PSİKOFARMAKOLOJİ DERNEĞİ
TURKISH ASSOCIATION FOR PSYCHOPHARMACOLOGY
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Glucose Metabolism & Psychiatric Disorders

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GATA Haydarpaşa - İstanbul

WPA Thematic Conference on Intersectional Collaboration: The Multidisciplinary Facets of Psychiatry
4th European Congress of the International Neuropsychiaric Association: Overlap and Integration in Neuropsychiatry
November 29- December 2, 2012, Athens -Greece

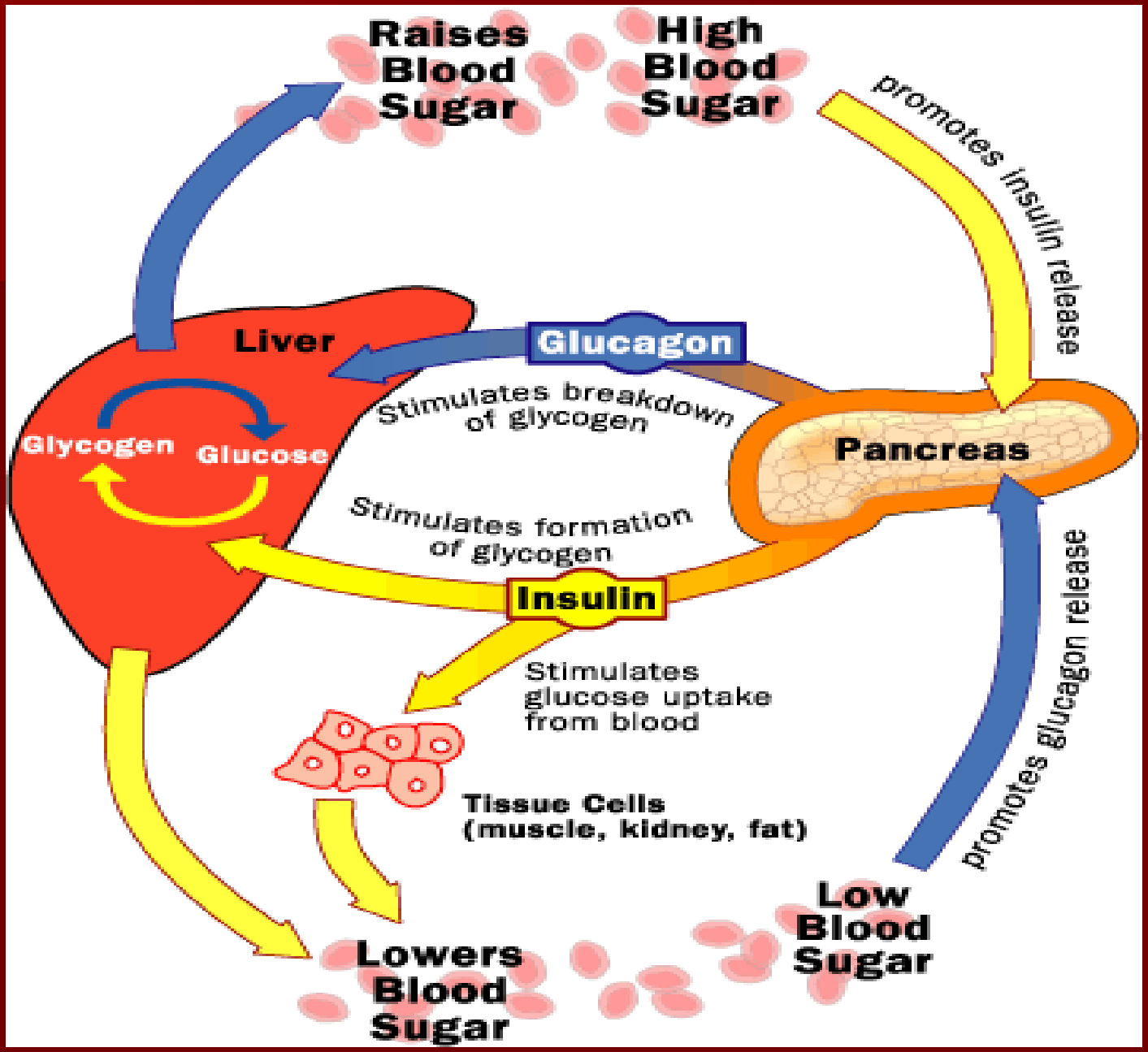
Disclosure

I have the following pharmaceutical companies and researchers have worked as a consultant and speaker:

Abdi İbrahim, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen -Cilag, Sanofi Aventis, Sanovel, Sifar, and Wyeth.

Background

- **Insulin**- a hormone produced in the pancreas that carries sugar from the blood into the cells to be used for energy. Insulin is a "***fat storage hormone***".
- **Glucagon-** a hormone to counter the blood sugar lowering effects of insulin. In a properly functioning body insulin and glucagon are in balance.
- ***Insulin resistance-*** *a consequence of heredity, excess body fat, hormone changes and even some medications that prevents our cells from using insulin to regulate blood sugar effectively.*


Raises Blood Sugar
High Blood Sugar
promotes insulin release
Liver
Glucagon
Glycogen
Glucose
Stimulates breakdown of glycogen
Pancreas
Stimulates formation of glycogen
Insulin
Stimulates glucose uptake from blood
promotes glucagon release
Tissue Cells (muscle, kidney, fat)
Low Blood Sugar
Lowers Blood Sugar

Selected Neuropeptide Transmitters

Adrenocorticotropin hormone (ACTH)
Angiotensin
Atrial natriuretic peptide
Bombesin
Calcitonin
Calcitonin gene-related peptide (CGRP)
Cocaine and amphetamine regulated transcript (CART)
Cholecystokinin (CCK)
Corticotropin-releasing factor (CRF)
Dynorphin
β - Endorphin
Leu-enkephalin
Met-enkephalin
Galanin
Gastrin
Gonadotropin-releasing hormone (GnRH)
Growth hormone
Growth hormone-releasing hormone (GHRH; GRF)
Insulin
Motilin
Neuropeptide S
Neuropeptide Y (NPY)
Neurotensin
Neuromedin N
Orphanin FQ/Nociceptin
Orexin
Oxytocin
Pancreatic polypeptide
Prolactin
Secretin
Somatostatin (SS; SRIF)
Substance K
Substance P
Thyrotropin-releasing hormone (TRH)
Urocortin (1, 2, and 3)
Vasoactive intestinal polypeptide (VIP)
Vasopressin (AVP; ADH)

Blood glucose levels mg/dL

	HEALTHY PERSONS Blood glucose levels	PREDIABETICS	DIABETICS
FASTING	70 - 99 mg/dL.	100 -125 mg/dL.	> 126 mg/dL
POSTPRANDIAL After 2 hours	70-140mg/dL	140 -199 mg/dL.	> 200mg/dL

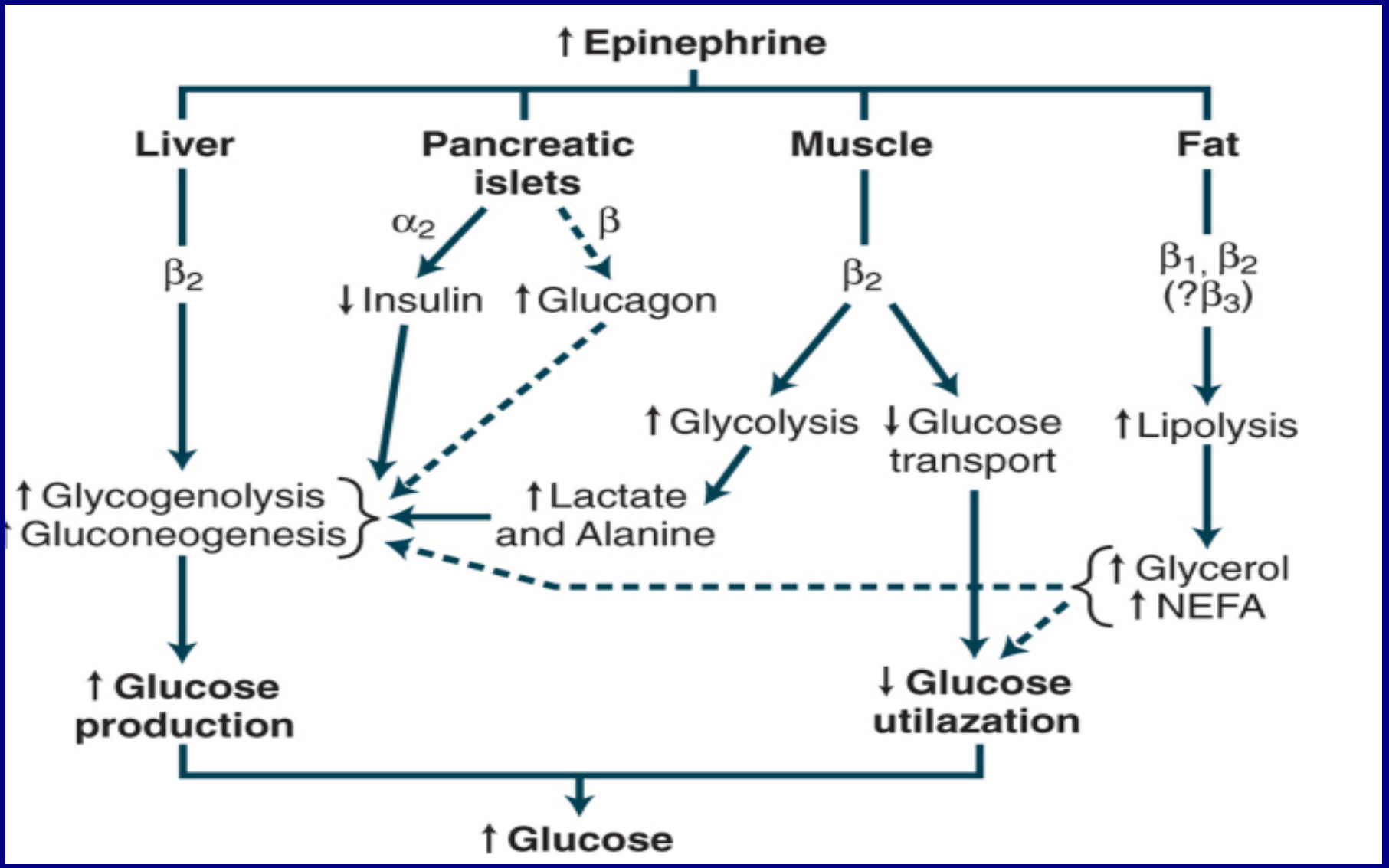
Hypoglycemia and mental functions

HYPOGLYCEMIA IS AT BLOOD GLUCOSE VALUES BELOW 70 MG/ DL .

- arterialized blood by :
  - **at 66 mg/ dL** the onset of counterregulatory hormonal response (glucagon, epinephrine, norepinephrine and growth hormone),
  - **at 56 mg/ dL** the onset of the sympathetic response ,
  - **at 50 mg/ dL** the onset of neuroglucopenic symptoms and deterioration in cognitive function tests began

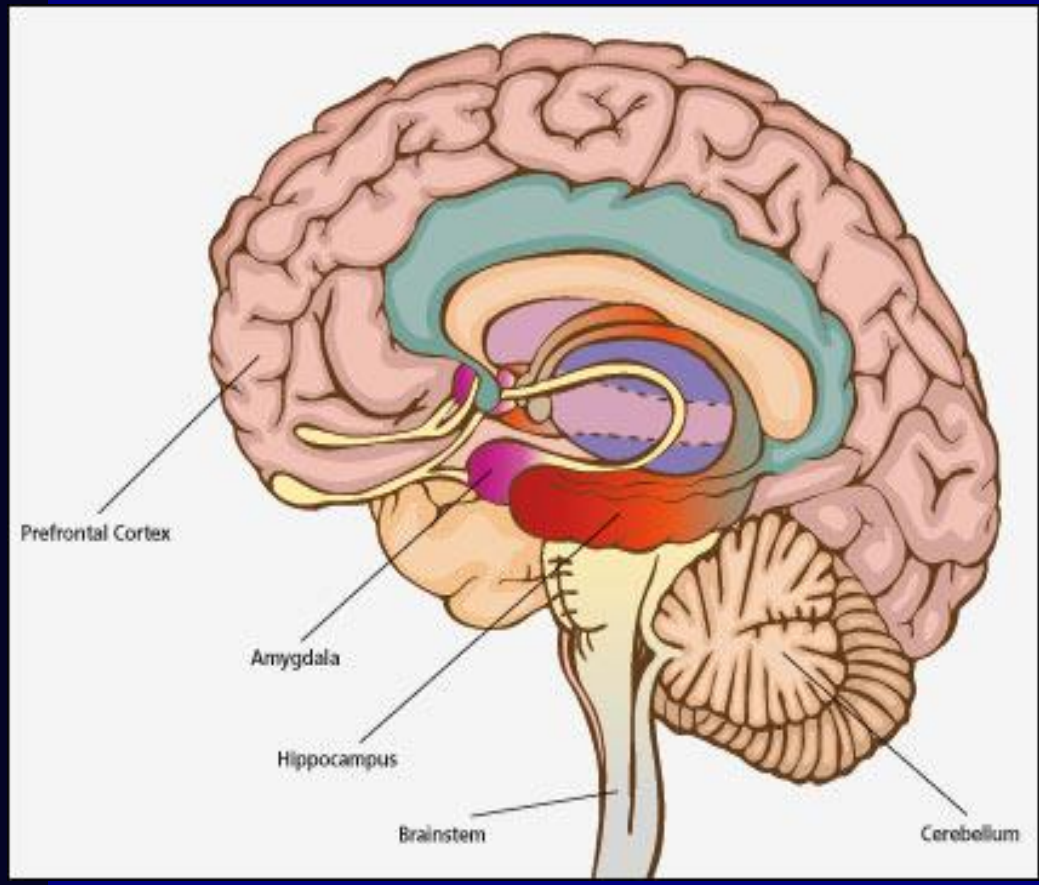
Mitrakou A , at al. Am J Physiol, 1991, 260 (Endocrinol Metab 23), E67-E74.

Counterregulatory effects of Epinephrine during Hypoglycemia



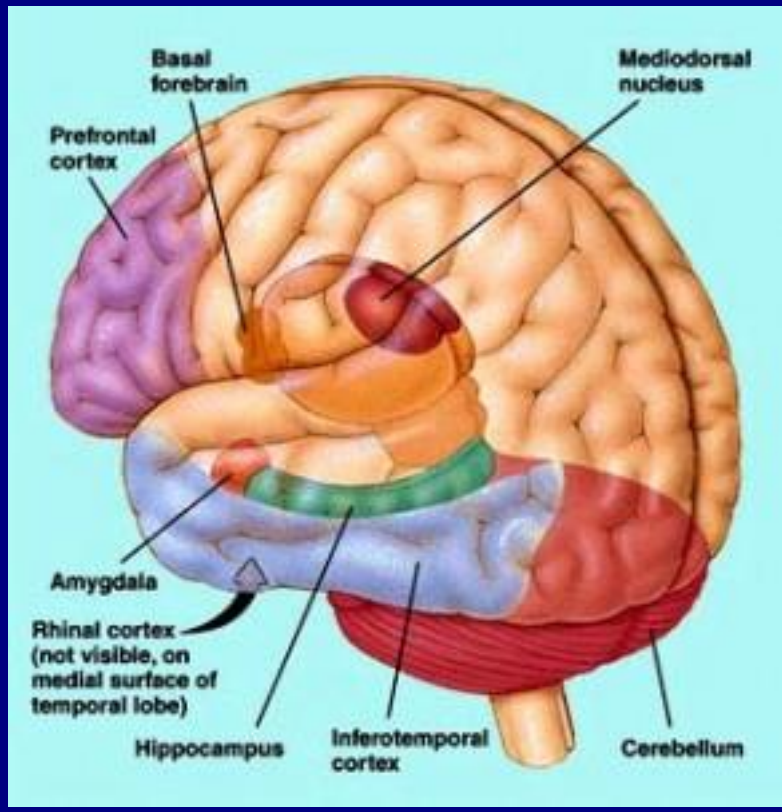
Signs of hypoglycemia cluster into three sets:

- **AUTONOMIC** (*sweating, palpitation, shaking and hunger*),
- **Neuroglucopenic** (*confusion, drowsiness, odd behavior, speech difficulty and incoordination*),
- **Malaise** (*nausea and headache*).



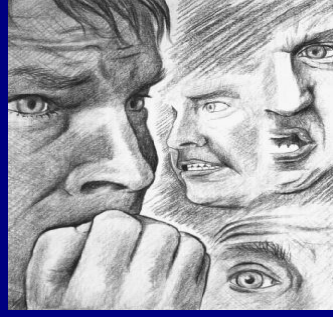
PANIC ATTACKS AND HYPOGLYCAEMIA HAVE SIMILAR SYMPTOMS

- PJ Lefevre proposes the term of "Adrenergic hormone postprandial syndrome" to describe autonomic symptoms (*anxiety, palpitations, sweating, irritability, tremor*...) that are experimentally observed after insulin infusion, at **plasma glucose levels of about 66 mg/dL.** It is likely that, in some individuals, after a meal, such autonomic counterregulation may occur.



