Stress, Obesity, Marijuana AND The New *Oncoming* Prediabetes Epidemic

Ron Innerfield, MD, FACE
Endocrinology,
Marshall University School of Medicine

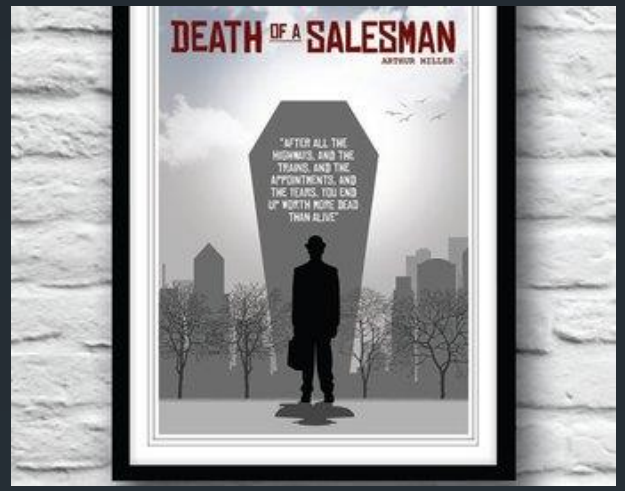
Questions to be Addressed

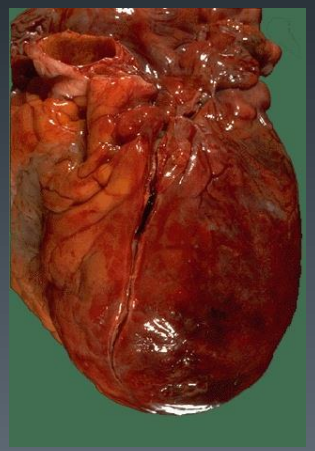
- 1) Is there stress in the modern world as we know it?
- 2) Does stress lead to obesity and/or marijuana?
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- 6) Should we *as physicians* be concerned?

Questions to be Addressed

- **1) Is there stress in the modern world as we know it?**
- 2) Does stress lead to obesity and/or marijuana?
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- 6) Should we *as physicians* be concerned?

- Name: Willie Loman
- Age: 63
- Smoked 2 PPD x 45 years
- BP 200/115 LASit
- PR 100 reg
- BMI 37
- LDL-C 125 mg/dl (direct)
- HDL-C 29 mg/dl
- Triglycerides 331 mg/dl
- Waist/Hip Ratio Increased
- Uric Acid 8.5 mg/dl
- FBS/2hrPC Glucose 91/185 mg/dl
- HbA1c 5.9%

