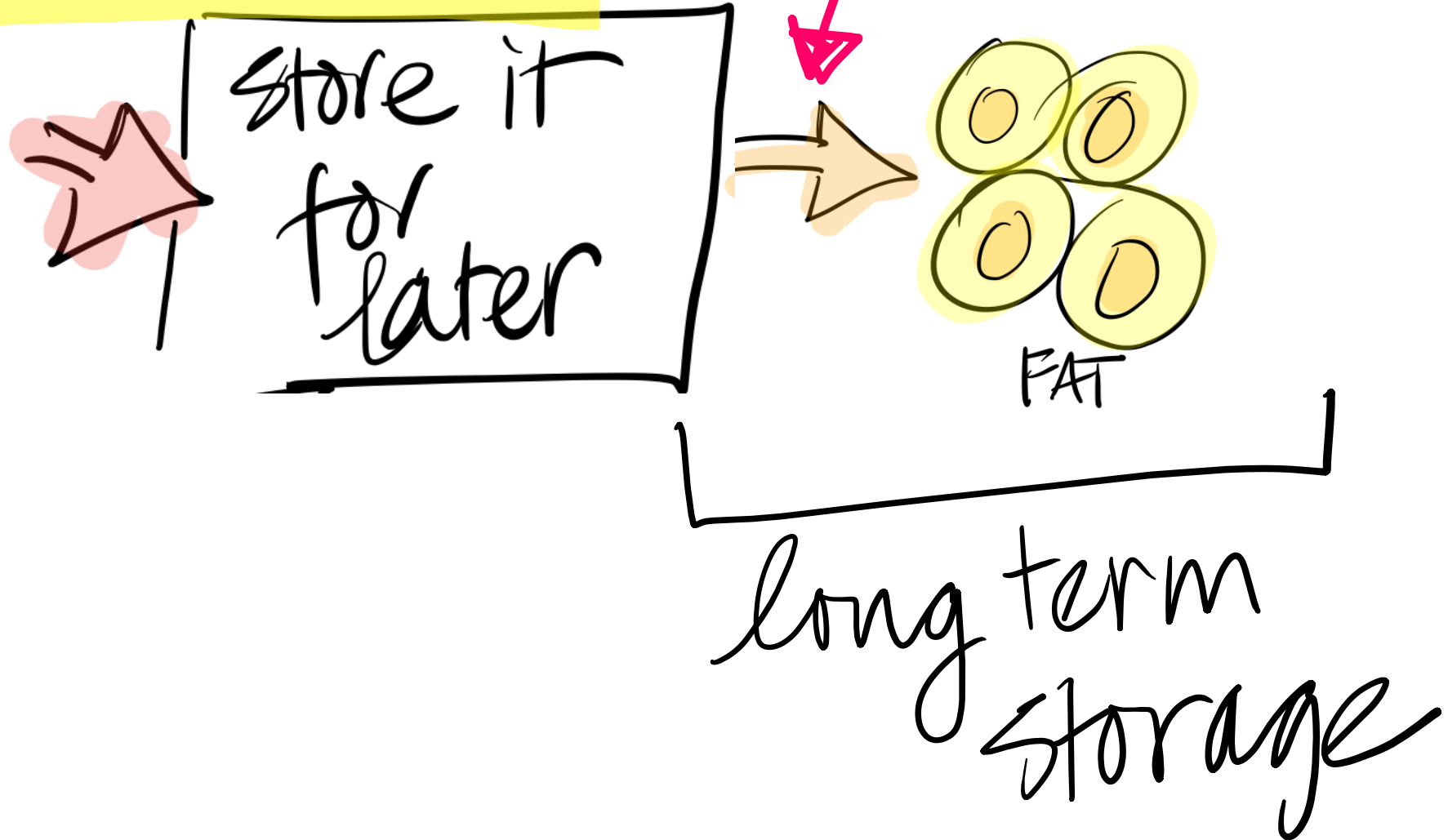
muscle
cell



This is equivalent to putting money in your wallet
→ short term storage.

Insulin is your FAT storage hormone!

INSULIN DOES THIS, too





store it
for
later



This is equivalent to putting money in the bank
→ long term storage.



However, when INSULIN is present → you CANNOT get your money out of the bank!



However, when INSULIN is present → you CANNOT get your money out of the bank!

Q: ①
When is
INSULIN
present?

A: when you eat*
...



However, when INSULIN is present → you CANNOT get your money out of the bank!

Q. (2)

When do you burn fat??

A: When you don't have insulin
& ↓↓ glycogen stores

Are you a Tofu? (That's thin on the outside, fat inside)

Extraordinary images from medical scans revealed here for the first time show that many people who have normal body weight are carrying around hidden layers of fat. Stored up around vital organs, they can put outwardly healthy people at risk

Jo Revell Health Editor

Sun 10 Dec 2006 09:02 EST First published on Sun 10 Dec 2006 09:02 EST

Ben Schwartz could hardly be described as overweight. The slimly-built 28-year-old does not like junk food and keeps busy all day, working as a runner for a television production company. Last week, with some trepidation, he had the chance to find out what his lifestyle was doing to his insides when he allowed himself to be put through a hi-tech MRI (magnetic resonance imaging) scanner.

Thanks to MRI, doctors can look at the body's composition in a new light. The remarkable images, revealed here for the first time, show how much 'internal fat' even slim people carry - and raise fresh questions about how healthy people are. Doctors are increasingly concerned that people can look slim on the outside but still have a problem with fat.

Schwartz lay on a trolley which slid inside the huge doughnut ring of the scanner as the radiographer, Julie Fitzpatrick, took picture 'slices' of his anatomy.

Professor Jimmy Bell, head of the molecular imaging group at the Medical Research Council's centre at Imperial College, London was able to analyse the images appearing on his computer screen in his office next door, as the scanner moved above Ben's abdomen, showing the paler regions of internal fat contrasting against the darker shapes of bones and organs.

Bell has spent years studying how human beings store and use their adipose tissue, or fat. He has carried out studies showing that people who would be considered slim can have large quantities of fat within them.

'This is particularly true of men who have a slim build but who do little or no exercise,' he said. 'We know now that 40 per cent of people have fat infiltration of the liver, which is linked to so many other health problems.'

He said of Schwartz: 'He is slim, he's not overweight, but you can see there are some areas where there is a bit of a build-up



Ben Schwartz's scan. Photograph: Public domain

of visceral fat. He doesn't have a lot of subcutaneous fat [the kind that lies just under the skin], but I can see there is quite a bit around the organs and some in the muscle.'

Thanks to this new technique, Bell and others are able to understand why appearances can be so deceptive. Someone like Schwartz, who is young, falls into the category of those who need to start changing their lifestyle. Unknowingly, he is on the way to becoming what is jokingly described as a 'Tofu' - Thin on the Outside, Fat on the Inside. Tofis probably need to worry more about their health than others, because the fat deposits they carry are hidden in the white fat that lies around their vital organs, streaked through their underused muscles, and wrapped around the heart. It is this fat that sends out the chemical signals which eventually lead to insulin resistance, diabetes and heart conditions, rather than the fat lying in dimples underneath the skin.

Someone like Schwartz could hardly be described as an over-eater. He spends half his day at a desk, the rest outside helping to arrange filming and setting up interviews for television documentaries. 'I don't have the time - or, frankly, the cash - to go to a gym,' he said. 'I love surfing and I try to go down once a month to Compton Bay in the Isle of Wight, but that's about it. Often I hardly eat in the day, and only really eat properly in the evening at home.'

Genes also play an enormous role. 'Our work so far has shown that you can take two men of the same age, with the same BMI [body mass index], and find one with five litres of fat within him and another with two litres,' said Bell, who works at Hammersmith Hospital, west London. 'We've even scanned people who are underweight and found up to seven litres of fat inside them.'

'What we don't yet possess is enough information about how different genetic groups store fat. But we do know that you can manipulate the way the body stores it by changing the diet.'

It would appear that nutritional alterations, such as eating more resistant starch, such as in lentils and pulses, means less fat is likely to be laid down in the abdomen. Bell is carrying out a trial on healthy volunteers to see what happens to their internal deposits of fat when they switch to a diet involving more grains and lentils.