Lefebvre PJ. Hypoglycemia or non-hypoglycemia. In: Rifkin H, Colwell JA, Taylor SI (eds) Diabetes Excerpta Medica Amsterdam London New York Tokyo, 1991,757-761.

Panic & Hypoglycemia have similar symptoms



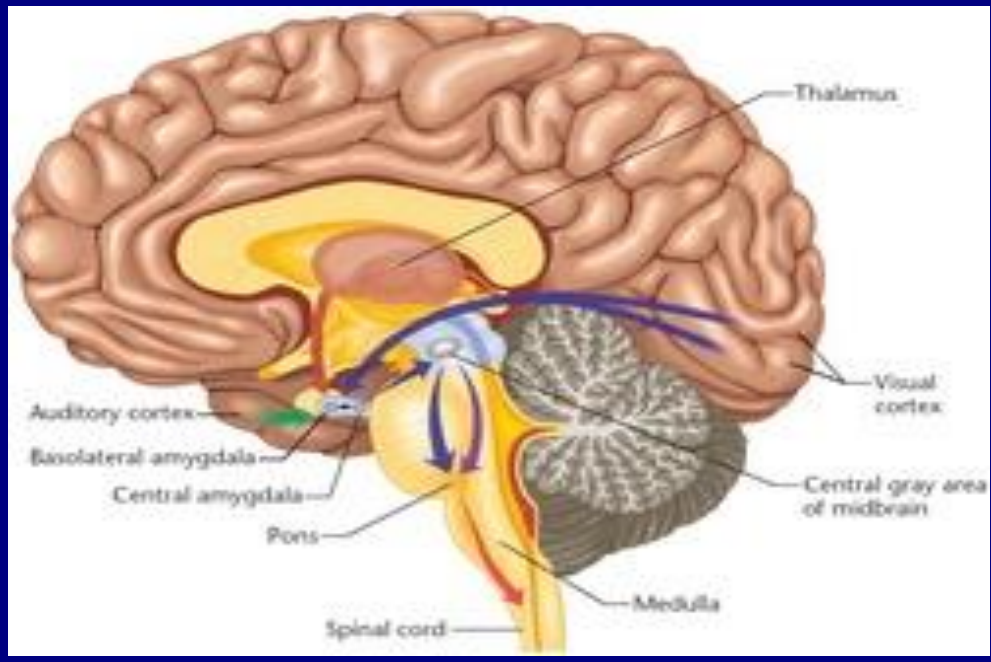
- A feeling of imminent danger or doom
- The need to escape
- Palpitations
- Sweating
- Trembling
- Shortness of breath or a smothering feeling
- A feeling of choking
- Chest pain or discomfort
- Nausea or abdominal discomfort
- Dizziness or lightheadedness
- A sense of things being unreal, depersonalization
- A fear of losing control or "going crazy"
- A fear of dying
- Tingling sensations
- Chills or hot flushes

TABLE I. *Standardized list of symptoms of hypoglycemia. Each sign could be quoted from 0 to 5 allowing the calculation of a "score". After [20, 24, 26].*

Sympathetic signs	Neuroglucopenic signs
Anxiety	Hunger
Palpitations	Dizziness
Irritability	Tingling
Tremors	Blurred vision
Sweating	Difficulty in thinking
	Faintness

Reactive Hypoglycemia and Psychological Effects

Reactive hypoglycemic states may manifest an abnormal personality profile as determined, for instance, by the Minnesota Multiphasic Personality Inventory (MMPI). These patients' personality profiles are characterized by hypersomatization and hypochondriacal complaints, emotional distress, anxiety, somatization, depression,and obsessive-compulsive scores than controls.



Johnson DD, Door KE, Swenson WM, Service FJ. Reactive hypoglycemia. JAMA, 1980, 243, 1151-1155

Berlin who studied eight patients with **suspected postprandial hypoglycemia (PPH)** in whom he evaluated beta-adrenergic sensitivity with the **isoproterenol sensitivity test**. While plasma epinephrine and norepinephrine responses after OGTT were similar than those of controls, both heart rate and systolic blood pressure were significantly higher (albeit remaining within the normal range) compared to controls. Moreover, after glucose intake, PPH patients had symptoms (*palpitations, headache, tremor, generalized sweating, hunger, dizziness, sweating of the palms,flush, nausea, and fatigue*).

This study shows that such patients with suspected postprandial hypoglycemia most often exhibit an increased beta-adrenergic sensitivity and emotional distress.

Berlin I, Grimaldi A, Landault C, Cesselin F, Puech AJ. J Clin Endocrinol Metab, 1994;79:1428-1433.

Hypoglycemia can also happen during sleep

- Nightmares,
- Night sweats ,
- Feeling tired, irritable, or confused after waking up

THE OTHER SIDE OF THE COIN

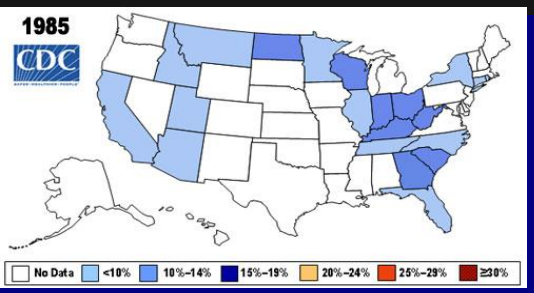
- Obesity & Metabolic Syndrome
- Diabetes Mellitus

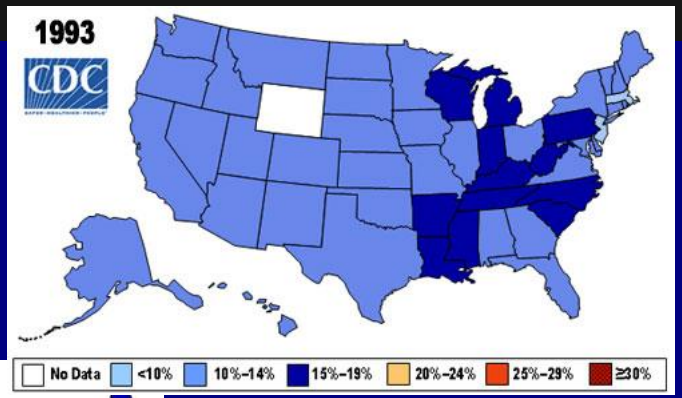
Obesity is becoming the most important health problem all over the world!

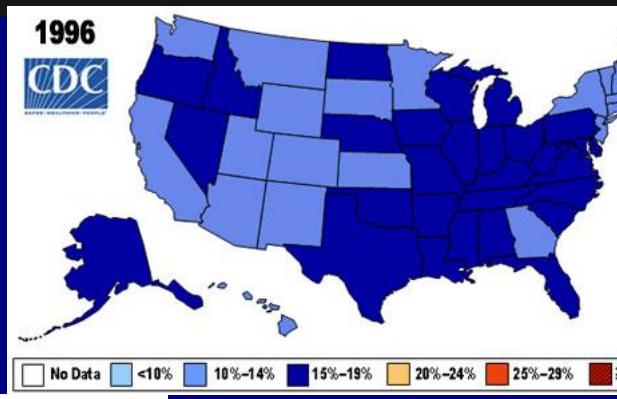
- Being overweight and obese are not only aesthetic problems, but they may also cause serious health problems such as metabolic syndrome and diabetes mellitus.
- Today, obesity and diabetes reached proportions of an epidemic worldwide.

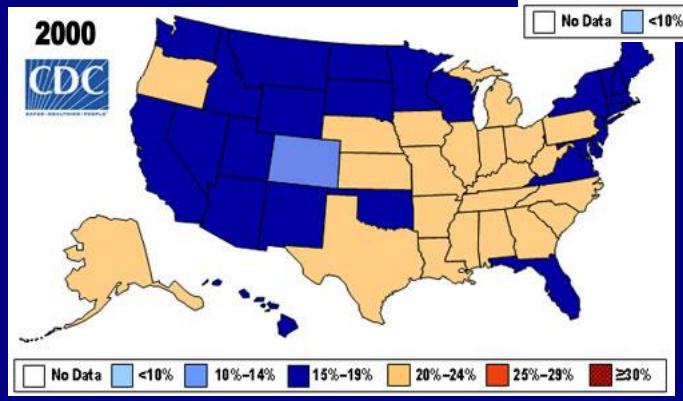
Obesity trends in the USA between 1985-2009:

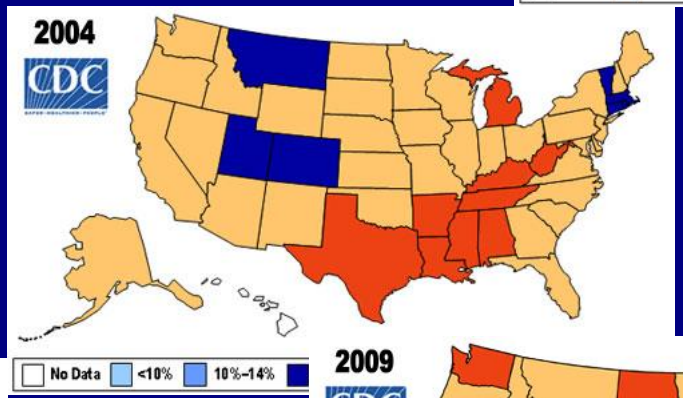
According to health statistics, the prevalence of obesity is increasing rapidly in the US!



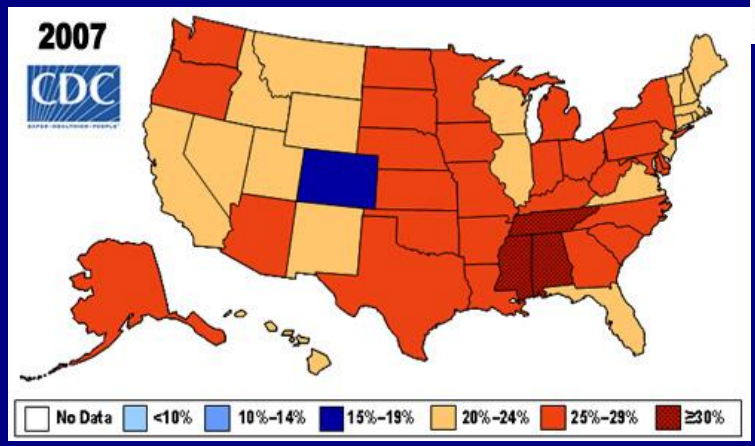


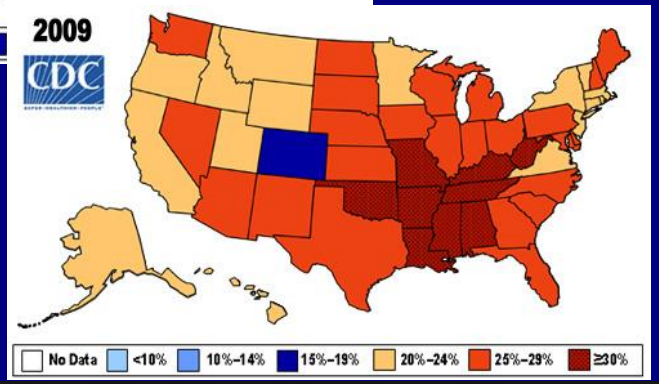






Percent of Obese (BMI > 30) in U.S. Adults

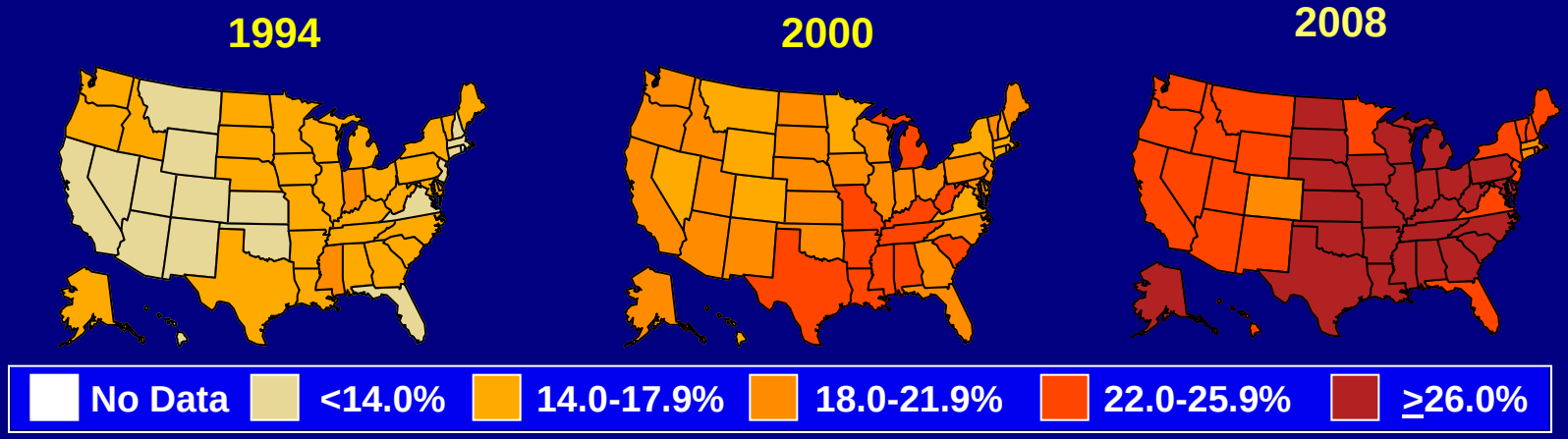




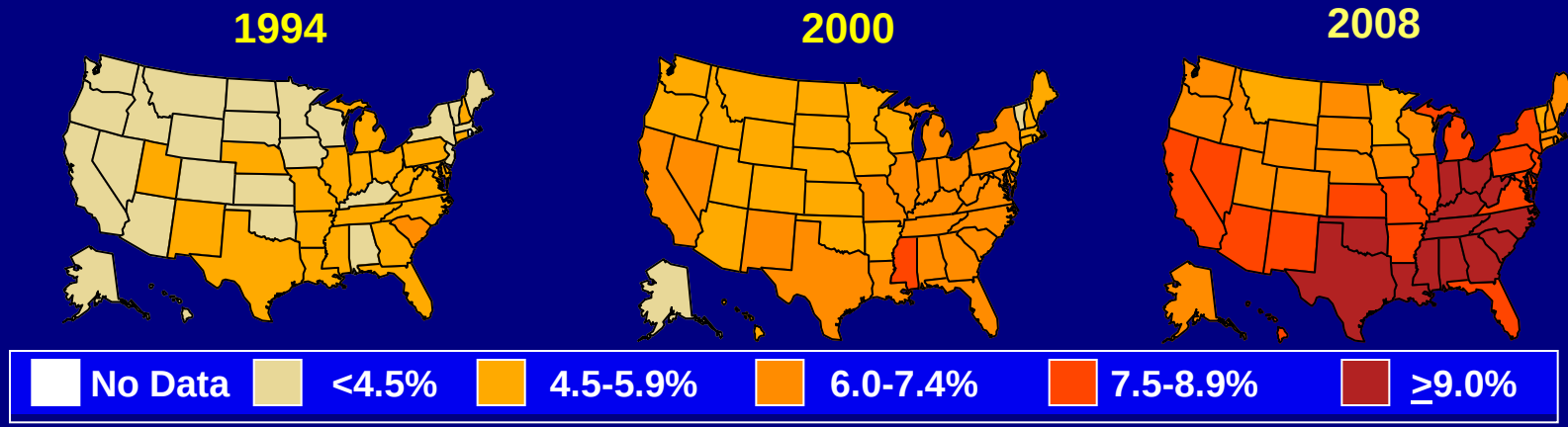
http://www.cdc.gov/obesity/data/trends.html

Obesity is associated with diabetes mellitus

Obesity (BMI ≥30 kg/m^2)