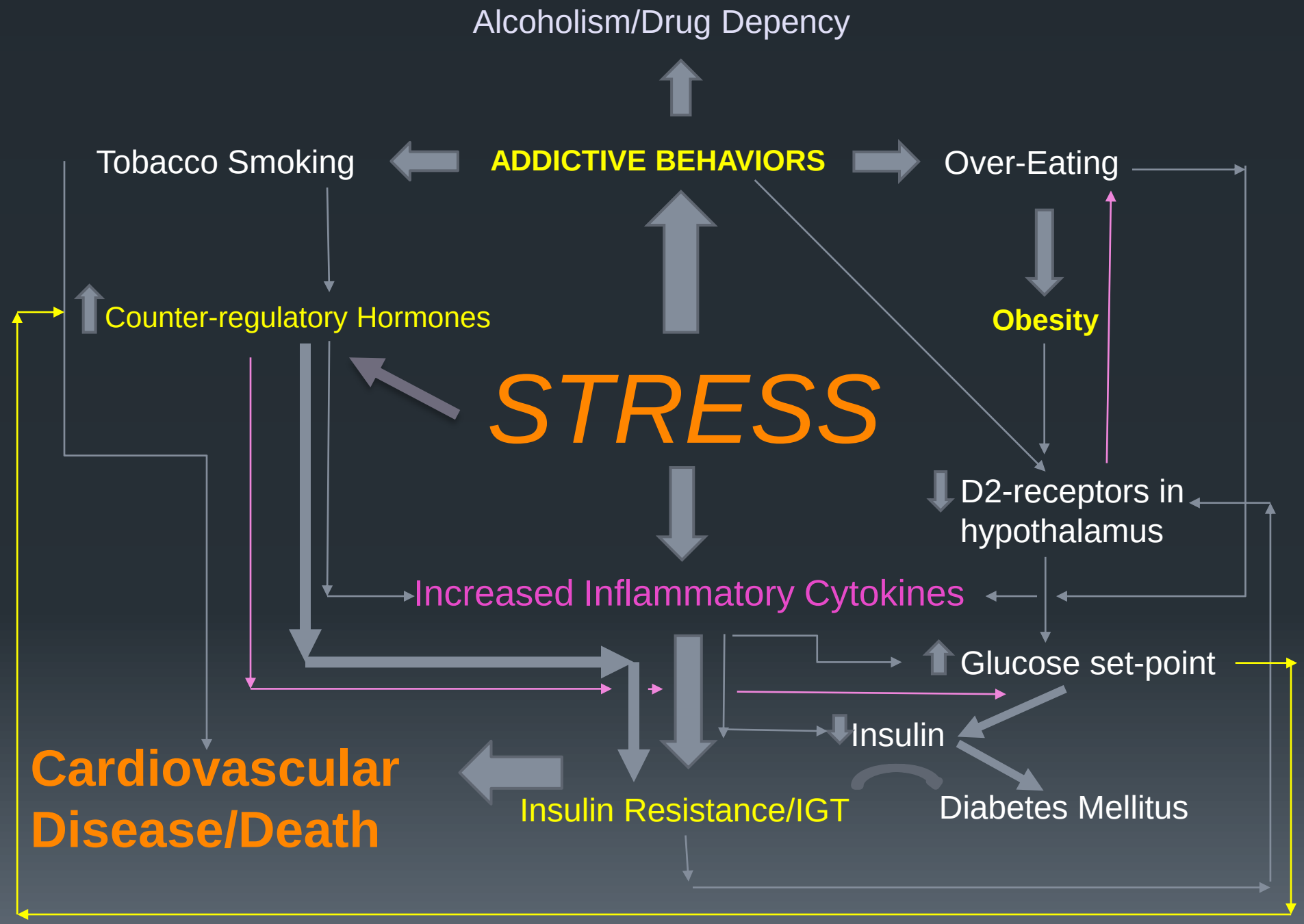




"After all the highways, and the trains, and the appointments, and the years, you end up worth more dead than alive"

- *Willy Loman*

DEATH OF A SALESMAN


Alcoholism/Drug Depency
Tobacco Smoking
ADDICTIVE BEHAVIORS
Over-Eating
Counter-regulatory Hormones
Obesity
STRESS
D2-receptors in hypothalamus
Increased Inflammatory Cytokines
Glucose set-point
Insulin
Cardiovascular Disease/Death
Insulin Resistance/IGT
Diabetes Mellitus

Control

- Lack of control over work has been related to a number of stress and illness indicators including:
  - Job dissatisfaction
  - Absenteeism
  - Development of coronary artery disease