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Thanks to MRI, doctors can look at the body's composition in a new light. The remarkable images, revealed here for the first time, show how much 'internal fat' even slim people carry - and raise fresh questions about how healthy people are. Doctors are increasingly concerned that people can look slim on the outside but still have a problem with fat.

Ectopic fat accumulation: an important cause of insulin resistance in humans

Hannele Yki-Järvinen

J R Soc Med 2002;**95**(Suppl. 42):39–45

FORUM ON LIPIDS IN CLINICAL MEDICINE, 12 OCTOBER 2001

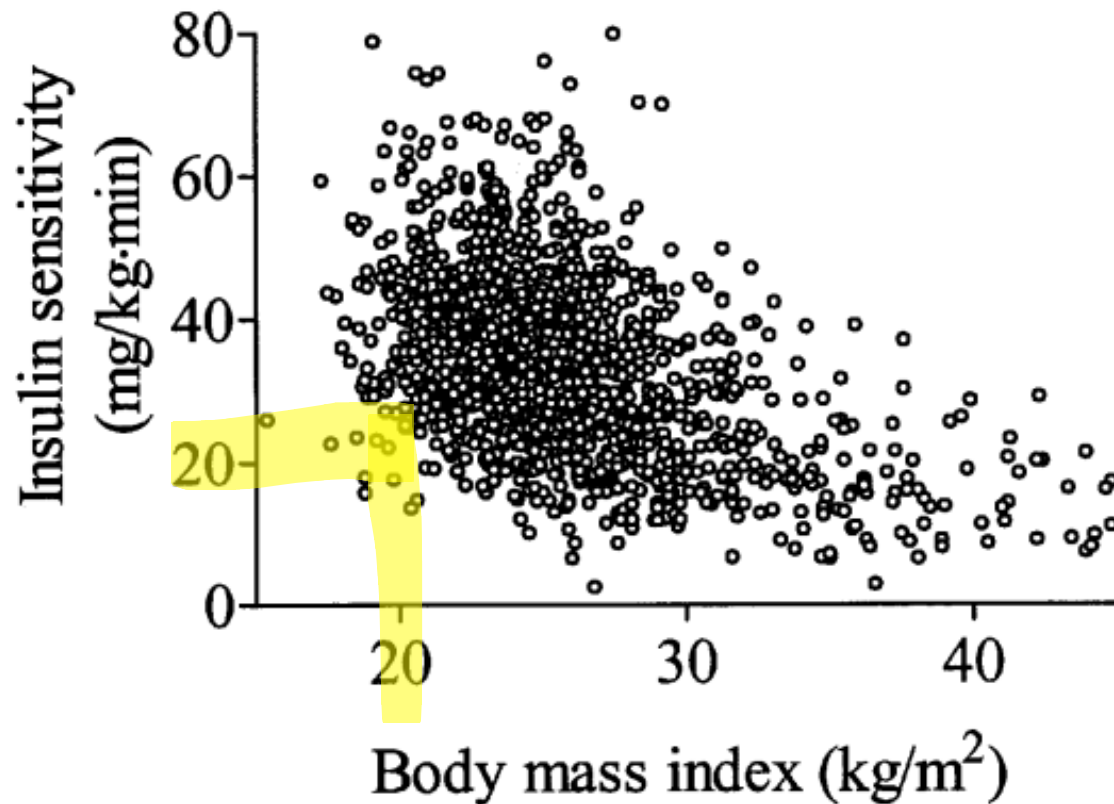
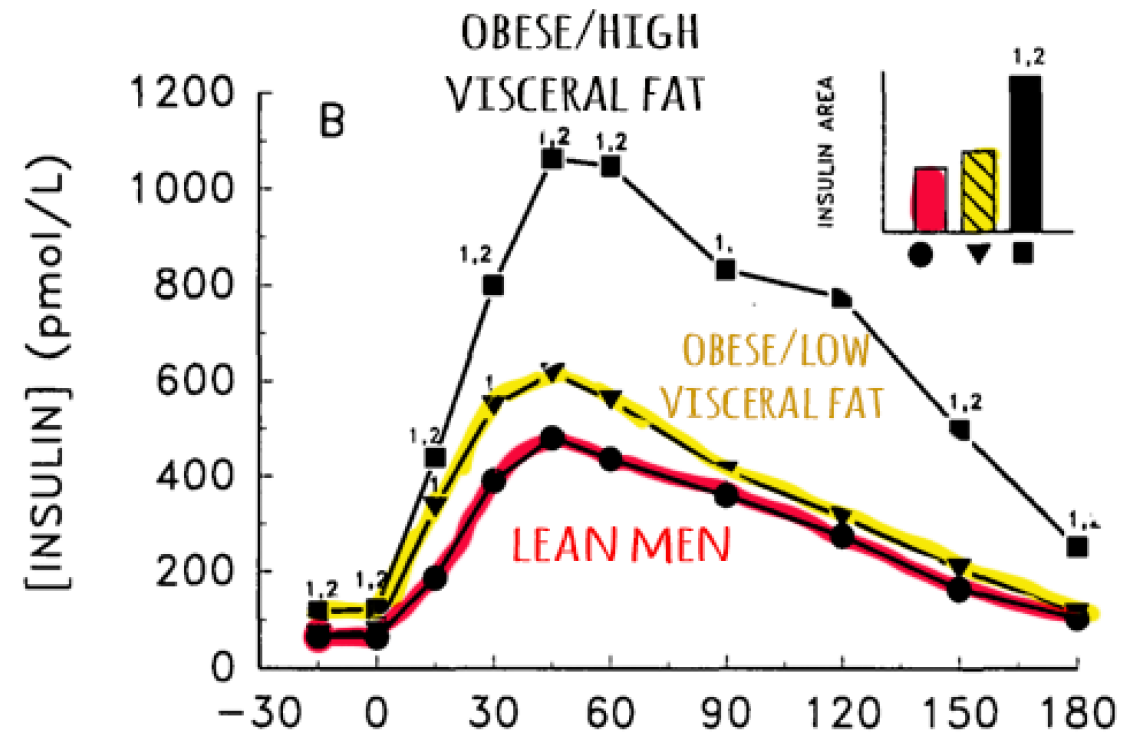
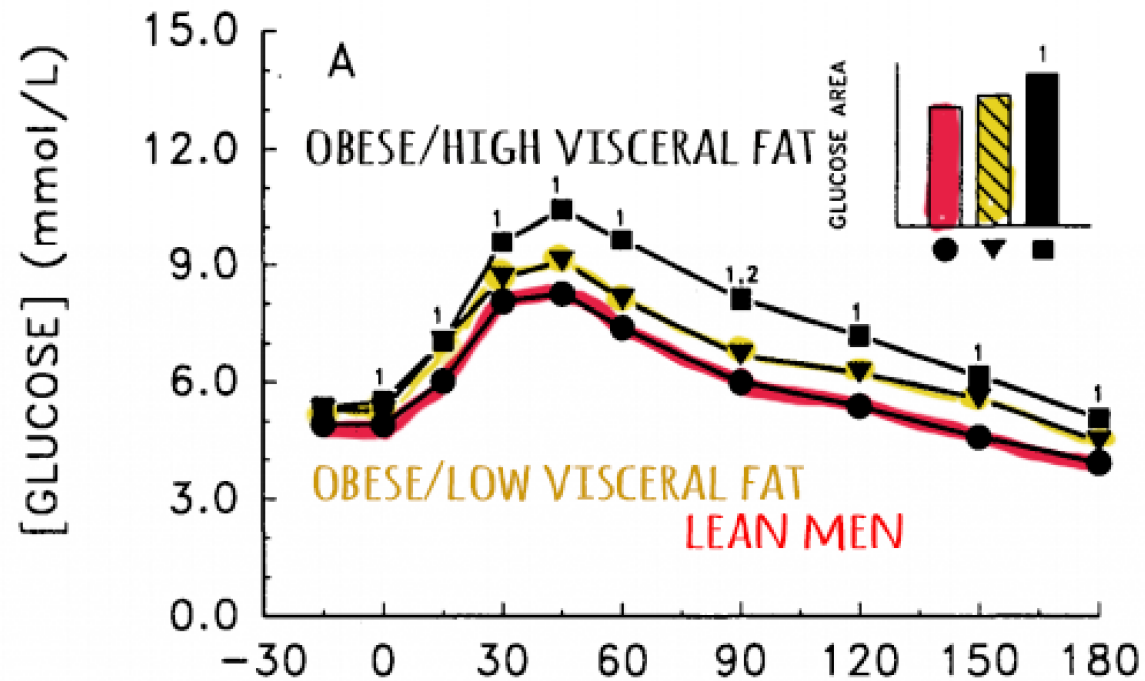