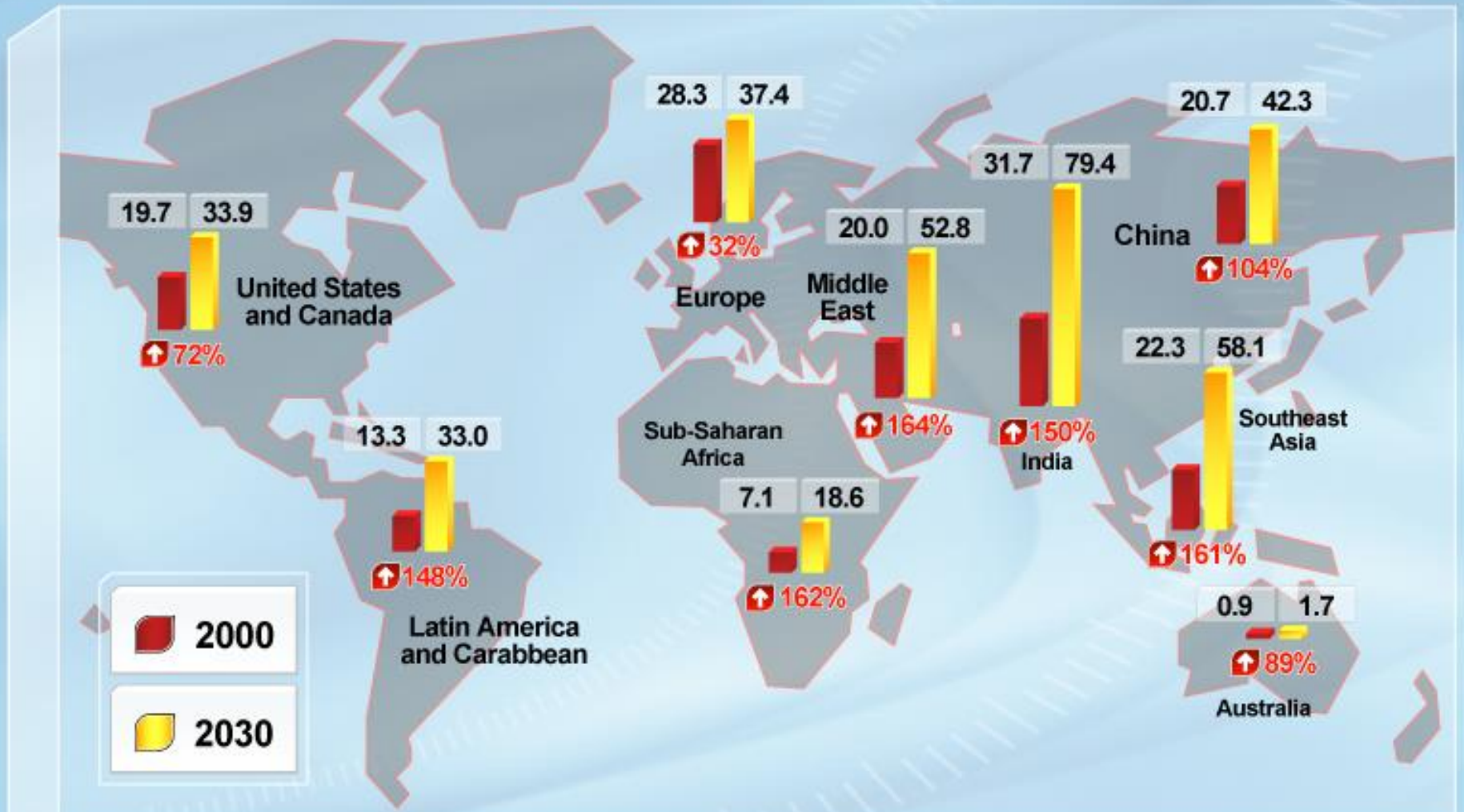


Diabetes



CDC's Division of Diabetes Translation. National Diabetes Surveillance System
available at http://www.cdc.gov/diabetes/statistics

WORLDWIDE PREVALENCE OF DIABETES IN 2000 AND ESTIMATES FOR THE YEAR 2030 (IN MILLIONS)



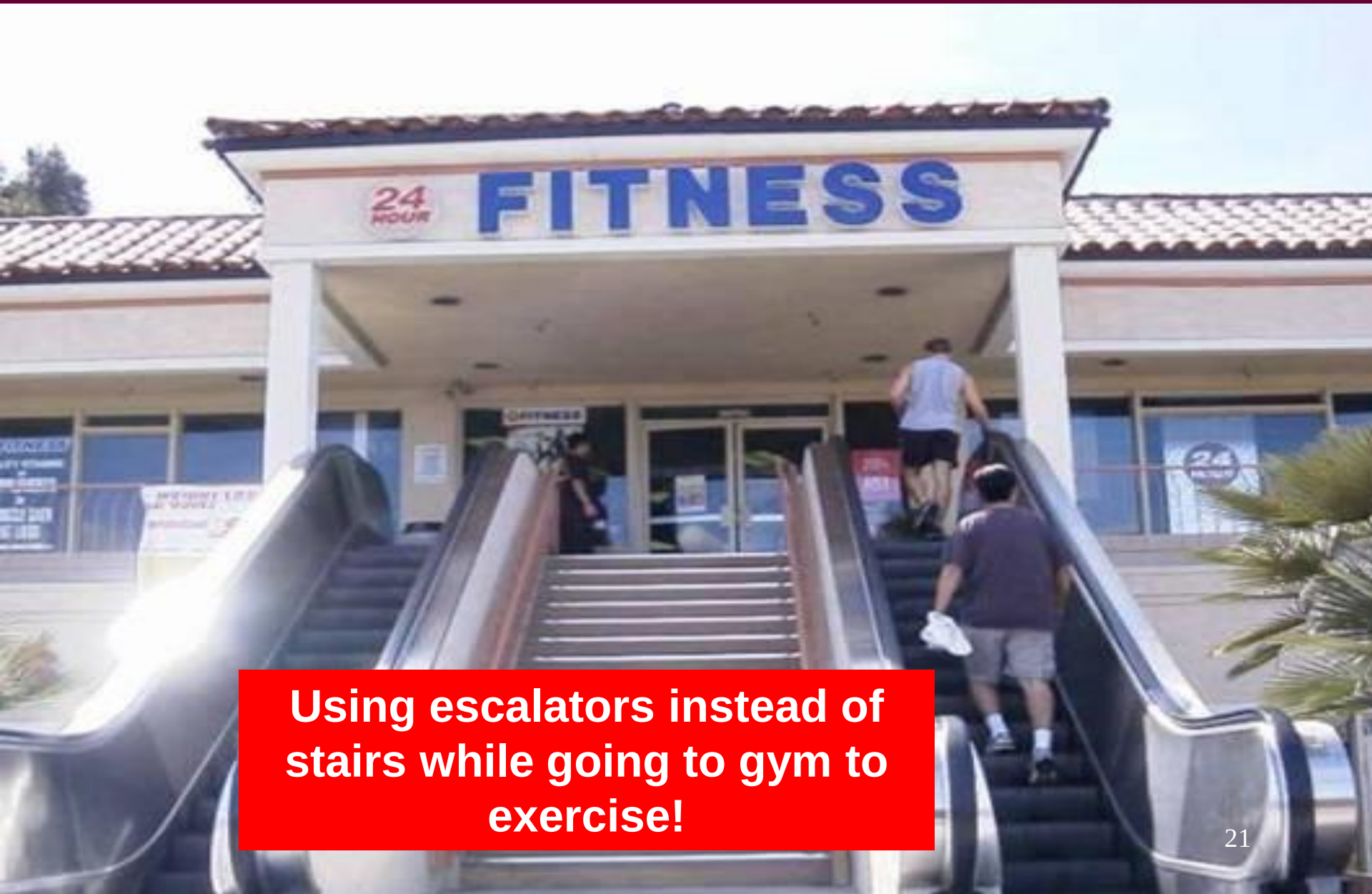
Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Hossain P et al. N Engl J Med 2007; 356: 213-5

Causes of weight gain and obesity

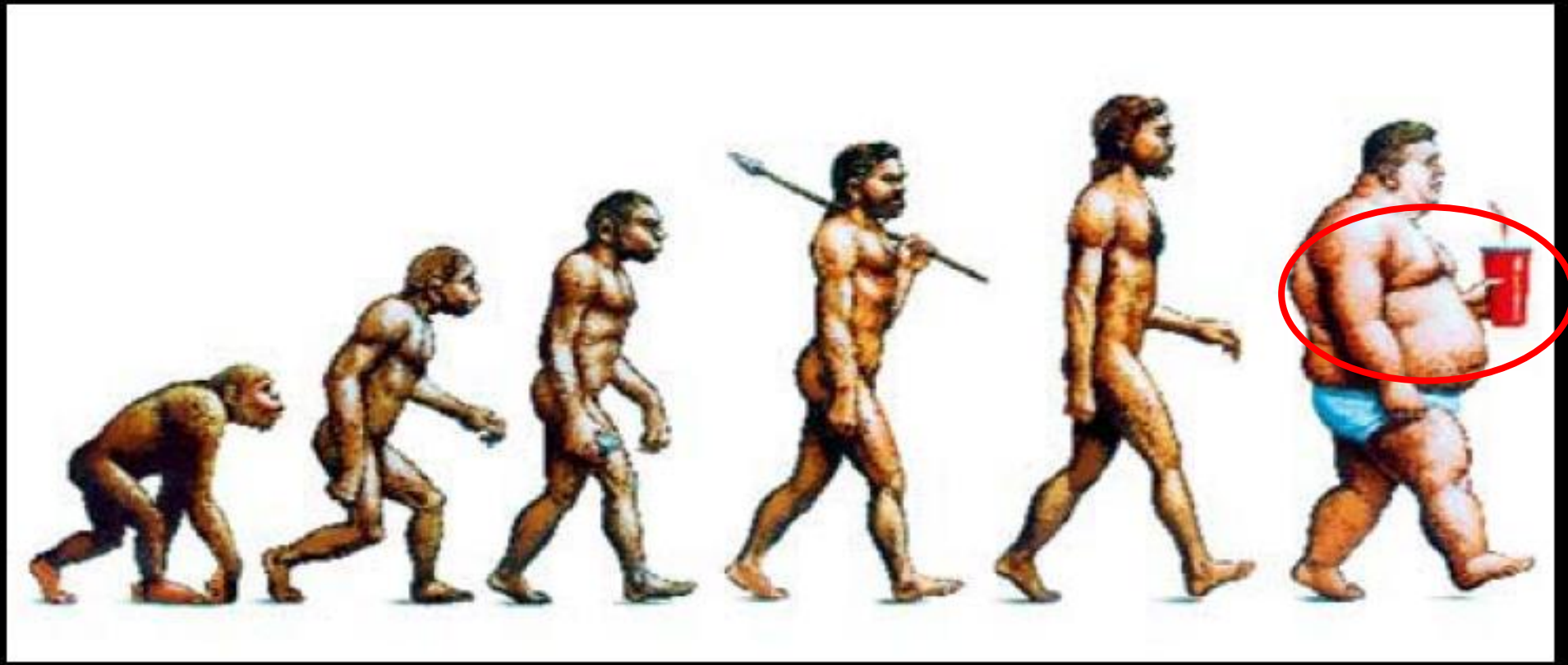
- Sedentary lifestyle:
- Bad eating habits:
  - Fast food-style, high-calorie diet, etc.

Sedentary lifestyle



Using escalators instead of stairs while going to gym to exercise!

A Further View of Evolution…



Day by day, food portion sizes are bigger!

1954
Burger King

2.8 oz
202 calories

2004

4.3 oz
310 calories

1955
McDonald's

2.4 oz
210 calories

2004

7 oz
610 calories

1900
Hershey's

2 oz
297 calories

2004

7 oz
1,000 calories

1916
Coca-Cola

6.5 fluid oz
79 calories

2004

16 fluid oz
194 calories

1950s
Movie popcorn

3 cups
174 calories

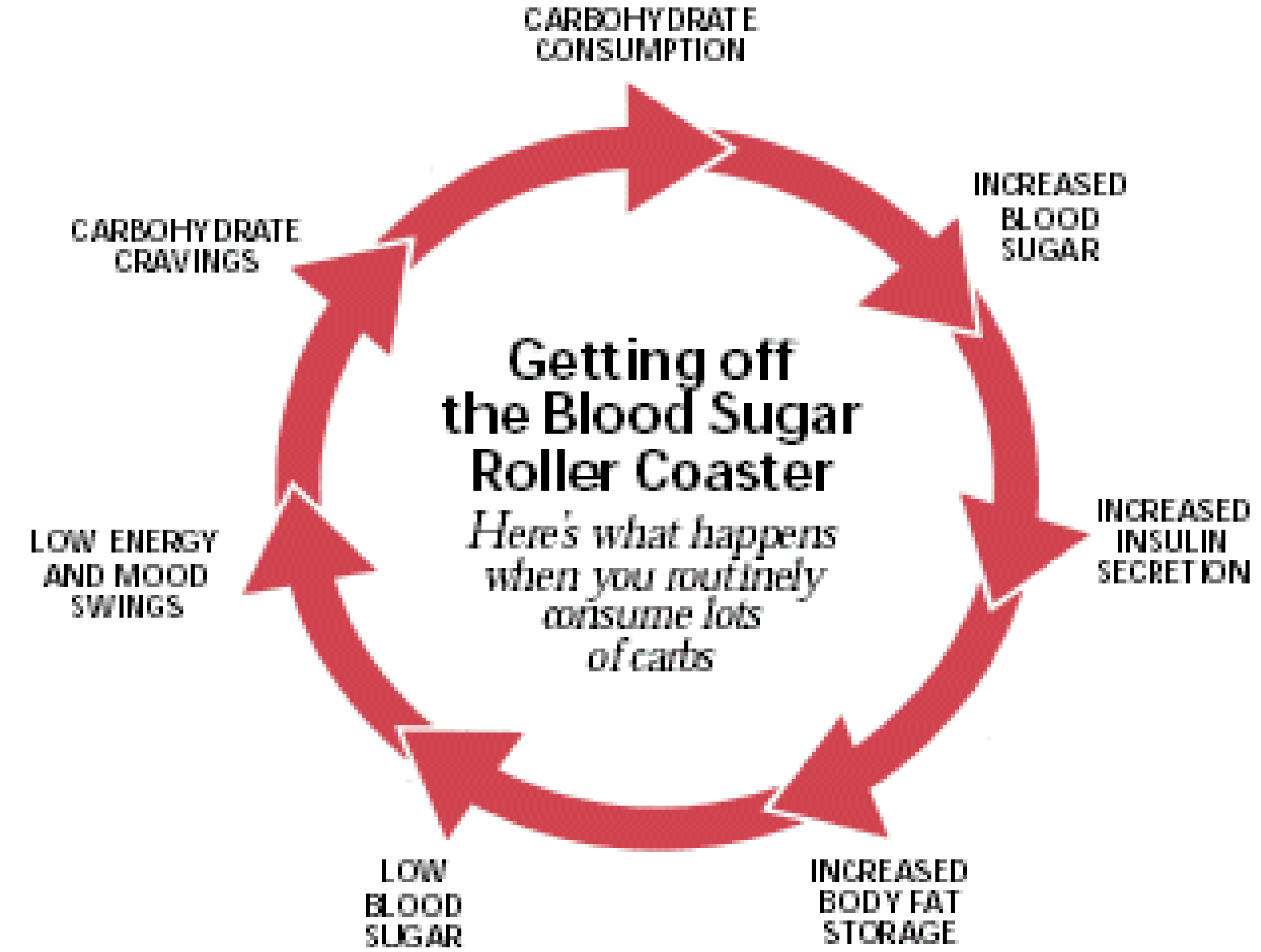
2004

21 cups (buttered)
1,700 calories

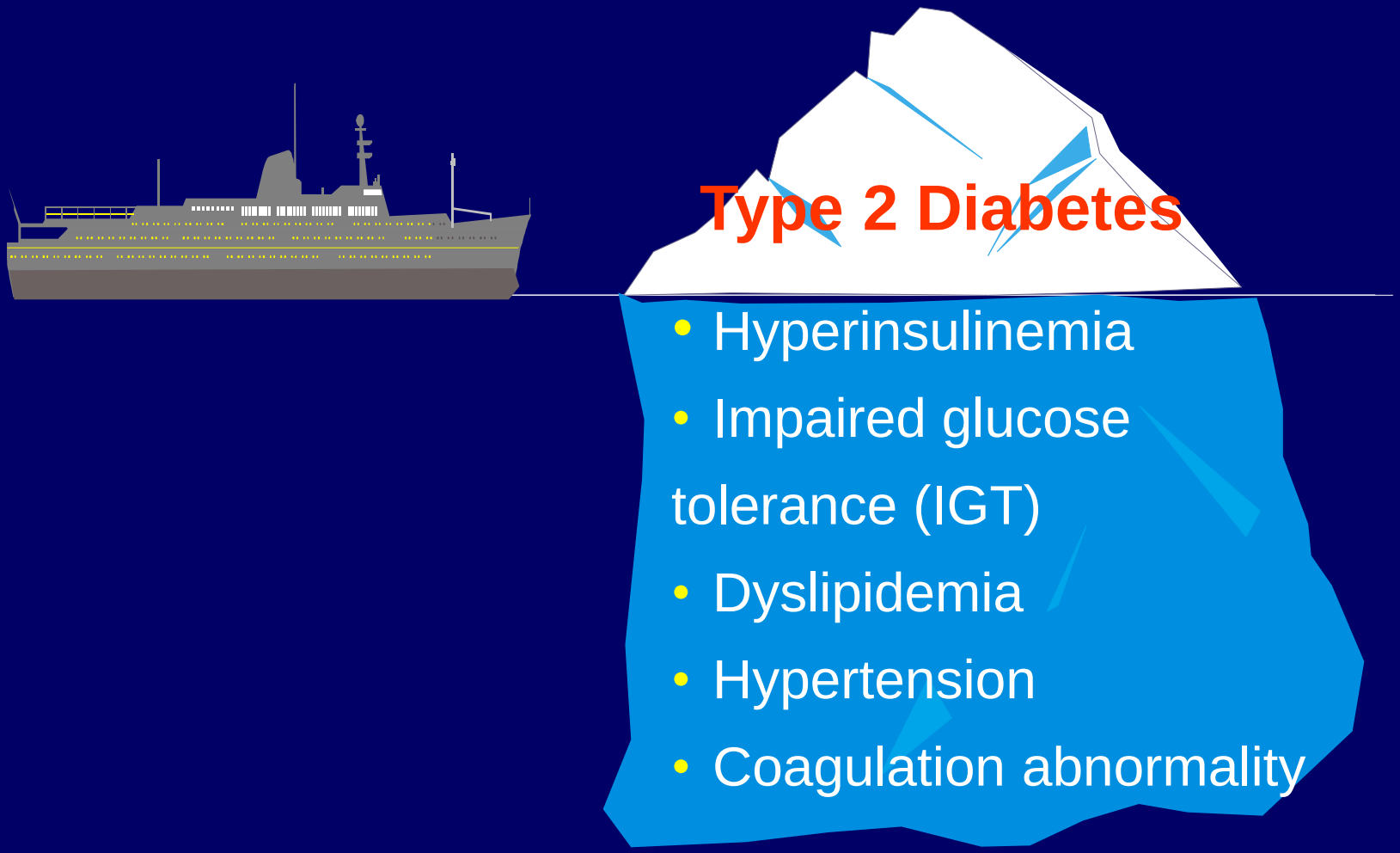
National Geographic, August 2004

Recently, a new generation has being created : the fast food nation!

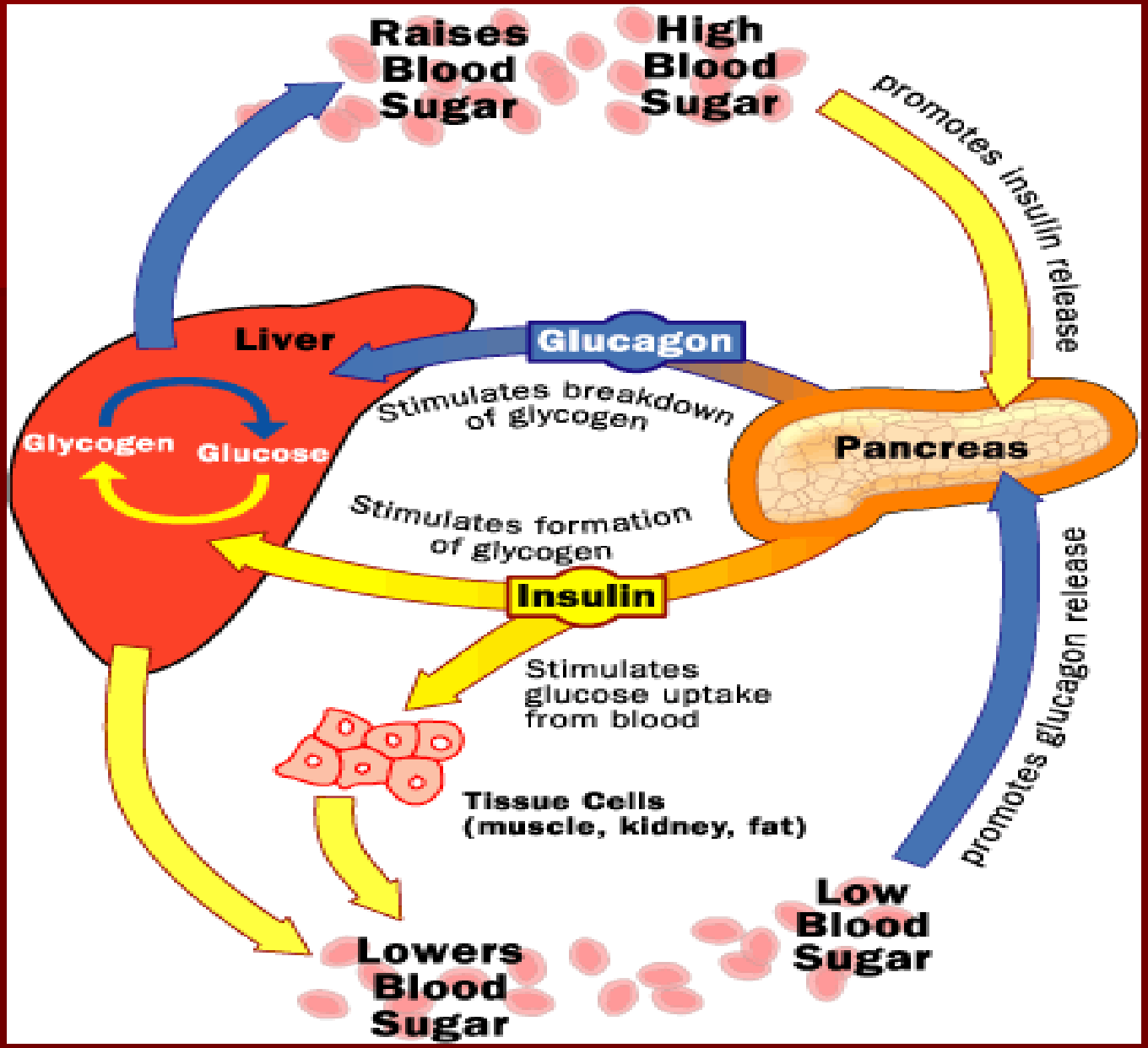
People are addicted to fast food life style, even in animals !


CARBOHYDRATE CONSUMPTION
INCREASED BLOOD SUGAR
INCREASED INSULIN SECRETION
INCREASED BODY FAT STORAGE
LOW BLOOD SUGAR
LOW ENERGY AND MOOD SWINGS
CARBOHYDRATE CRAVINGS
Getting off the Blood Sugar Roller Coaster
Here's what happens when you routinely consume lots of carbs

Insulin Resistance - Hidden Dangers



IGT = impaired glucose tolerance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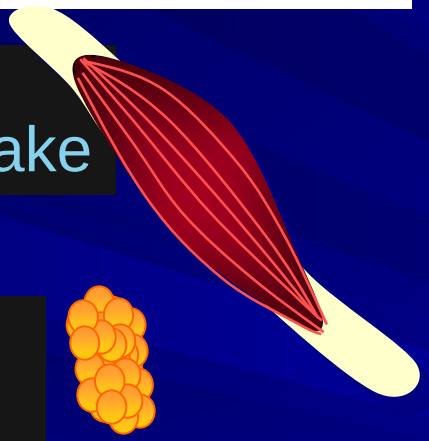
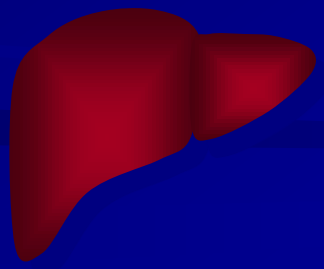
Pancreas
Stimulates formation of glycogen
Insulin
Stimulates glucose uptake from blood
Tissue Cells (muscle, kidney, fat)
promotes glucagon release
Low Blood Sugar
Lowers Blood Sugar

Dual Metabolic Abnormalities in Type 2 Diabetes

Insulin Resistance

- Decreased Glucose Uptake
- Unrestrained Lipolysis
- Excessive Hepatic Glucose Output

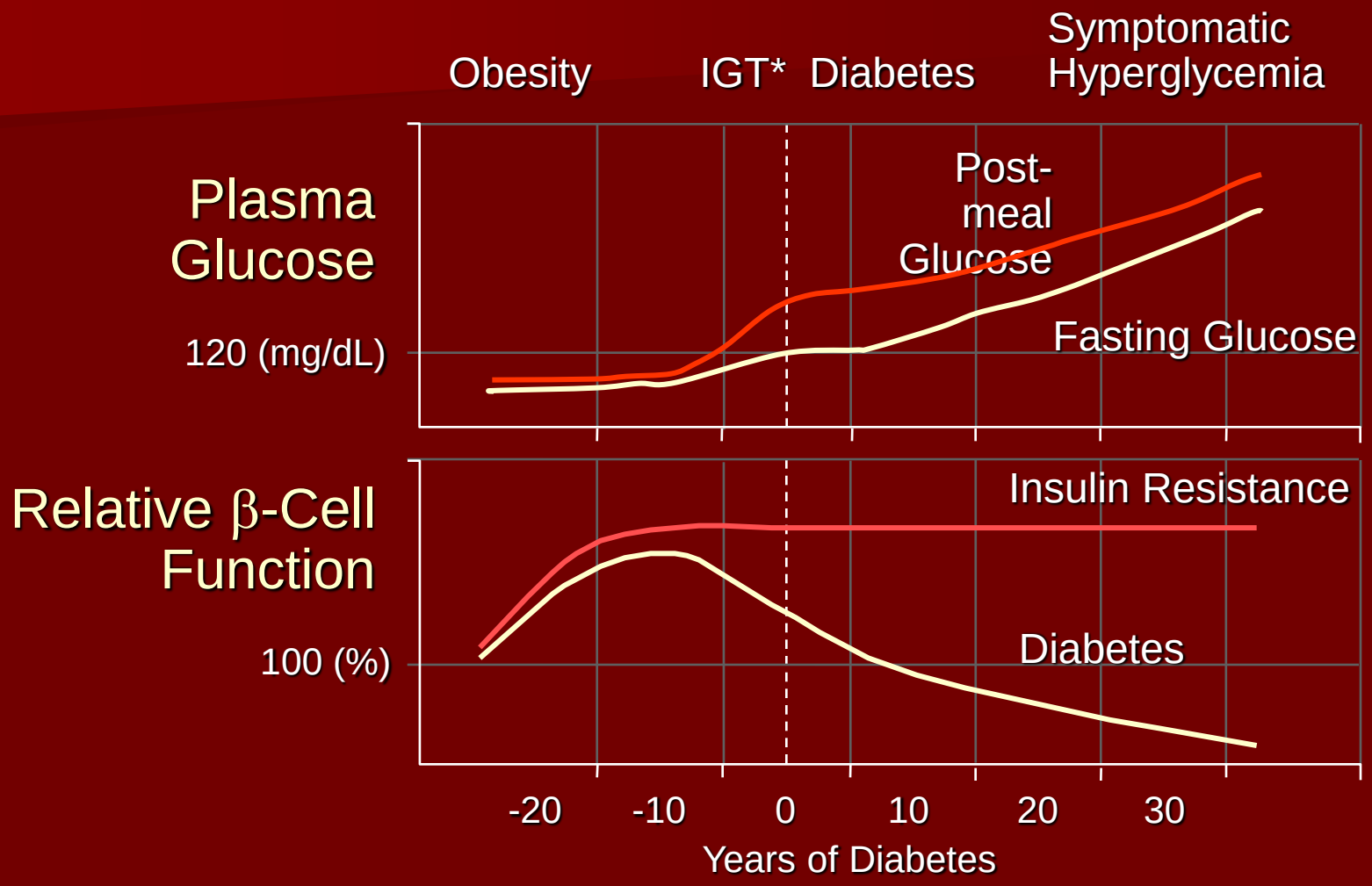




Insulin Deficiency

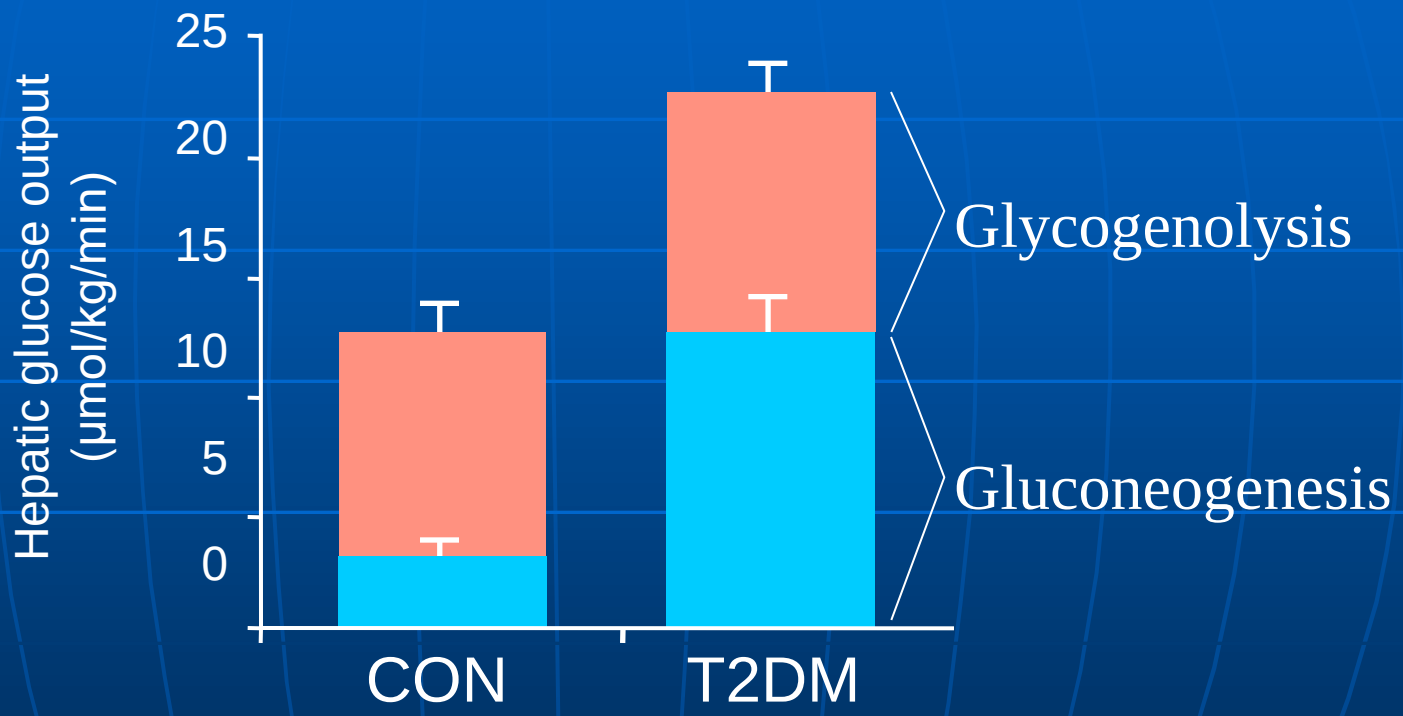
- Decreased Insulin Secretion

Natural History of DM II



*IGT = impaired glucose tolerance

Hepatic Insulin Resistance
(T2DM)



Adapted from Consoli A. *Diabetes* 1989;38:550–557.