Figure 1 Relationship between body mass index and insulin sensitivity, measured using the euglycaemic clamp technique, in 1394 healthy non-diabetic European men and women whose data have been included in the European Group for Insulin Resistance (EGIR) database [data used by permission from the EGIR]

Visceral Obesity in Men

Associations With Glucose Tolerance, Plasma Insulin, and Lipoprotein Levels

MARIE-CHRISTINE POULIOT, JEAN-PIERRE DESPRÉS, ANDRÉ NADEAU, SITAL MOORJANI, DENIS PRUD'HOMME, PAUL J. LUPIEN, ANGELO TREMBLAY, AND CLAUDE BOUCHARD

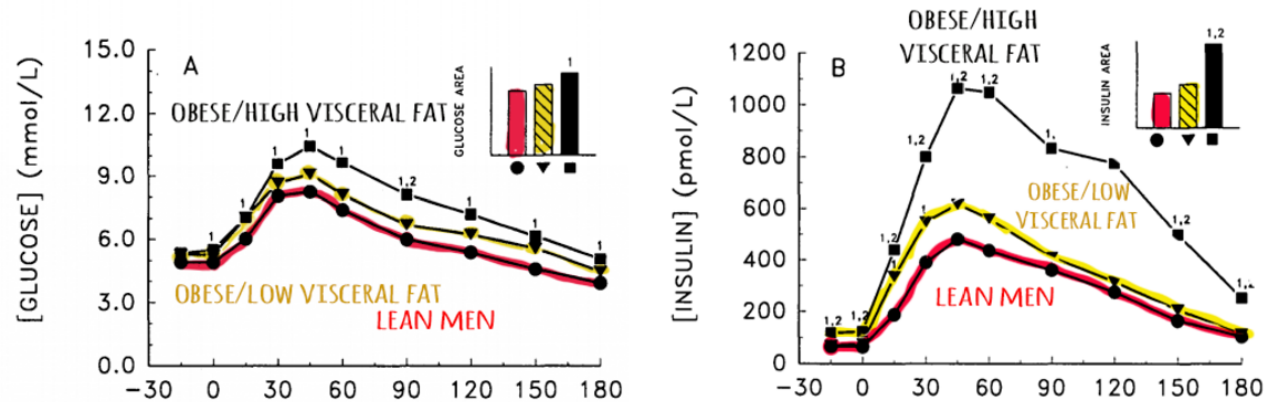


Plasma glucose and insulin levels during a 75-g oral glucose tolerance test in lean control men (●) and in obese men with either low (T) or high (●) levels of visceral adipose tissue.

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Plasma glucose and insulin levels during a 75-g oral glucose tolerance test in lean control men (●) and in obese men with either low (▲) or high (■) levels of visceral adipose tissue.

<https://doi.org/10.2337/diab.41.7.826>

- The obese men in this study had identical amounts of total body fat.
- The obese groups only differed in the amount of intra-abdominal fat levels.
- The low intra-abdominal fat group's responses were essentially the same as the lean group's response.
- It was only the men with high intra-abdominal fat that had greater glucose and insulin responses.

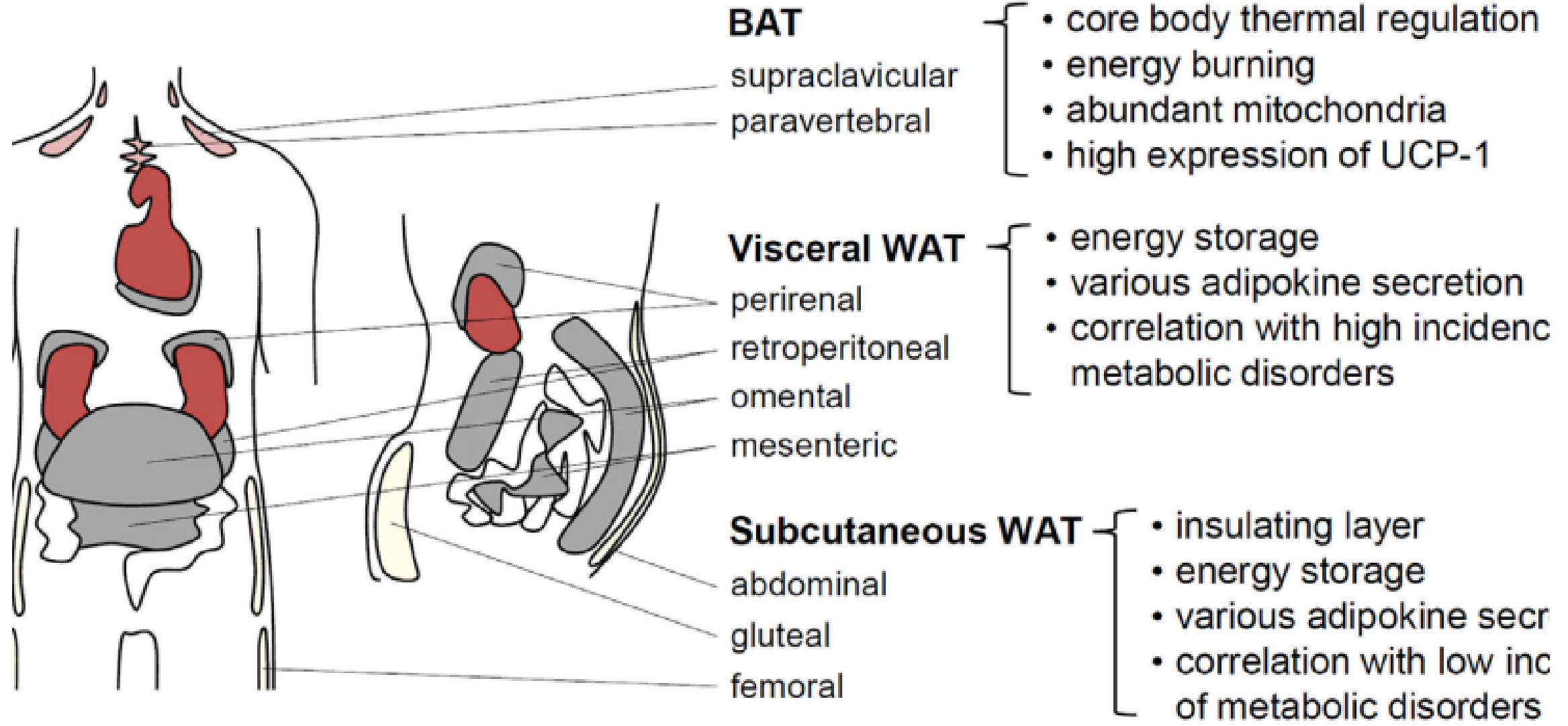
It is the **intra-abdominal** component of excess fat, and **not total fat**, that is *strongly associated with impaired insulin action.*