Insulin Resistance: Inherited and Acquired Influences

Inherited

Rare Mutations

- Insulin receptor
- Glucose transporter
- Signalling proteins

Common Forms

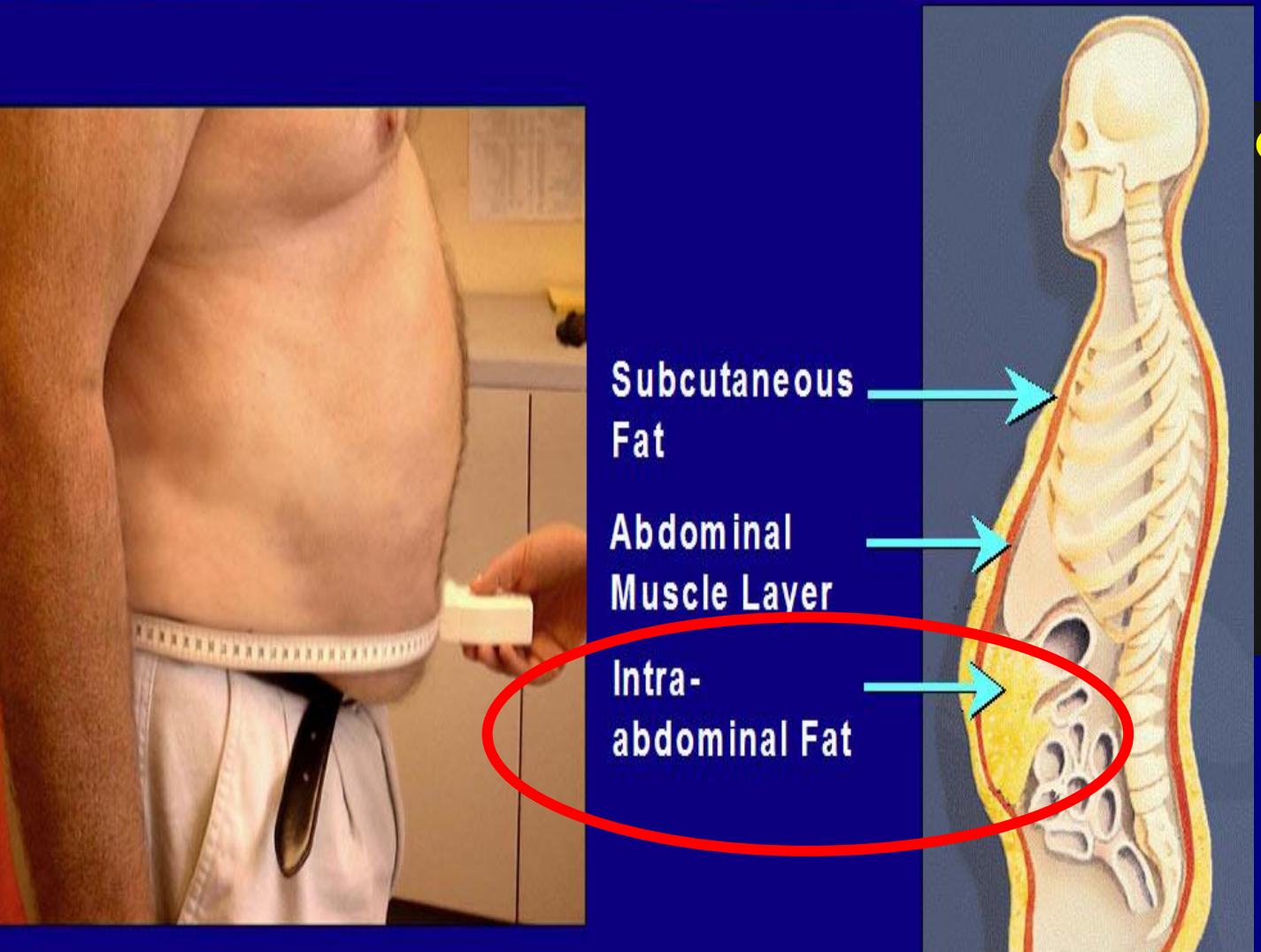
- Largely unidentified

Acquired

- Inactivity
- Obesity
- Stress
- Medications
- Glucose toxicity
- Lipotoxicity

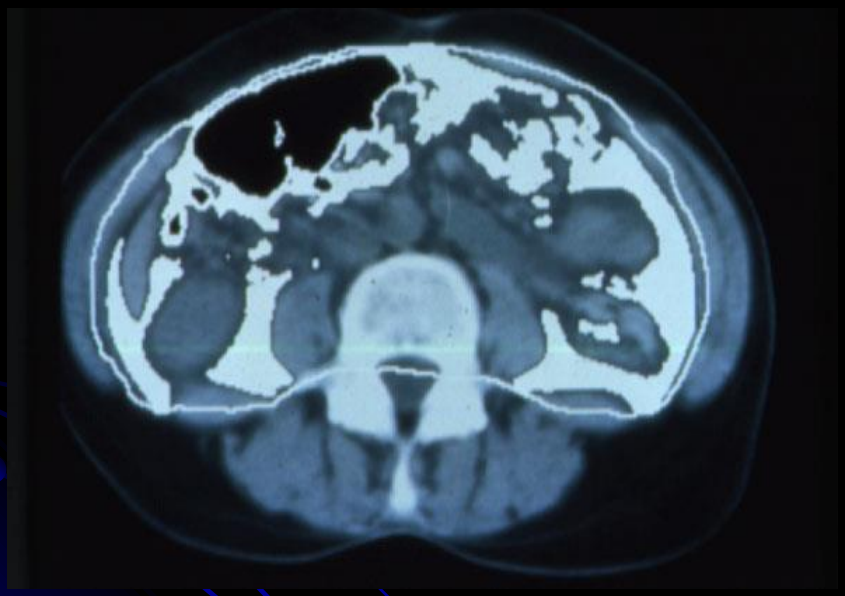
INSULIN RESISTANCE

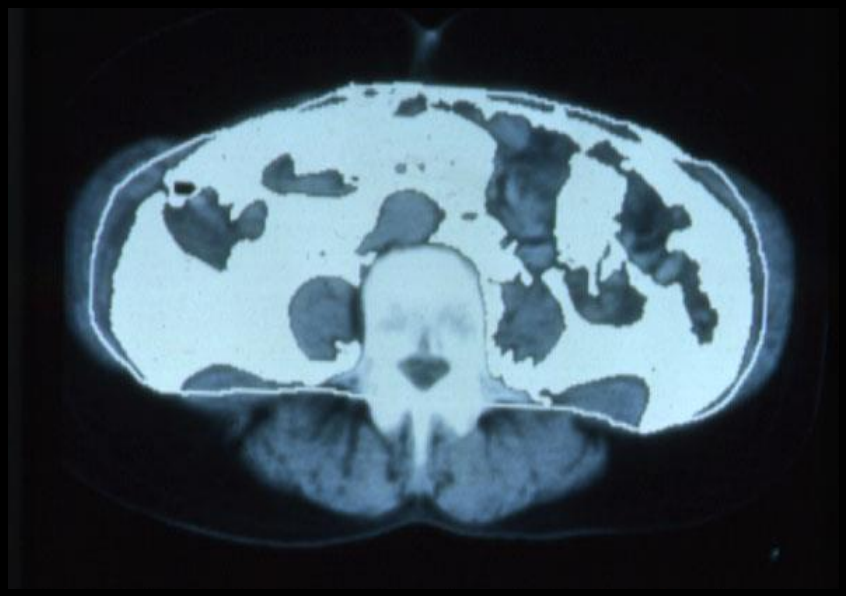
The most important measurement tools of weight gain and obesity are body mass index (BMI) and waist circumference.



- Waist circumference is a more important index than BMI.

Role of body fat distribution

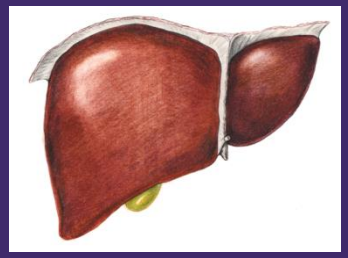


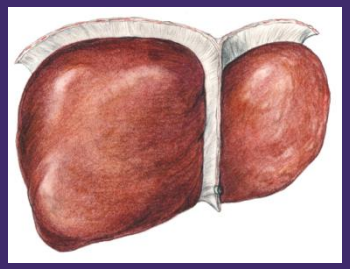


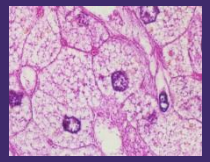
- Normal

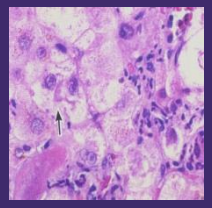
Type 2 diabetes

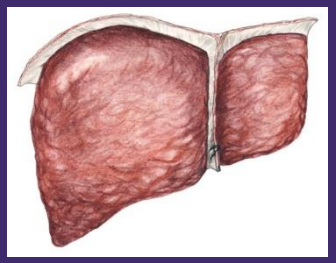
Abdominal (visceral) obesity, is a leading cause of cardiovascular disease (CVD), insulin resistance, type 2 diabetes, dyslipidaemia, inflammation, and thrombosis.











What are the settings for NAFLD

obesity

50%

steatosis

33%

steatohepatitis

50%

fibrosis

15%~30%

cirrhosis

30%~40%

liver-related morbidity and mortality

metabolic disorders

T2DM

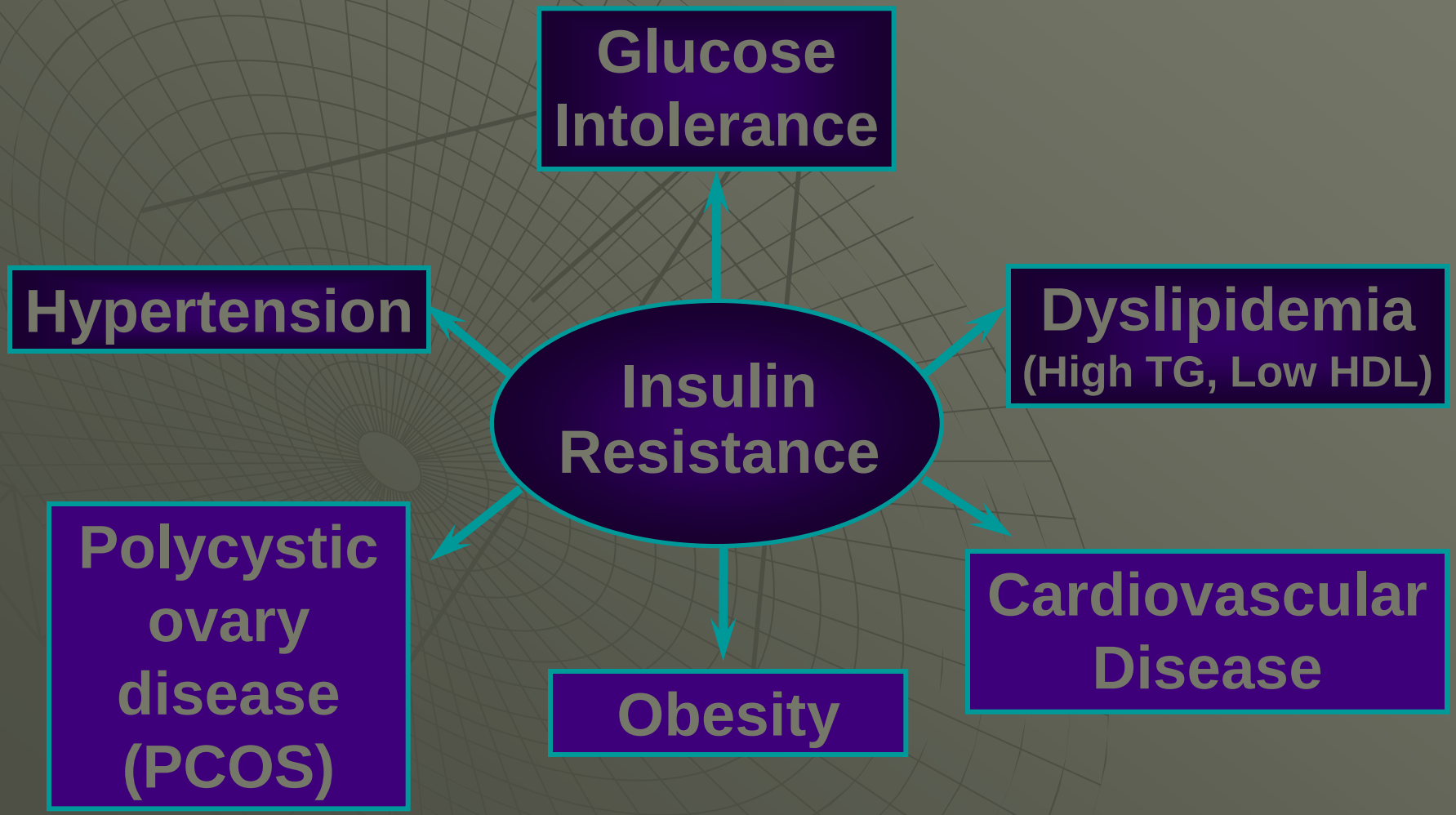
CVD, malignancy

Patrick L. Altern Med Rev, 2002, 7:276-291

What is Metabolic Syndrome (METS)?

- METS is the name for a group of risk factors linked to being overweight or obese.
- These risk factors include increased heart disease and other health problems, such as diabetes and stroke.

Insulin Resistance Syndrome (Metabolic Syndrome)



What is the Metabolic Syndrome (METS) Criteria:

- **Waist circumference**

Male	≥94* (102)** cm
Female	≥80* (88)** cm

PLUS two or more of:

•Blood Pressure	≥130/ ≥85 mm Hg
•Fasting Glucose	≥100* (110)** (100)***mg/dL
•Triglyceride	≥150 mg/dL
•HDL Cholesterol:	
Male	<40 mg/dL
Female	<50 mg/dL

The basic criteria of METS is measure of waist circumference. It's limits 94 cm (according to IDF criteria)- 102 cm (according to ATP IIIA criteria) for men and 80 (IDF)-88 cm (ATP IIIA) for women. PLUS two or more of the waist circumference: one of them blood pressure greater than 130/ ≥85 mm Hg ; AND/ OR Fasting glucose level greater than 100 (IDF) -110 (ATPIIIA) mg/dl, AND/ OR Triglyceride level greater than 150 mg/dL ; AND/ OR HDL cholesterol level lower than 40 mg/ dl for men, lower than 50 mg/dl for women.

**The National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATPIII), JAMA:2001

***ATP IIIA criteria

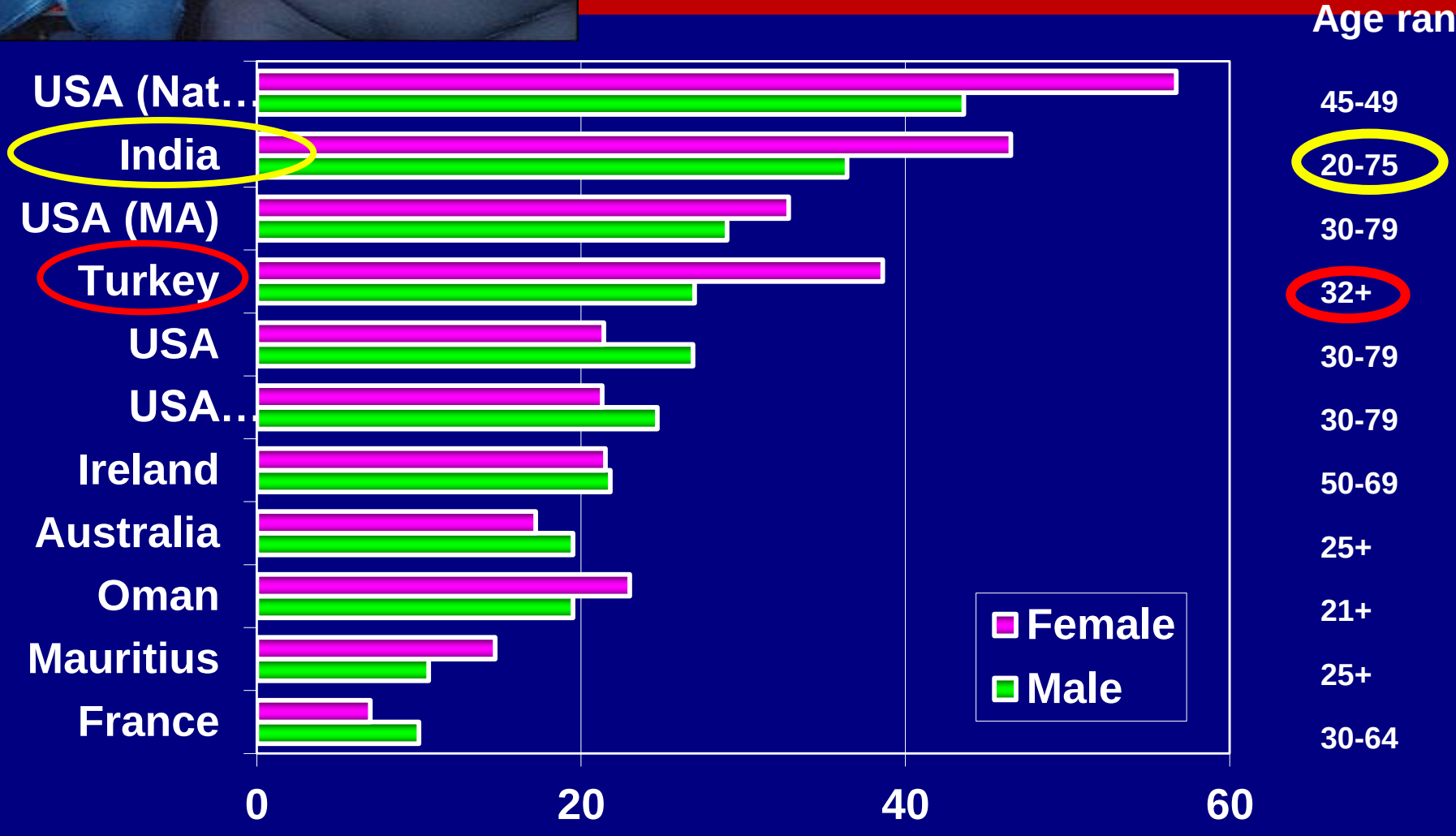
*International Diabetes Fedaration (IDF), Consensus Worldwide Definition of the Metabolic Syndrome April,14th,2005 Berlin

METS PREVALENCE IN TURKEY, by Turkish METS Research Society , 2005 (n = 4264)

	Male %	Female %	Total %
Rural	26.9	41.1	33.9
Urban	28.6	38.8	33.8
General	28	39.6	33.9