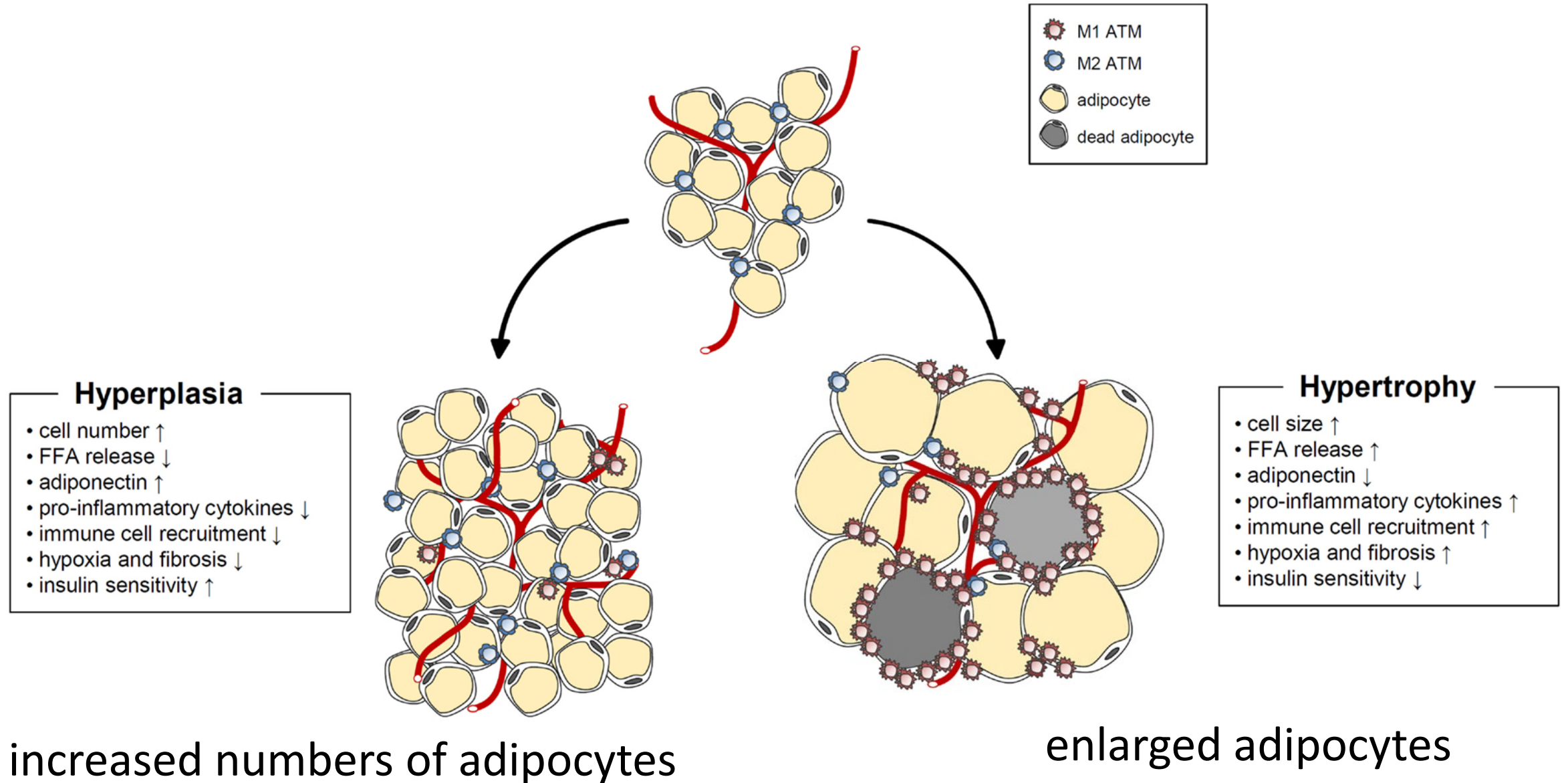
Adipose Tissue Remodeling: Its Role in Energy Metabolism and Metabolic Disorders

*Sung Sik Choe, Jin Young Huh, In Jae Hwang, Jong In Kim and Jae Bum Kim**

Department of Biological Sciences, National Creative Research Initiatives Center for Adipose Tissue Remodeling, Institute of Molecular Biology and Genetics, Seoul National University, Seoul, South Korea

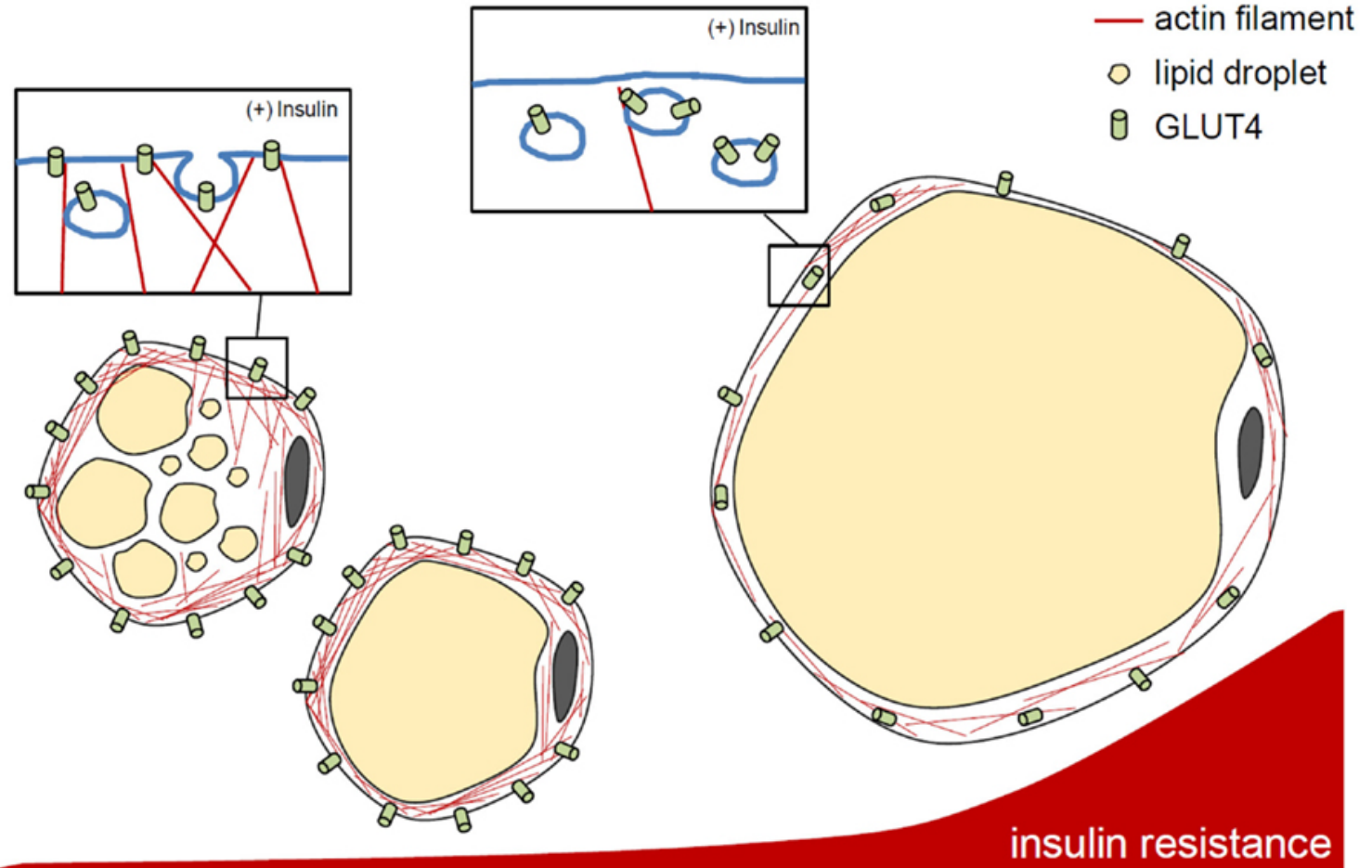


Two Modes of Adipose Tissue Expansion



Small adipocyte

- small cell size
- multilocular lipid droplets
- organized cortical actin
- intact GLUT4 translocation



When the adipocyte becomes hypertrophied, the cytoskeleton is unable to hold in place the glucose transporters, thus impairing insulin responsiveness.

Hypertrophic adipocyte

- large cell size
- unilocular-like lipid droplet
- disorganized cortical actin
- impaired GLUT4 translocation

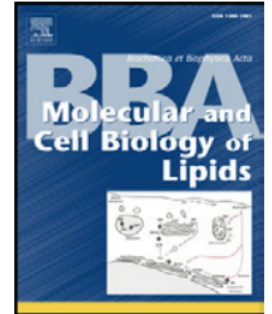


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Review

Adipose tissue expandability, lipotoxicity and the Metabolic Syndrome – An allostatic perspective

Sam Virtue^{*}, Antonio Vidal-Puig^{*}

Institute of Metabolic Science, Metabolic Research Laboratories, University of Cambridge, Box 289, Level 4, Addenbrooke's Hospital, Cambridge CB2 0QQ, UK

The adipose tissue expandability hypothesis

While it is clear that obesity is associated with diabetes based on population studies, there is some controversy as to the mechanisms by which this occurs on an individual level. One hypothesis, which perhaps links many others, is that of limited adipose tissue expandability. The adipose tissue expandability hypothesis can be stated as follows; adipose tissue has a defined limit of expansion for any given individual. As an individual gains weight a point will eventually be reached when their adipose tissue can no longer store more lipid. Once adipose tissue storage capacity is exceeded then net lipid flux to non-adipose organs will increase and lipids will begin to be deposited ectopically. Ectopic lipid accumulation in cells such as myocytes hepatocytes and beta cells then causes toxic effects such as insulin resistance and apoptosis.

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once you
hit the
limit

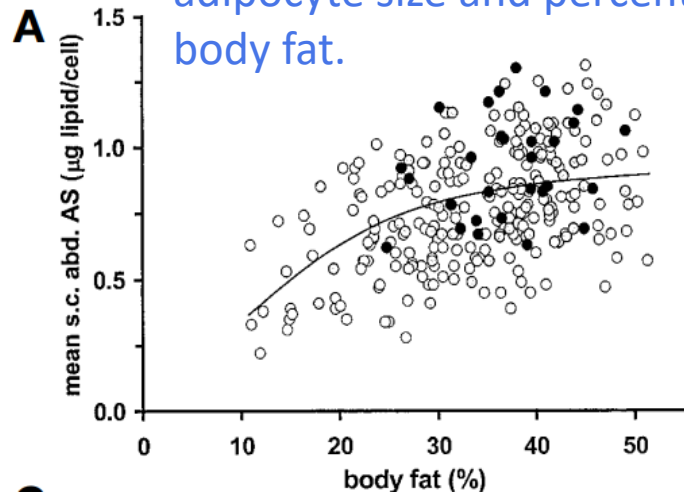
→ insulin resistant!!

Enlarged subcutaneous abdominal adipocyte size, but not obesity itself, predicts Type II diabetes independent of insulin resistance

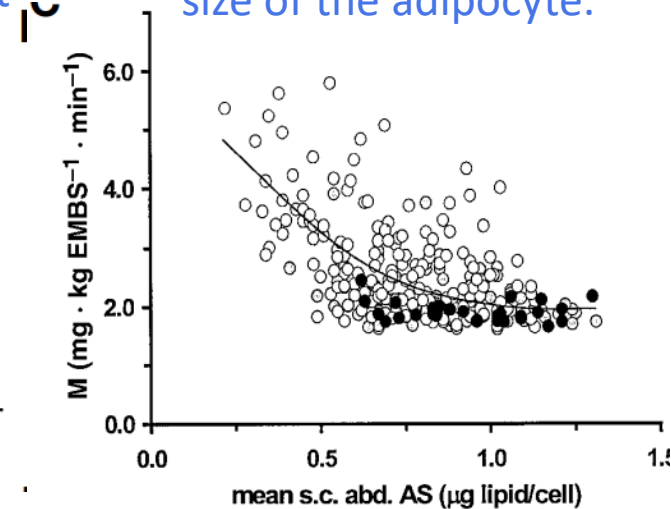
C. Weyer, J. E. Foley, C. Bogardus, P. A. Tataranni, R. E. Pratley

Clinical Diabetes and Nutrition Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona, USA

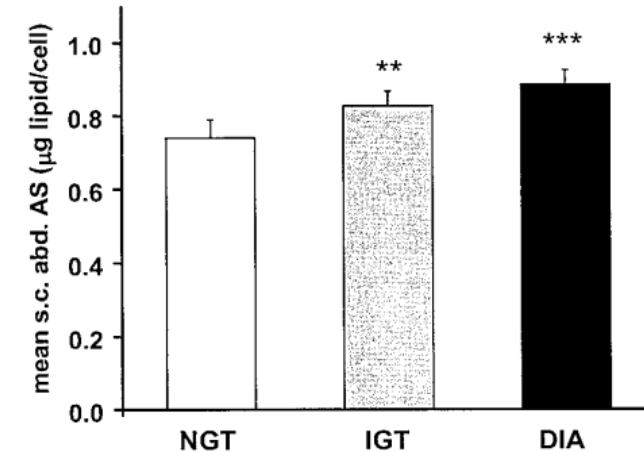
There was a positive correlation between adipocyte size and percent body fat.



The rate of insulin stimulated glucose disposal was inversely related to the size of the adipocyte.



The relationship between insulin stimulated glucose disposal and the average size of adipocyte.



Cross-sectional studies indicate that enlarged subcutaneous abdominal adipocyte size is associated with hyperinsulinaemia, insulin resistance and glucose intolerance.