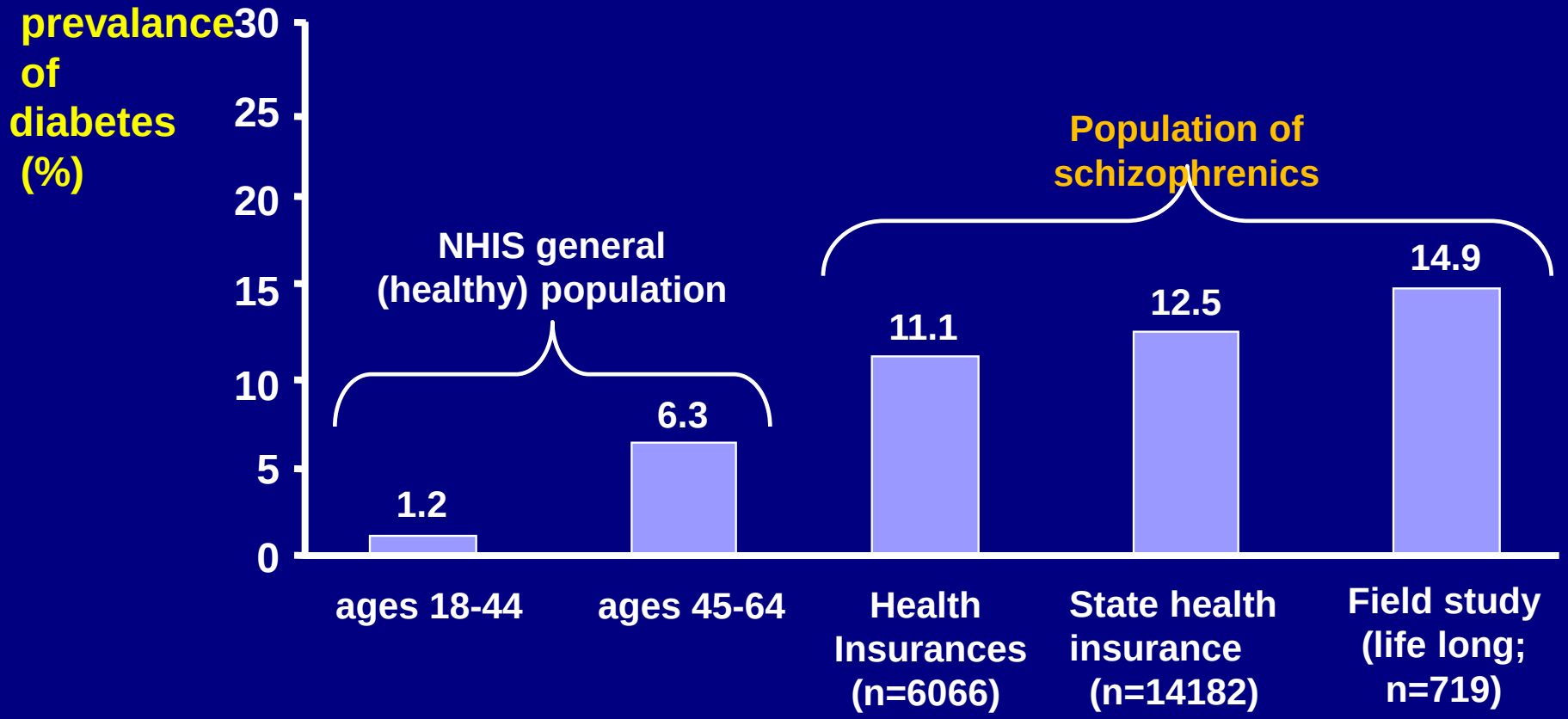
Turkish METS Research Society screened over four thousands people in Turkey.
They found that were met 40% for metabolic syndrome according to the IDF criteria !

METS is very common all over the world



Turkish people have a high risk in terms of METS

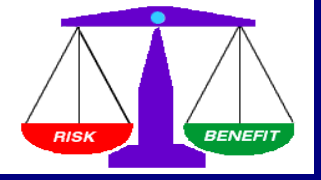
Before the atypical antipsychotic age , an epidemiological study (PORT study) conducted during 1991-1996, demonstrated that patients with schizophrenia compared to healthy controls was found 3 times more DM.



NHIS, 1994

PORT Study 1991-1996

Dixon et al. 2000

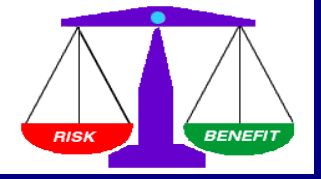


Risky People (*Turkish*)

+

Risky group (*Schizophrenics*)

Schizophrenia and Glucose Metabolism Disorders are comorbid!



Metabolic syndrome risk of atypical antipsychotics

Researches have demonstrated that the risk of clinically significant weight gain, glucose and lipid metabolism disorders, ranked in terms of risk of metabolic syndrome:

Clozapine > Olanzapine >

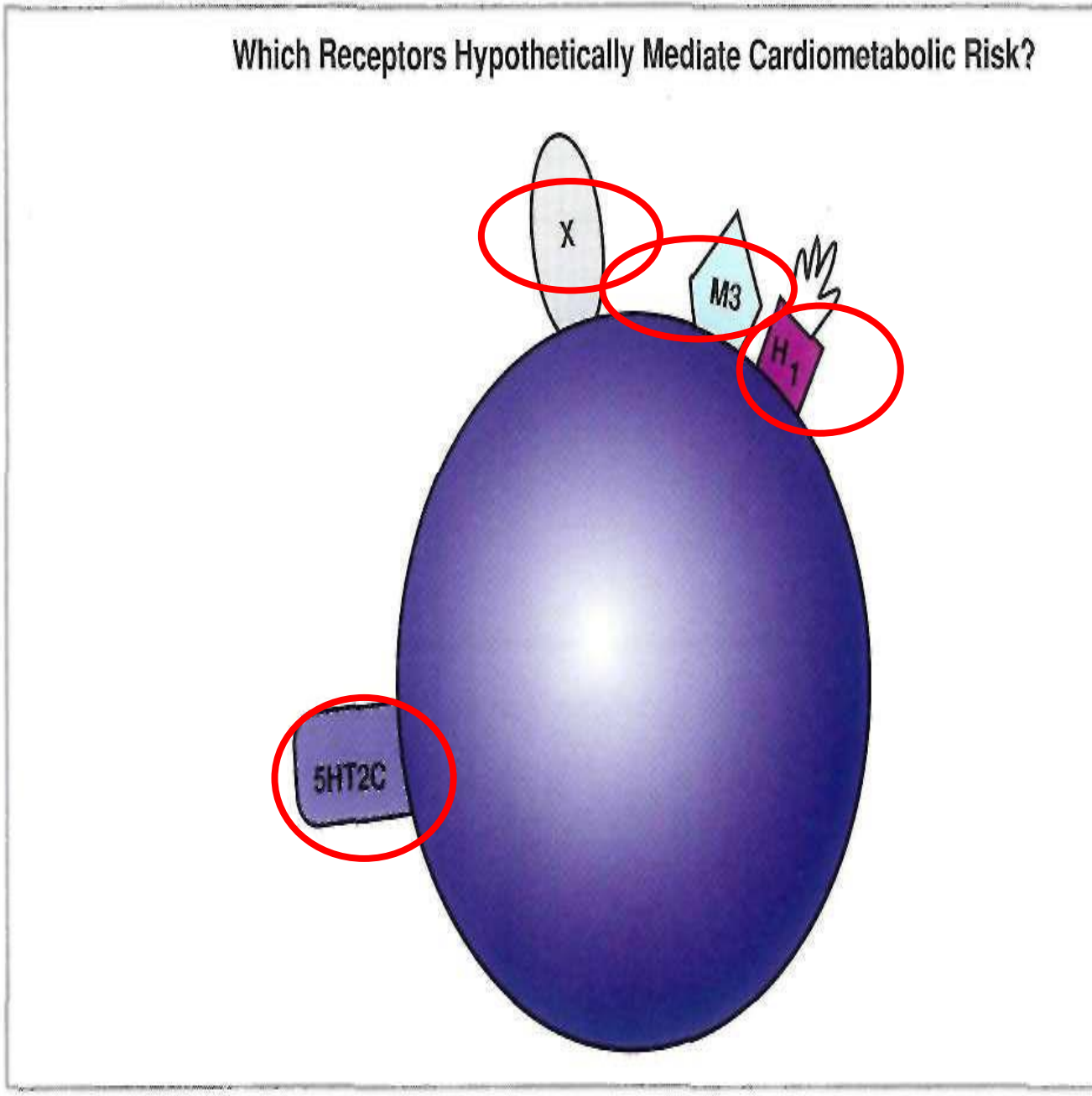
Quetiapine= Risperidone >

Ziprasidone = Aripiprazole

Newcomer JW. CNS Drugs 2005;19(1):1-93

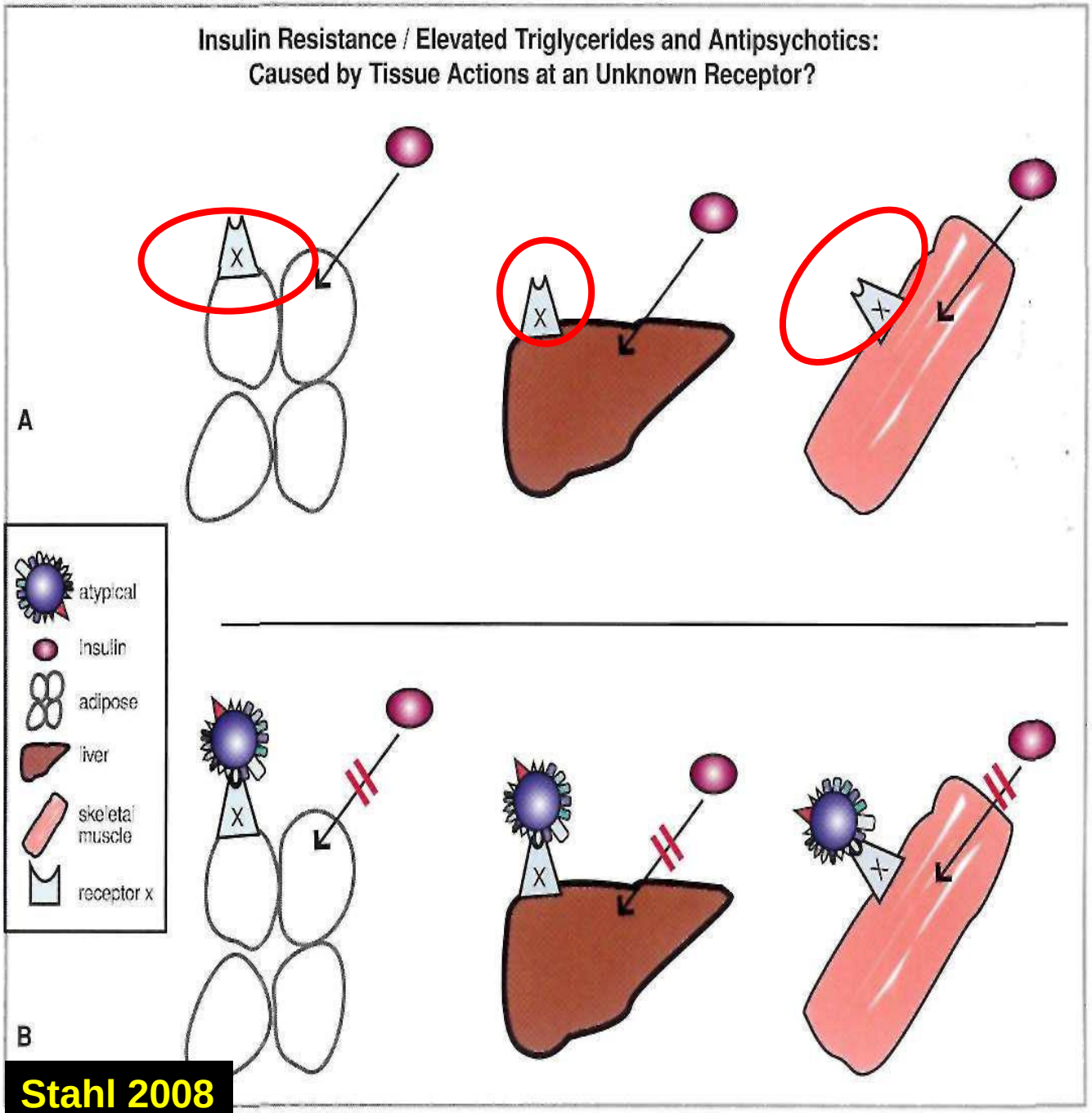
Researches have founded that the risk of clinically significant ranked in terms of risky of metabolic syndrome olanzapine and clozapine have the greatest risky , quetiapine and risperidone have mildly risky, and finally ziprasidone and aripiprazole have the lowest risky.

The H1 histamine M3 cholinergic , and the 5HT2C receptors associated with increased weight gain.



Stahl 2008

Some atypicals (olanzapine, clozapine, etc.) may lead to insulin resistance and elevated triglycerides independently of weight gain, although the mechanism is not yet established.



Stahl 2008

Neural Correlates of Weight Gain With Olanzapine

Jose Mathews, MD; John W. Newcomer, MD; Jennifer R. Mathews, PhD; Christina L. Fales, PhD; Kathy J. Pierce, PhD; Brandon K. Akers, AB; Ioana Marcu, AB; Deanna M. Barch, PhD

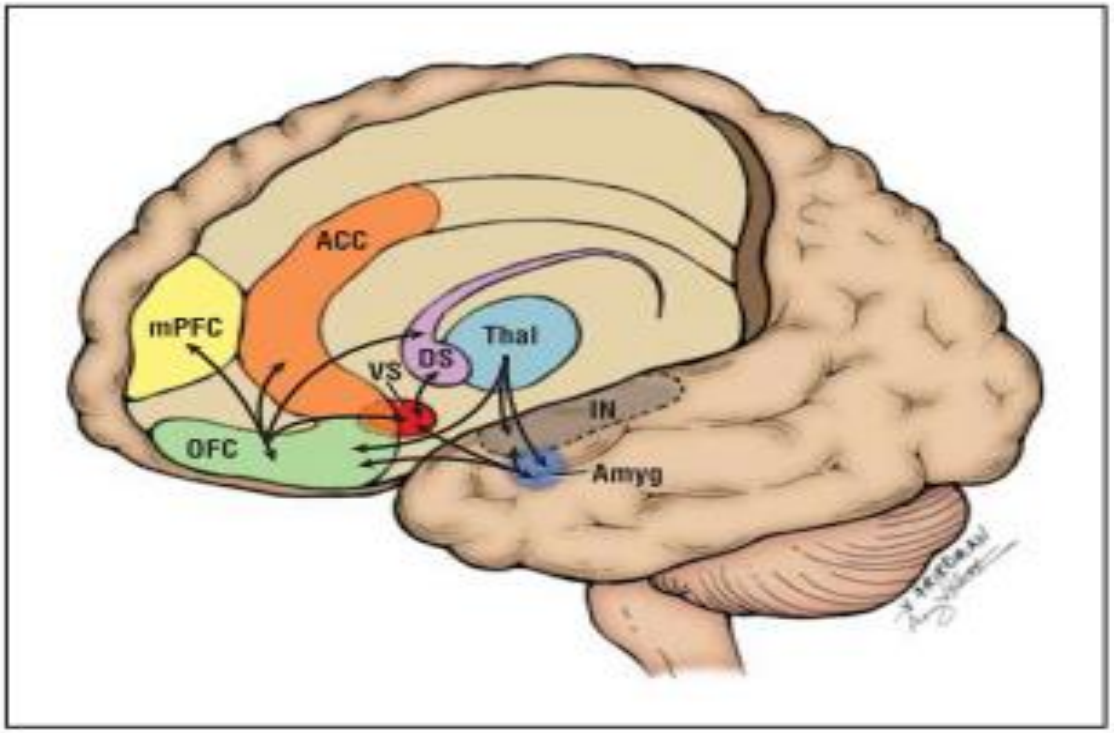


Figure 1. A schematic depiction of the approximate anatomical locations and connections of the taste reward pathways. Information from taste receptors project to the thalamus (Thal) via the nucleus tractus solitaries. This taste information along with information from other sensory modalities (eg, smell and appearance of food) then converge on the insula (IN), amygdala (Amyg), and orbitofrontal cortex (OFC). From here they access the other major components of the reward processing circuit including the highly interconnected striatum (ventral striatum [VS] and dorsal striatum [DS]), anterior cingulate cortex (ACC), and medial prefrontal cortex (mPFC).