Asians prone to TOFI - thin on the outside, fat on the inside

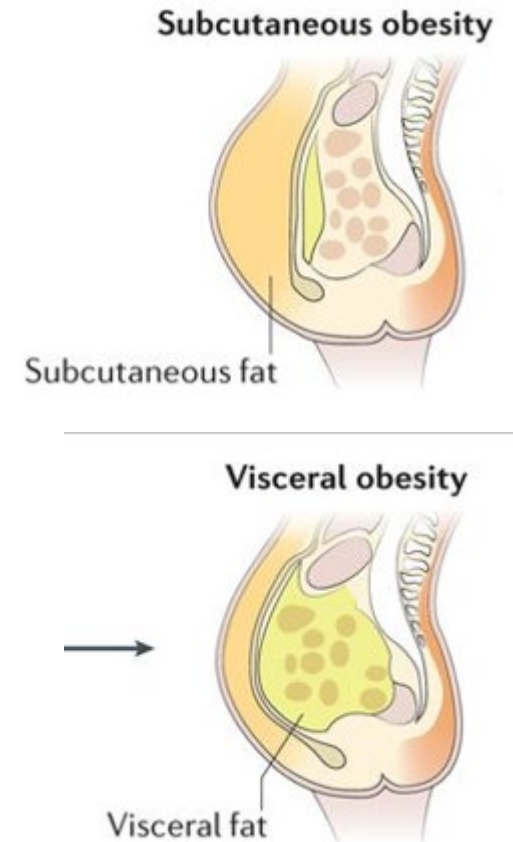
MATT STEWART · 20:18, Oct 13 2015

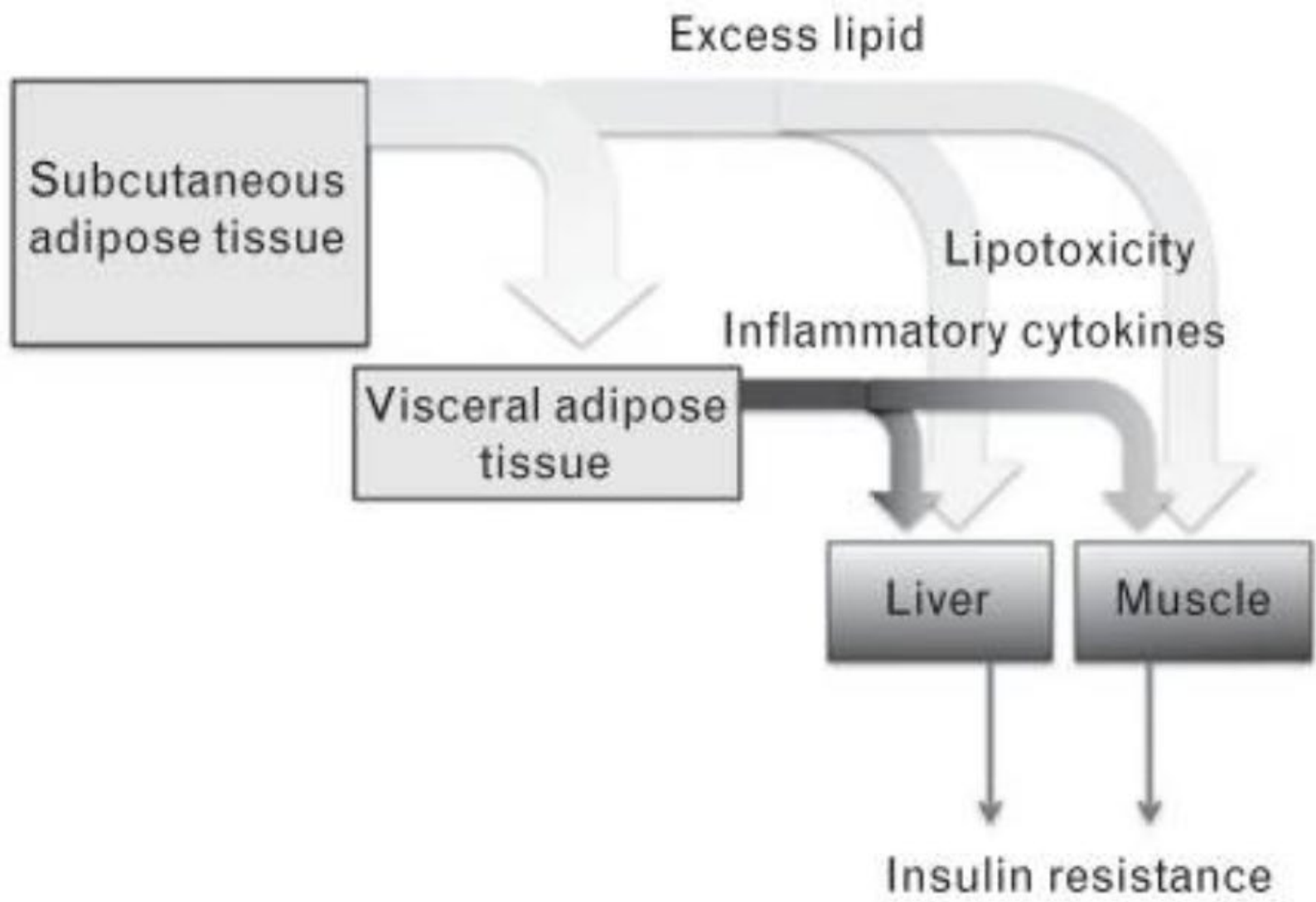


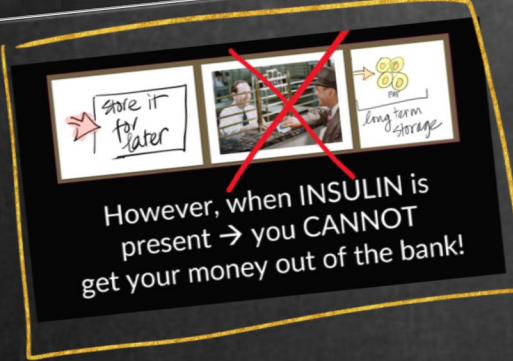
"Surprisingly perhaps, when matched against their European, Maori or Pacific counterparts, Asian consumers are at greater risk of poor metabolic health and that highlights the need for food and beverage products that provide better nutrition."

Scientists suspect the answer to why some people are more prone to diseases such as diabetes lies in how body fat is stored.

Even small amounts of weight could lead to fat spilling over from connective tissue into vital organs such as muscle, liver and pancreas, causing "metabolic mayhem", Cameron-Smith said







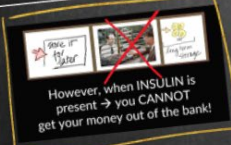
Q. (2)
When do you burn fat??

A: When you don't have insulin
& ↓↓ glycogen stores

← Recall this -
insulin is the reason that

the adipocytes are overfilled





Q. ②
When do you
burn fat??

A: When you don't have insulin
& ↓↓ glycogen stores

← Recall this -
insulin is the
reason that
the adipocytes are overfilled




A possible
solution -



stop triggering insulin
release.

Q. ② When do you burn fat??
A: When you don't have insulin & ↓ glycogen stores

← Recall this -
insulin is the reason that the adipocytes are overfilled



A possible solution -

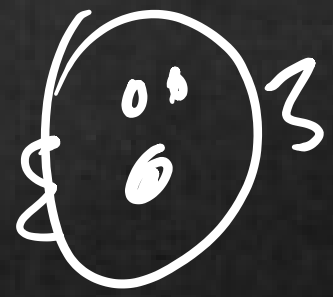


stop triggering insulin release.

HOW??

FAST

DON'T EAT!





stop triggering insulin release.

A possible solution -



HOW??

FAST ← DON'T EAT!

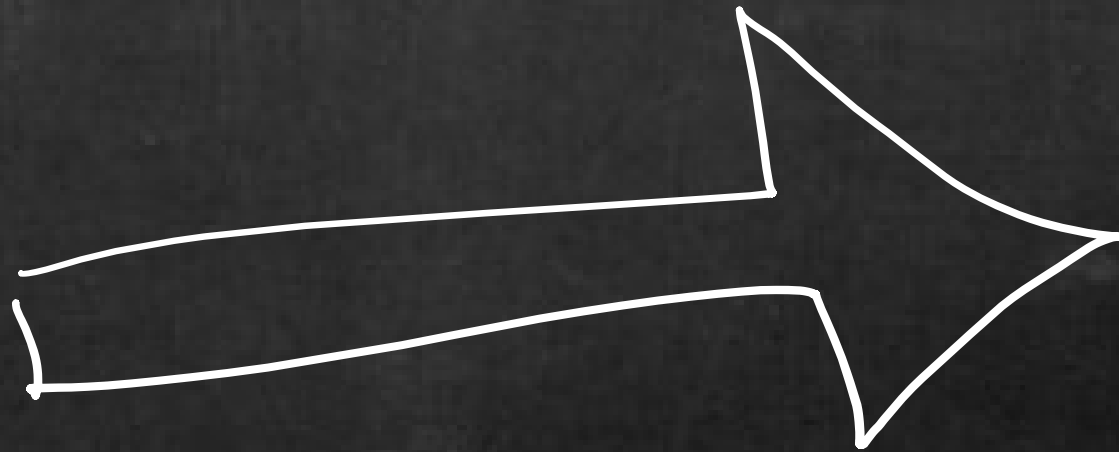


Why?

T2D & IRZ can be reversed



YOUR BRAIN needs
you to fast, too.



Intermittent metabolic switching, neuroplasticity and brain health

Mark P. Mattson^{1,2}, Keelin Moehl¹, Nathaniel Ghena¹, Maggie Schmaedick¹ and Aiwu Cheng¹

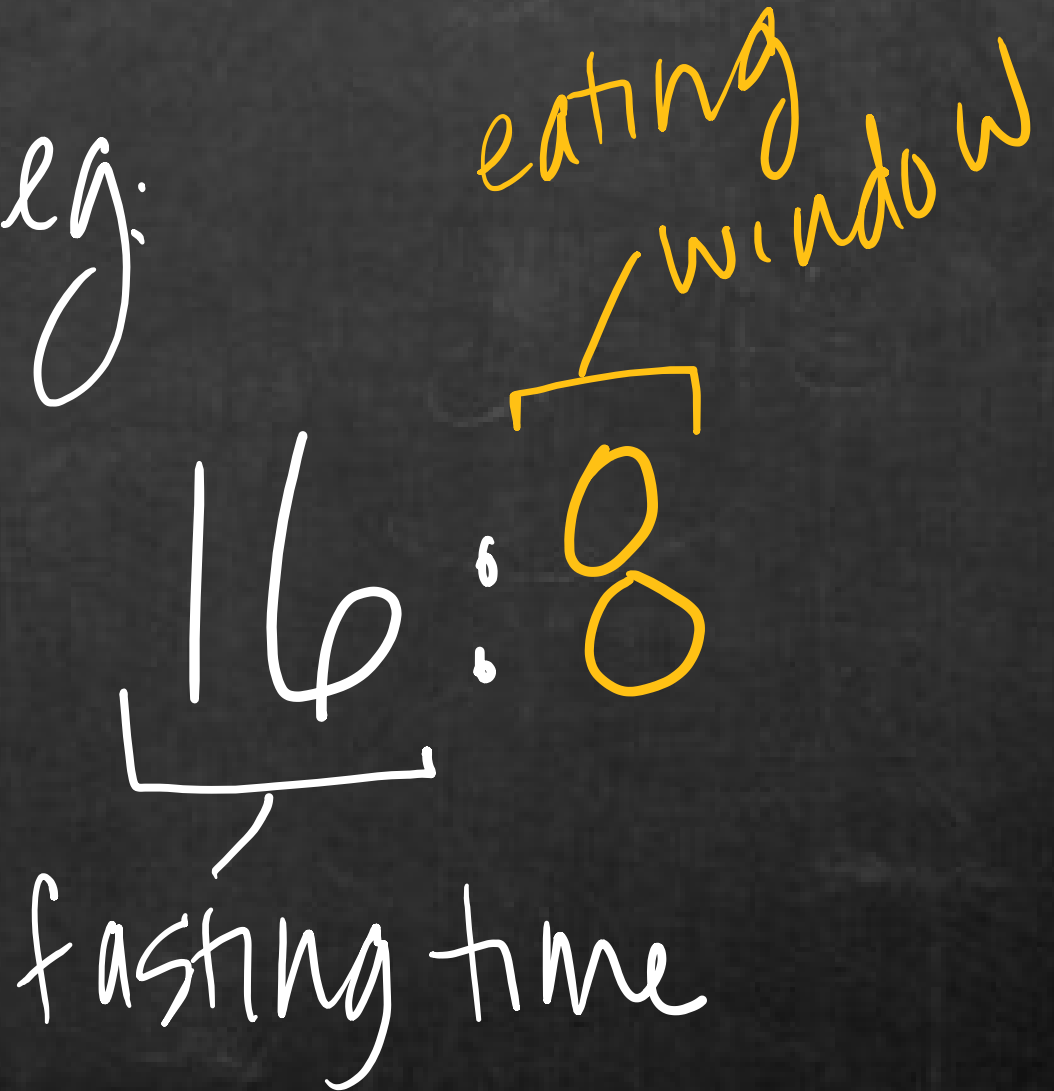
Abstract | During evolution, individuals whose brains and bodies functioned well in a fasted state were successful in acquiring food, enabling their survival and reproduction. With fasting and extended exercise, liver glycogen stores are depleted and ketones are produced from adipose-cell-derived fatty acids. This metabolic switch in cellular fuel source is accompanied by cellular and molecular adaptations of neural networks in the brain that enhance their functionality and bolster their resistance to stress, injury and disease. Here, we consider how intermittent metabolic switching, repeating cycles of a metabolic challenge that induces ketosis (fasting and/or exercise) followed by a recovery period (eating, resting and sleeping), may optimize brain function and resilience throughout the lifespan, with a focus on the neuronal circuits involved in cognition and mood. Such metabolic switching impacts multiple signalling pathways that promote neuroplasticity and resistance of the brain to injury and disease.



INTERMITTENT FASTING

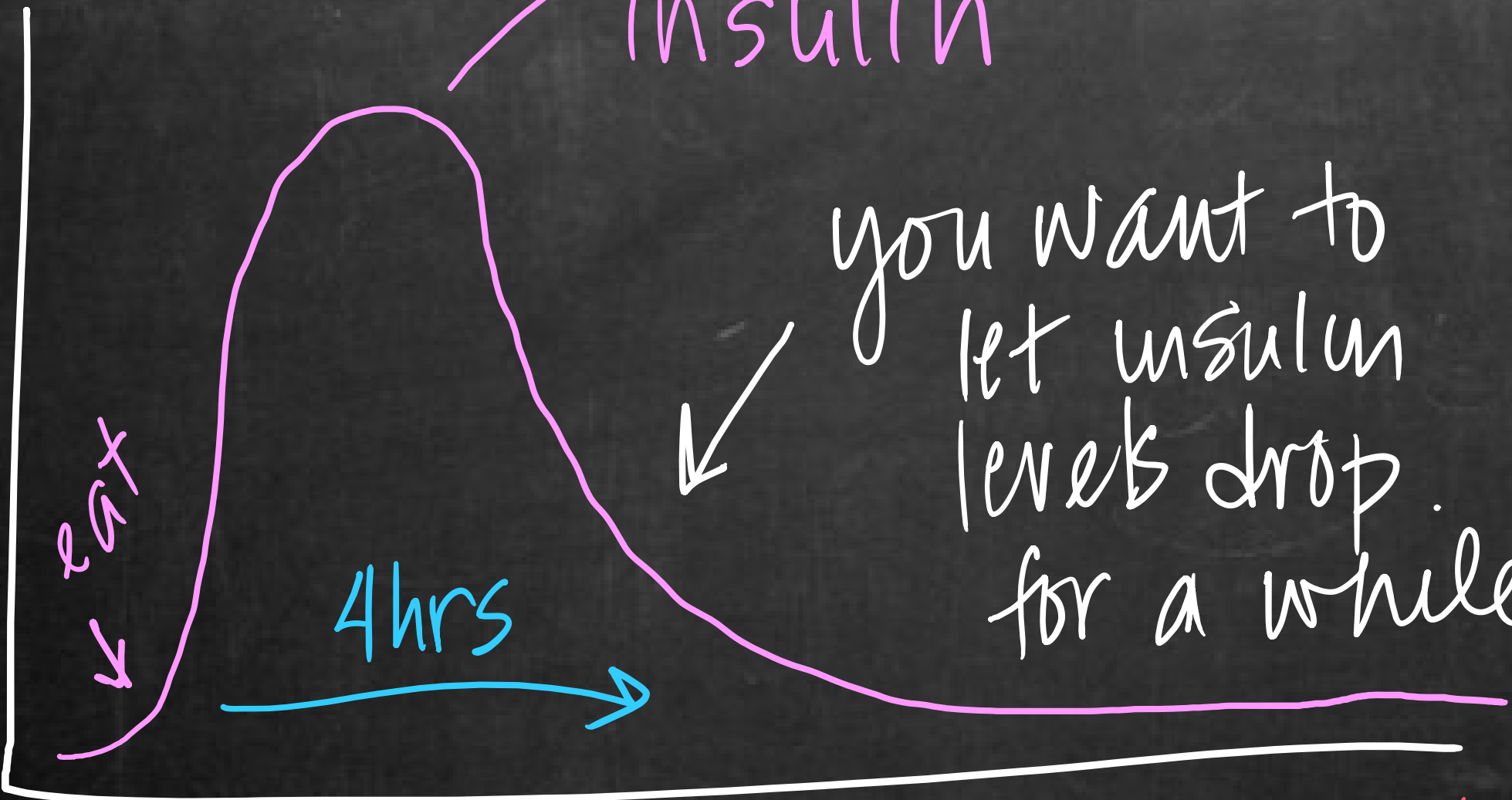


eg:



insulin

insulin



time (hours)

you want to let insulin levels drop for a while →

← use fat for energy



FASTING
Heal Your Body Through
Intermittent, Alternate-Day, and Extended Fasting

Dr. Jason Fung
Fasting

<https://idmprogram.com/>

↑ amazing results
from his clinic



↑ amazing results
from his clinic

When the
adipocytes
shrink



insulin resistance ↓↓



Fasting and exercise



Glucose-to-ketone switch
(bioenergetic challenge)

↑ Ketones
↑ Ghrelin
↑ Myokines

↑ Ketones
↑ BDNF, FGF2
↑ CREB, PGC1 α
↑ SIRT1, SIRT3
↑ Autophagy,
DNA repair

↓ Glucose
↓ Leptin
↓ Insulin
↓ Cytokines

↓ mTOR
↓ Protein synthesis
↓ Cytokines



Cellular stress resistance
(molecular recycling and repair
pathways)

Eating, resting and sleeping



Ketone-to-glucose switch
(recovery period)

↓ Ketones
↓ Ghrelin
↓ Myokines

↓ Ketones
↓ BDNF
↓ CREB
↓ SIRT1, SIRT3
↓ Autophagy

↑ Glucose
↑ Leptin
↑ Insulin
↑ Cytokines

↑ mTOR
↑ Protein synthesis
↑ Mitochondrial
biogenesis



Cell growth and plasticity pathways
(mitochondrial biogenesis,
synaptogenesis and neurogenesis)