Arch Gen Psychiatry.
Published online August 6, 2012.
doi:10.1001/archgenpsychiatry.2012.934

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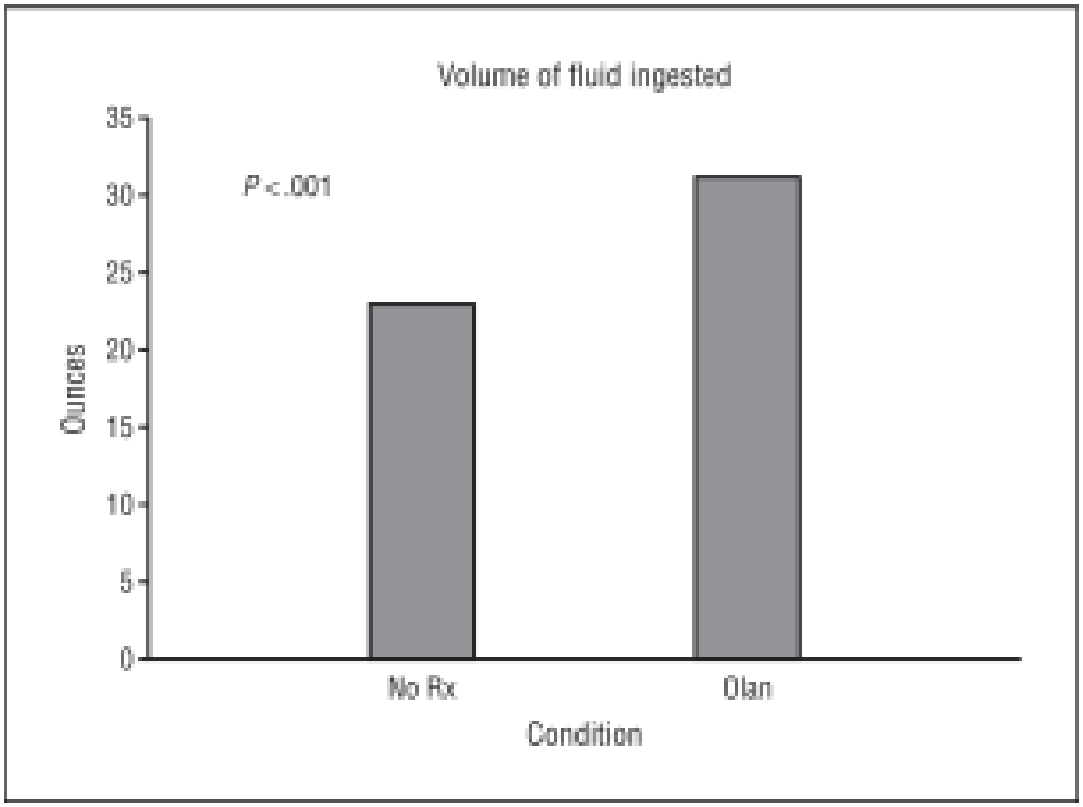

Figure 2. Increased consumption of liquid breakfast after a 7-day treatment with olanzapine (Olan). The *P* value reflects the results of a *t* test. Rx indicates prescription.

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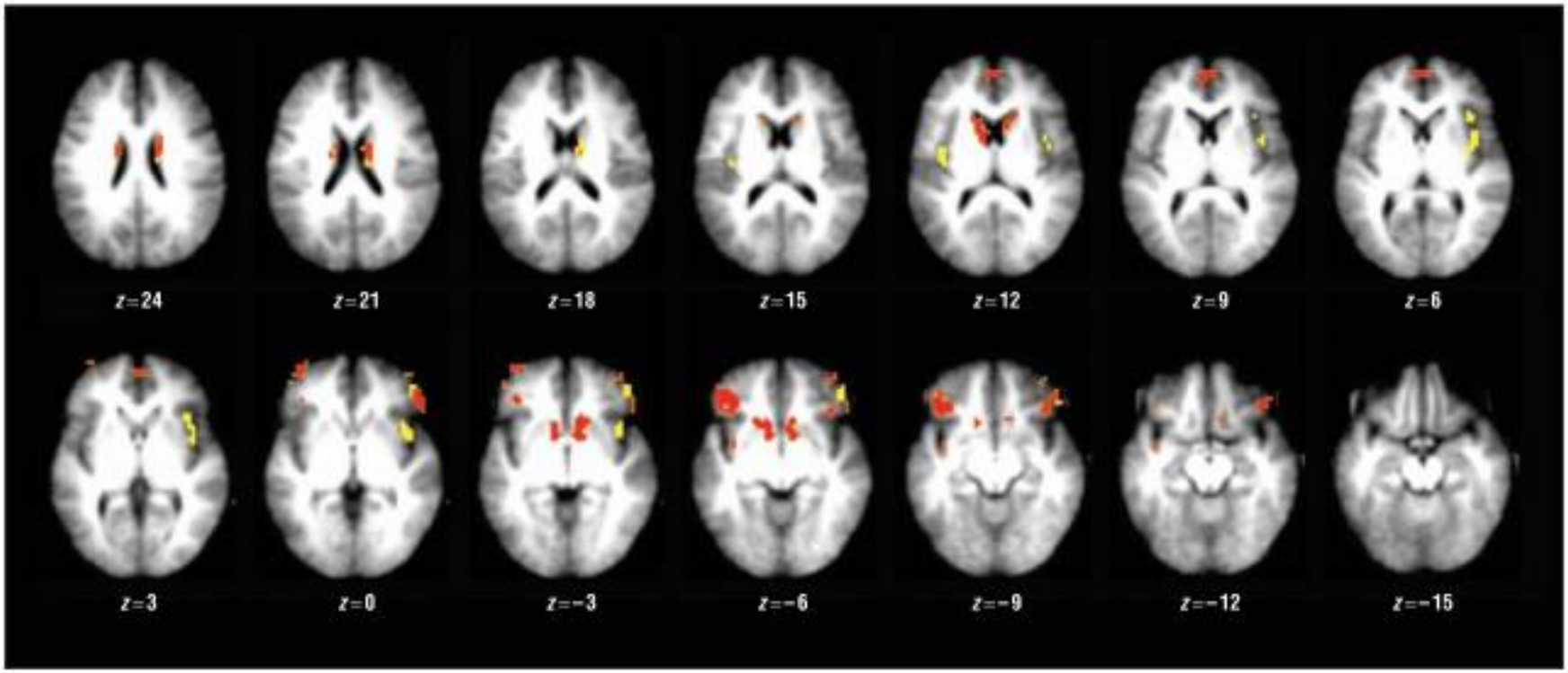


Figure 3. Activation maps of cue-related anticipatory response. Right is on the right and left is on the left. Regions displaying a cue type (reward vs tasteless) × time point interaction are in yellow and regions displaying a further interaction with treatment (treatment × cue type × time point) are in red. All the significant task-related brain activations depicted here have a *P* value of <.05 at the mask level, which corresponds to a *z* value of more than 2.58 (*P*< .005) per voxel and a minimum cluster size of 10 voxels.

Table 4. Brain Regions Identified in Analysis of Reward Anticipation (Cue-Related Activity)

Region	Brodmann Area	Cluster Size, Voxels	*x*	*y*	*z*	*z* Score	Effect Size, ω^2
			Cue × Time Point				
Inferior frontal cortex	47	29	46	33	−3	4.75	0.20
Claustrum		57	38	4	3	3.67	0.14
Insula	13	12	−38	−12	12	3.28	0.12
Caudate		22	11	−10	20	3.71	0.14
			Cue × Session × Time Point				
Inferior frontal cortex	47	28	40	25	−9	4.51	0.19
Inferior frontal cortex	47	69	−39	28	−6	4.75	0.21
Caudate		41	9	8	−5	5.30	0.24
Claustrum		10	−37	−4	−8	3.40	0.11
Inferior frontal cortex	10	13	38	45	−4	3.87	0.15
Lentiform nucleus		34	−10	7	−5	4.99	0.22
Inferior frontal cortex	47	20	49	27	−1	3.97	0.15
Middle frontal gyrus	10	17	−37	52	0	3.86	0.15
Anterior cingulate	32	36	0	49	7	4.62	0.19
Caudate		12	11	14	12	3.24	0.11
Caudate		19	−11	8	12	3.32	0.11
Caudate		19	13	−6	22	3.37	0.13
Caudate		11	−15	−7	22	3.28	0.11

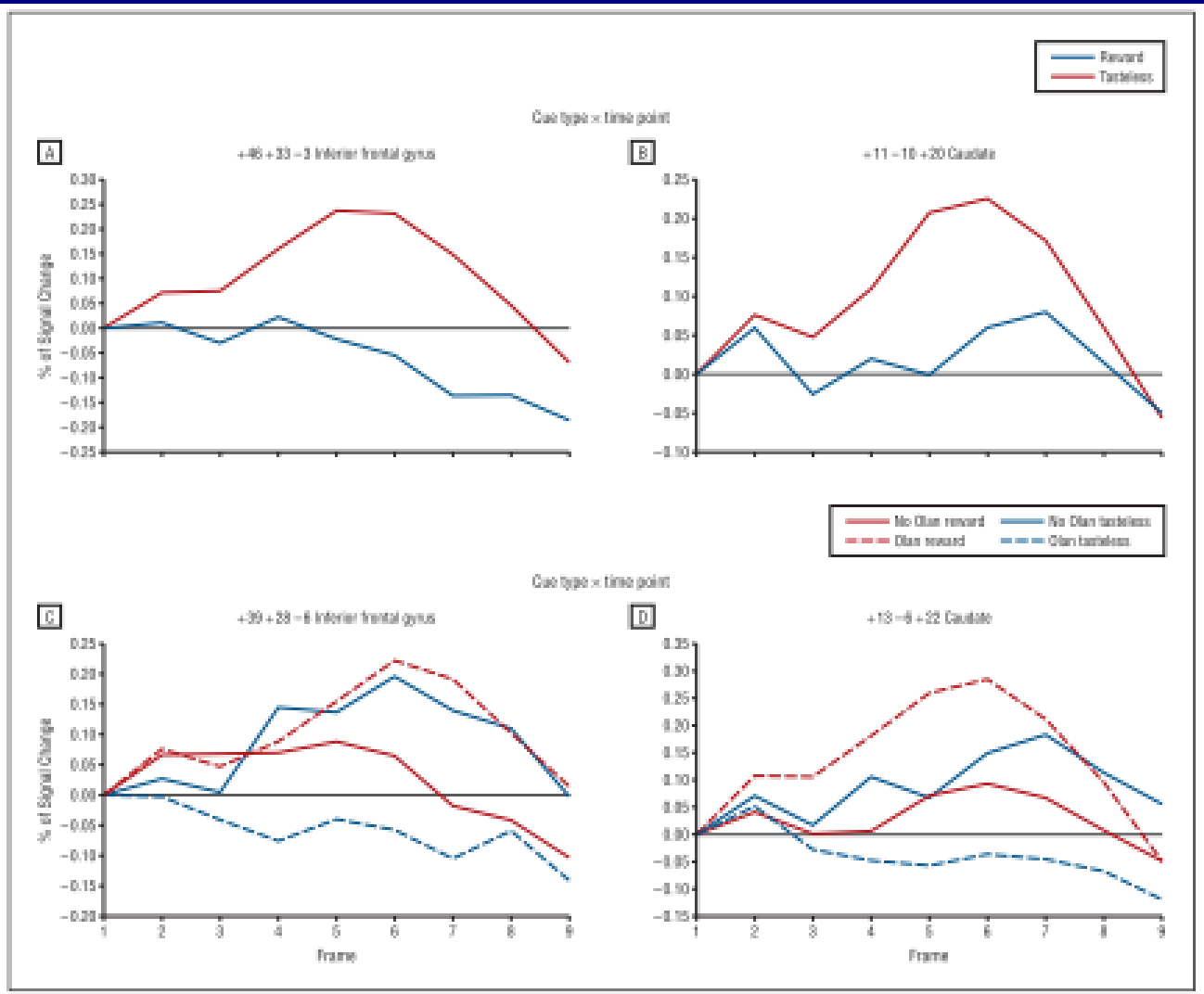


Figure 4. Examples of graphs plotting the time courses of the hemodynamic response curve to cue-related activity. Each time point on the x-axis represents 1 frame (2 seconds). A and B, Examples of the cue type × time point analysis, irrespective of treatment with olanzapine (Olan). C and D, Examples of further interaction with treatment (treatment × cue type × time point), where the red dotted line represents responses after olanzapine treatment for the rewarding taste while the blue dotted line represents the responses to the tasteless liquid after olanzapine treatment. All the significant task-related brain activations depicted here have a *P* value of <.05 at the mask level, which corresponds to a *z* value of more than 2.58 (*P*<.005) per voxel and a minimum cluster size of 10 voxels.

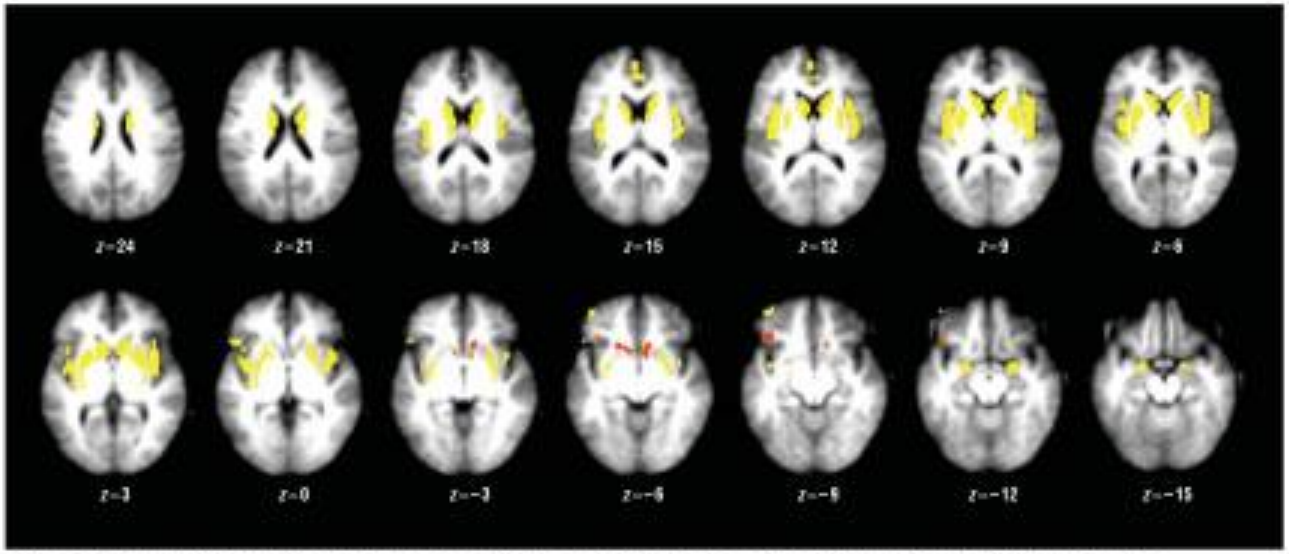


Figure 5. Activation maps of liquid receipt–related response. Right is on the right and left is on the left. Regions displaying a liquid type (reward vs tasteless) × time point interaction are in yellow and regions displaying a further interaction with treatment (treatment × liquid type × time point) are in red. All the significant task-related brain activations depicted here have a *P* value of <.05 at the mask level, which corresponds to a *z* value of more than 2.58 ($P<.005$) per voxel and a minimum cluster size of 10 voxels.

Table 5. Brain Regions Identified in Analysis of Reward Receipt (Liquid Receipt–Related Activity)

Region	Brodmann Area	Cluster Size, Voxels	*x*	*y*	*z*	*z* Score	Effect Size, ω^2
		Receipt × Time Point					
Insula	13	87	−36	−18	13	5.68	0.26
Lentiform nucleus		18	30	−14	7	5.11	0.23
Caudate		51	13	−7	21	6.30	0.31
Amygdala		46	22	−5	−12	5.55	0.26
Caudate		27	−14	−15	21	5.97	0.29
Caudate		103	−12	0	12	5.12	0.24
Putamen		92	−30	−13	−2	4.67	0.20
Caudate		150	13	7	9	4.73	0.20
Insula	13	115	36	12	6	3.97	0.15
Inferior frontal gyrus		17	−47	16	0	4.13	0.16
Insula	13	89	−33	6	12	4.05	0.17
Caudate		37	−16	19	8	3.67	0.14
Middle frontal gyrus	11	12	−42	44	−8	4.31	0.17
Amygdala		31	−20	−6	−15	4.47	0.18
Medial frontal gyrus	10	27	−3	45	13	3.22	0.11
		Receipt × Session × Time Point					
Inferior frontal gyrus	47	14	−39	20	−8	4.23	0.17
Caudate		20	8	11	−5	4.69	0.20
Putamen		12	−11	10	−5	3.96	0.15