- Enhanced synaptic plasticity and neurogenesis
- Enhanced performance (cognition, mood, motor and ANS function)
- Resistance to neuronal degeneration and enhanced recovery from injury



Sugar brain

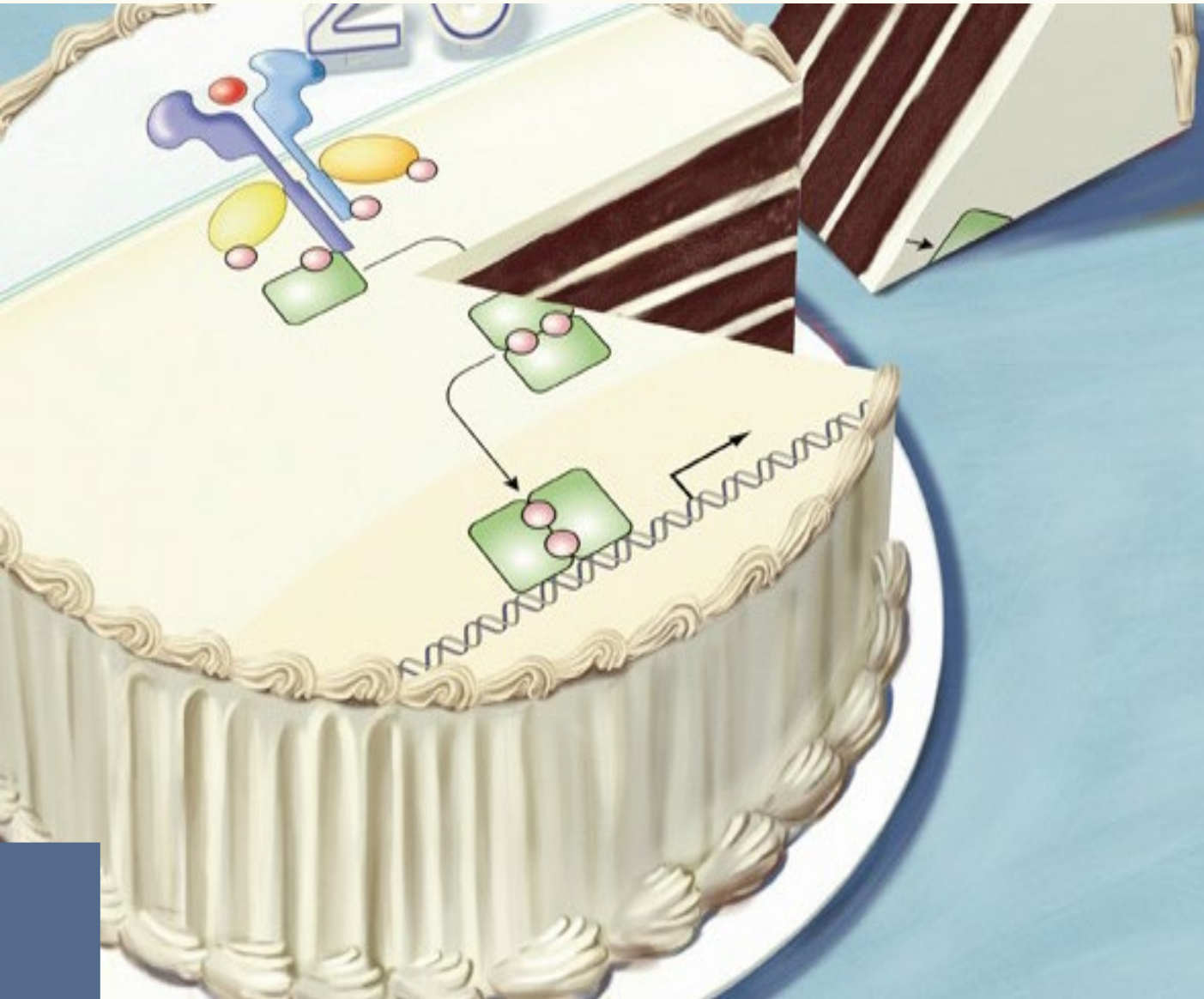
Carbs and sugar in our diet is a huge part of the problem.



Snacking is a problem

Snacking promotes continuous insulin release and keeps stuffing the adipocytes.

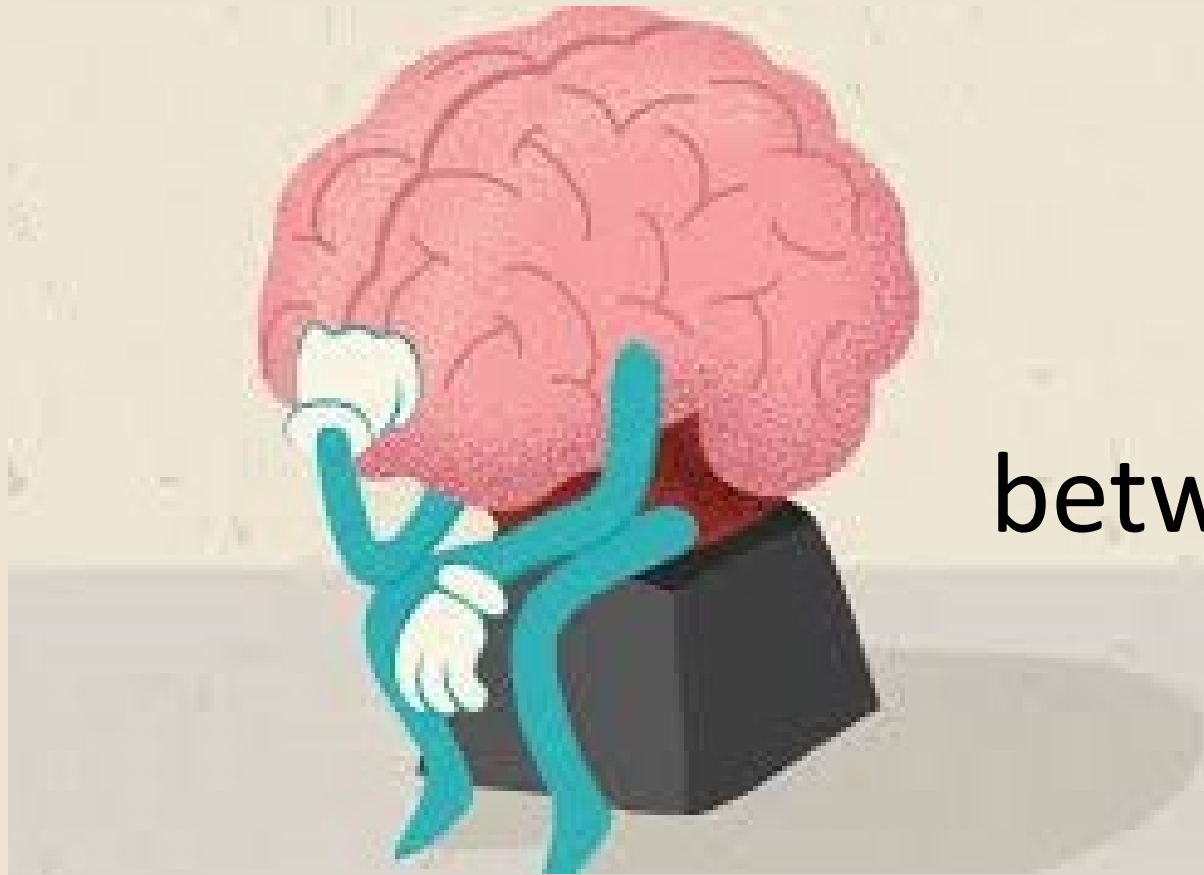




Insulin signaling

**Is only
part of the
problem**





Our Brain

Thrives when it switches between ketones and glucose.

**Fixing IR will
heal your heart**



Intermittent Fasting

**Current
Solution**



“

Your body is resilient

IR+T2D
do not
have to be
life
sentences

ThankYou