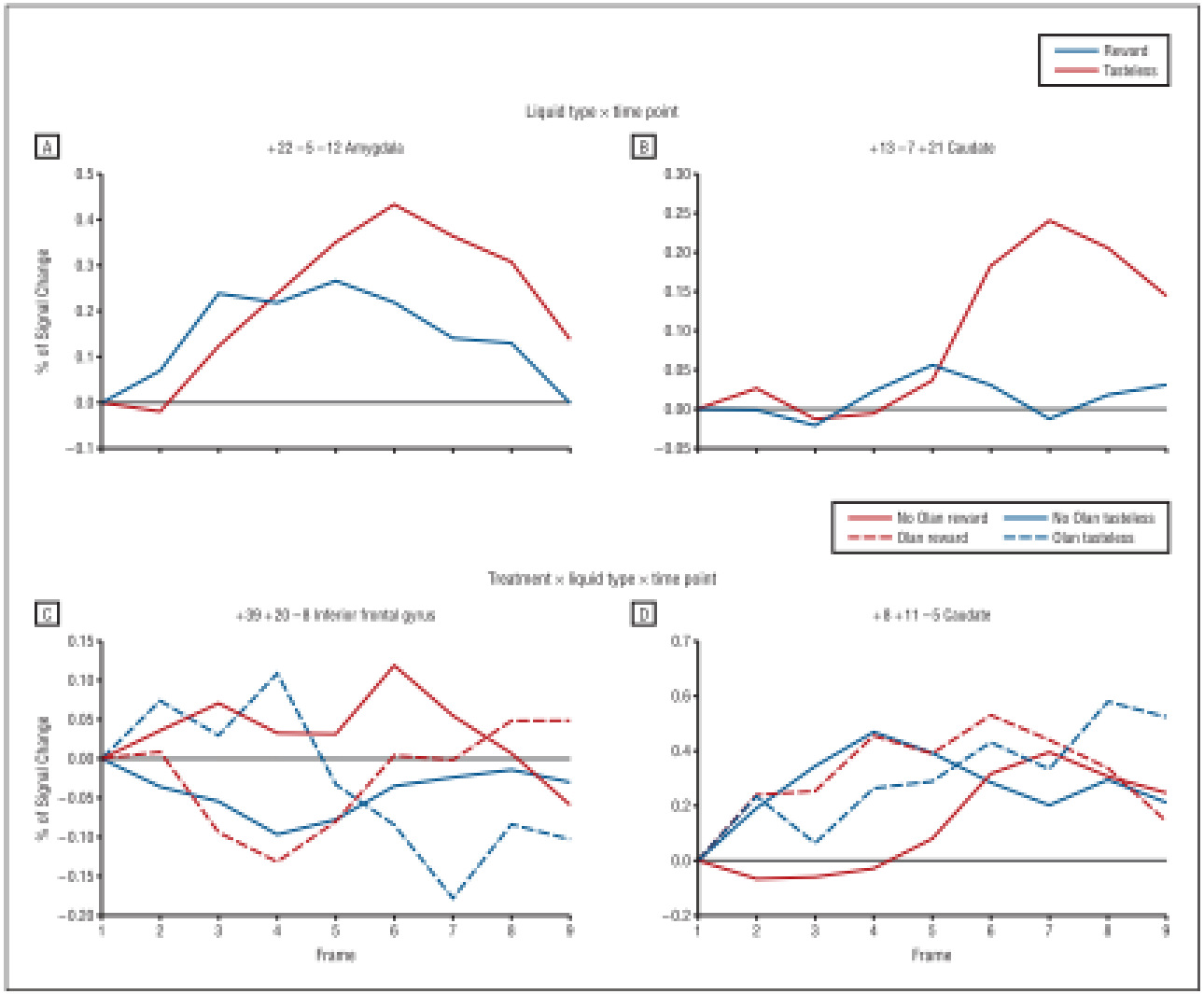
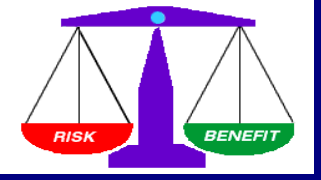


Figure 6. Examples of graphs plotting the time courses of the hemodynamic response curve to receipt-related activity. Each time point on the x-axis represents 1 frame (2 seconds). A and B, Examples of the liquid type × time point analysis, irrespective of treatment with olanzapine (Olan). C and D, Further interaction with treatment (treatment × liquid type × time point). In the inferior frontal gyrus (C), the response to rewarding taste receipt goes down after olanzapine treatment (solid red line compared with the dashed red line) while the converse is noted in the caudate (D). All the significant task-related brain activations depicted here have a *P* value of <.05 at the mask level, which corresponds to a *z* value of more than 2.58 (*P*<.005) per voxel and a minimum cluster size of 10 voxels.



What psychiatrists can do about metabolic side effects of SGAs?

While a patient progresses along the metabolic highway to premature death, factors determining outcome include:

- **unmanageable** *(e.g. the patient's genetic make-up and age),*

-**modestly manageable** (*e.g. change in lifestyle, such as diet, exercise, and quit smoking)*

-**most manageable**:

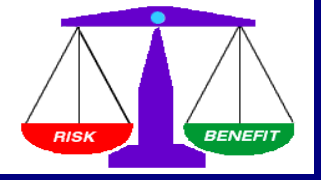
-the selection of antipsychotic

-switching from one to other SGAs

-monitoring

PHARMACOLOGICAL APPROACH

- Metformin is an oral antidiabetic drug in the biguanide class.
  - DM type II,
  - polycystic ovary syndrome,
  - insulin resistance
  - Metformin works by suppressing glucose production by the liver.
- Chromium picolinate works by stimulating the activity of insulin.



Olanzapine-induced metabolic abnormalities: Switching from olanzapine to aripiprazole

Mesut Cetin , Servet Ebrinc , Cengiz Basoglu, Umit Basar Semiz,

Ayhan Algul, Mine Karagozoglu

Department of Psychiatry, Gulhane Haydarpasa Training Hospital, Kadikoy, Istanbul, Turkey

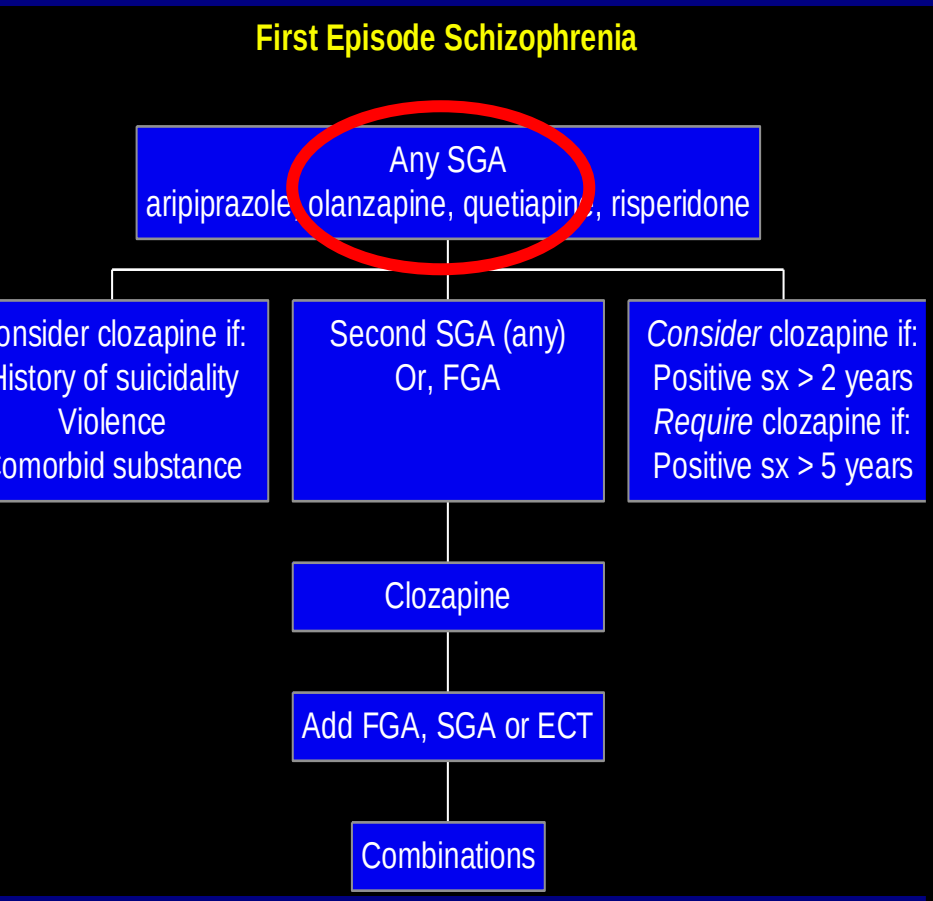
This is our switching study from olanzapine to aripiprazole . We found that weigth gain in patients with schizophrenia, as a side effect of olanzapine, can be managed effectively by switching from olanzapine to aripiprazole.

Cetin M et al. Association of European Psychiatrists (AEP), 15th European Congress of Psychiatry, Madrid, Spain, March 17−21, 2007

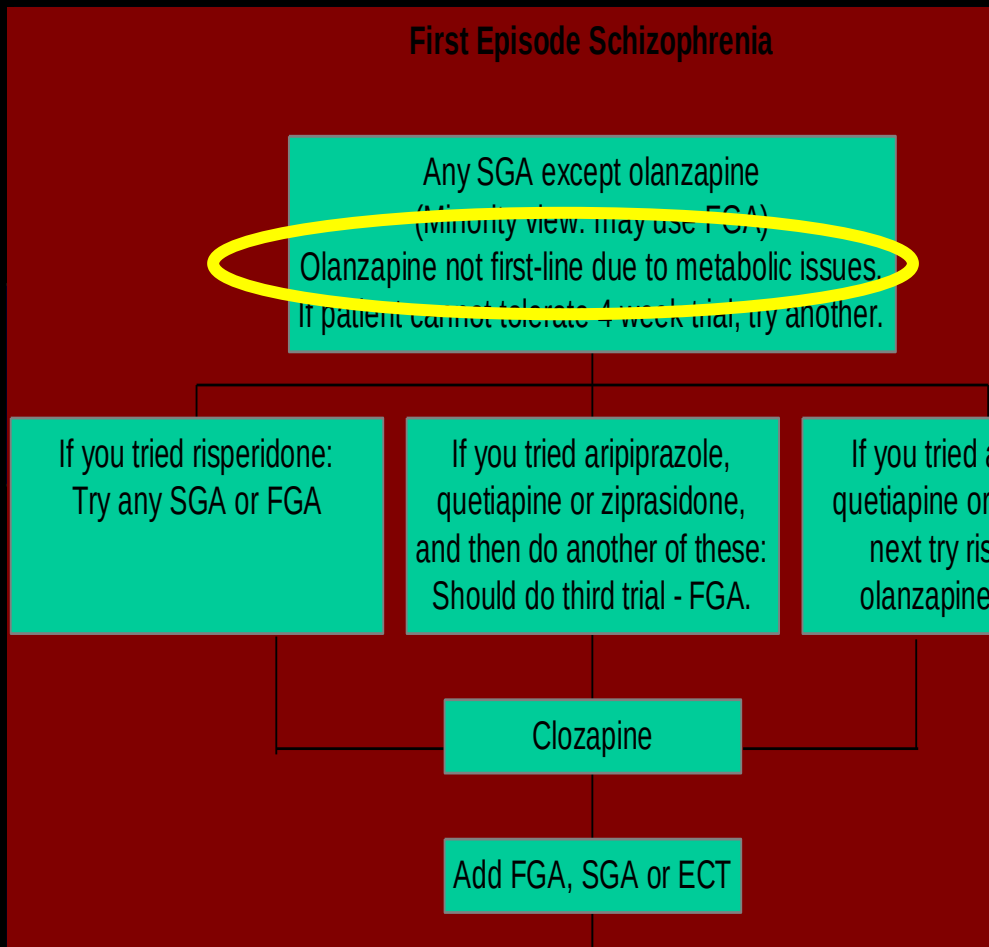
CHANGING CONCEPTS of TREATMENT GUIDELINES

Because of its METS risk, many treatment guidelines now do not recommend olanzapine as first-line.

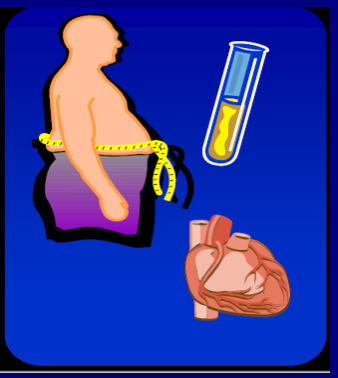
2006 TMAP Algorithm



2008 PAPHSS Schizophrenia Algorithm



Monitoring Recommendations



(van Winkel et al JCP 2006;67:14 93-1500

If the patient has pre-existing diabetes, hypertension, or obesity, do not consider olanzapine, clozapine!

- **Baseline:** fasting triglycerides and HDL cholesterol, fasting glucose, blood pressure, weight, abdominal circumference (AC)
- **Follow up at one month:** fasting glucose, blood pressure, weight, abdominal circumference (AC)
- **Follow up at 3 months:** same, plus lipids metabolic problems develop, switch another antipsychotic, or treat medically
- **If FG elevated, get glucose tolerance test.** If abnormal, this predicted 96% of patients who developed diabetes.

HANDY PORTION GUIDE

Vegetables

Choose as much as you can hold in both hands

Fruits, Grain products, Milk

Choose an amount up to the size of your fist

Meat and alternatives

Choose an amount up to the size of the palm of your hand and the thickness of your little finger

Cheese

Choose an amount the size of two fingers (index and middle finger)

Fat and oils

Limit fat to an amount the size of the tip of your thumb

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

IMPROVEMENTS IN CARDIOMETABOLIC RISK FACTORS INDUCED BY REGULAR EXERCISE

Insulin Resistance

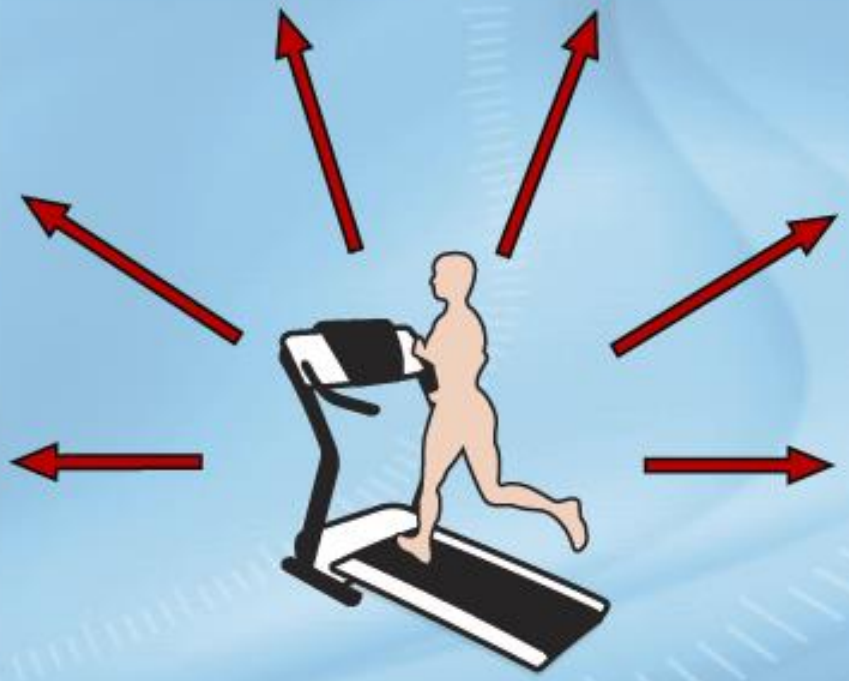
A 30-85% improvement

Atherogenic Dyslipidemia

Increased HDL cholesterol (~5%) and decreased triglycerides (~15%) and a shift in the distribution of LDL particle size (from small to large)

Abdominal Obesity

A 30% reduction in intra-abdominal fat



Hypertension

A 4 mm Hg reduction in both systolic and diastolic blood pressure

Thrombosis

Induces an anti-thrombotic state (decreased coaguability and increased fibinolysis)

Systemic Inflammation

Approximately 30% reduction in inflammatory markers

Moderate intensity endurance exercise on most days of the week

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

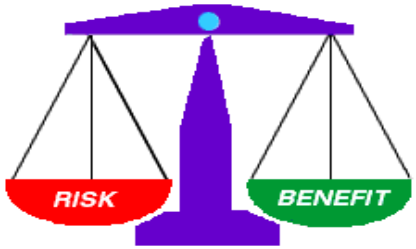
Conclusions

Primarily high rate of refined carbohydrate consumption and the following factors cause extreme increases of blood insulin levels: Unhealthy eating habits, sedantary life style, and other environmental factors.

Hypoglycemic can mimic and/or provoke panic attack symptoms (palpitations, tremor, sweating, dizziness, and blurry vision).

Based on cognitive perspective panic disorder is a disorder of misinterpretation of physiological reactions. Hence, hypoglycemia symptoms, which reflect blood insulin level changes, should be well known in psychiatry. As panic disorder and hypoglycemia provoke each other, the treatment strategies should target both conditions.

Long lasting high insulin levels initially lead to reactive hypoglycemia and in later stages insulin resistance, metabolic syndrome, and diabetes mellitus occur. Also as some medications used in pscyhiatry cause insulin resistance, they should be avoided in early stages of treatment especially in patients with positive family history of DM.



Conclusions

Treatment of psychiatric disorders are long-term treatments.

So:

-less side effects,

-does not disrupt the quality of life of patients,
-low cost drugs are easily available, forms developed.

Psychopharmacology is one of the fastest changing areas of medicine .Therefore, the clinical practice and guidelines need to be updated frequently.

PSİKOFARMAKOLOJİ DERNEĞİ
TURKISH ASSOCIATION FOR PSYCHOPHARMACOLOGY
İSTANBUL 2005

Psychopharmacology Therapeutics Update 2012 Meeting

'Therapeutic Decisions for Challenging & Evolving Psychiatric Diagnosis'

15 - 18 November 2012
Antalya -Turkey

http://www.psikofarmakoloji2012.org

“primum non nocere”

Hippocrates BC 4. century

Thank you for your attention