Taylor

The Newsletter of
THE AMERICAN INSTITUTE OF
STRESS

Volume 2 Number 4, 1989

More on Job Stress Due to Lack of Control

A study of 4800 men with a history of heart attack reviewed records and information obtained from national health data bases and government employee services. The men's jobs were rated to provide scores that would reflect certain psychological demands. These included the need to work quickly or excessively, as well as the degree of decision-making authority and intellectual challenge. We typically tend to think of heart attacks due to job stress as occurring in ambitious, hard-driving, competitive individuals at executive or upper management levels. However, the results of this study showed that most heart disease occurred at lower echelons such as assembly line personnel, garment district workers, waiters, and cooks. These are all high-stress occupations because they combine a high degree of demand with little control. The heart attack rate for the total sample was only 1.5 per cent. However, the rate for men in high-stress jobs was nearly three times as much. There was no evidence of increased risk for "high status, presumably success-oriented, managerial or professional occupations." As one sociologist noted, "an assembly line worker, for instance, has virtually no control over the methods and tools he uses, whom he works with, when he works, or in the design of the product . . . lawyers and doctors, on the other hand have control over almost everything they do." Interestingly enough, the percentage of men in high-stress jobs appeared to decrease with age, suggesting that they possibly move out of stressful jobs as they get older, or somehow adapt to the situation. Other studies suggest that workers in low-control jobs are also more likely to smoke and have higher blood pressures than those engaged in occupations where they can make decisions. Data from the Framingham study also reveal that women in low-control jobs have more heart attacks. Heart disease risks are twice as great among women in low-control clerical jobs as compared to housewives and self-employed females. These concerns and other observations have been responsible for the markedly increased interest in stress management training in the workplace on the part of corporations and unions.

(Psychology Today, April, 1989)

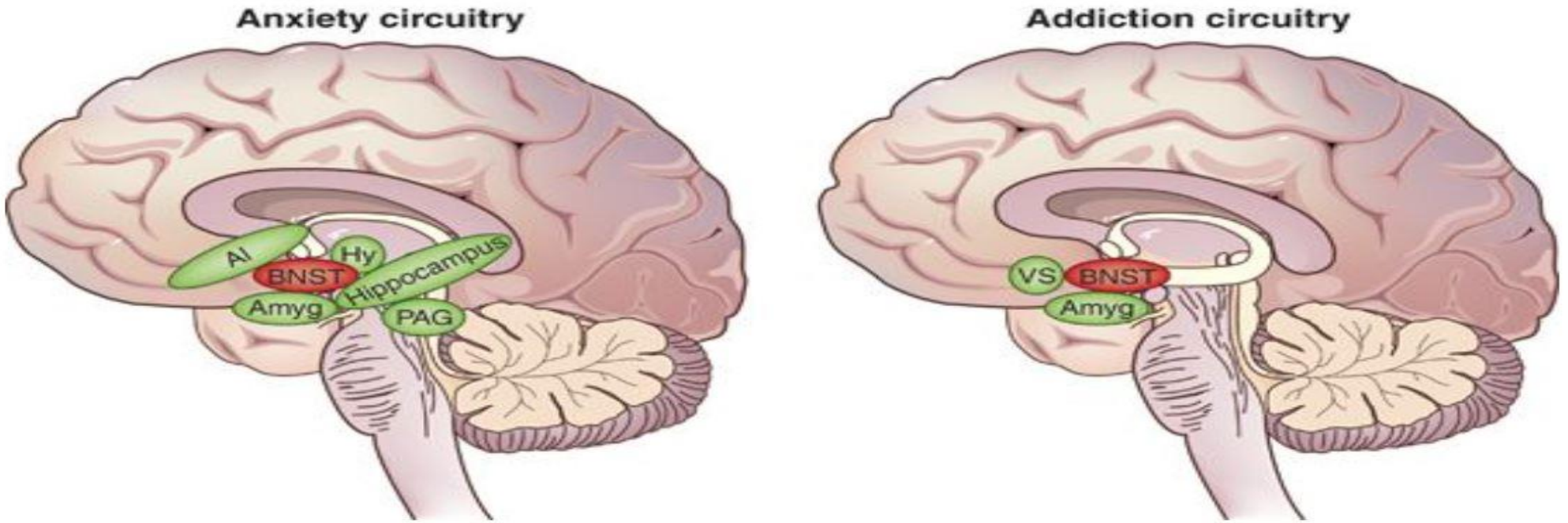
"Man needs not only knowledge but ignorance too. Knowledge alone, or ignorance alone, leads him into darkness . . . The world is so filled with the matter of knowledge that men would go mad if they

Work-Related Factors Contributing to Stress

- Lack of control over work
- Lack of control over economic impact
- Unrealistic expectations
- Too high a work load, impossible deadlines
- Too low a workload, no or few challenges
- Low task variety, under-utilization of skills
- Low pay
- Undervalued position

Stress at work

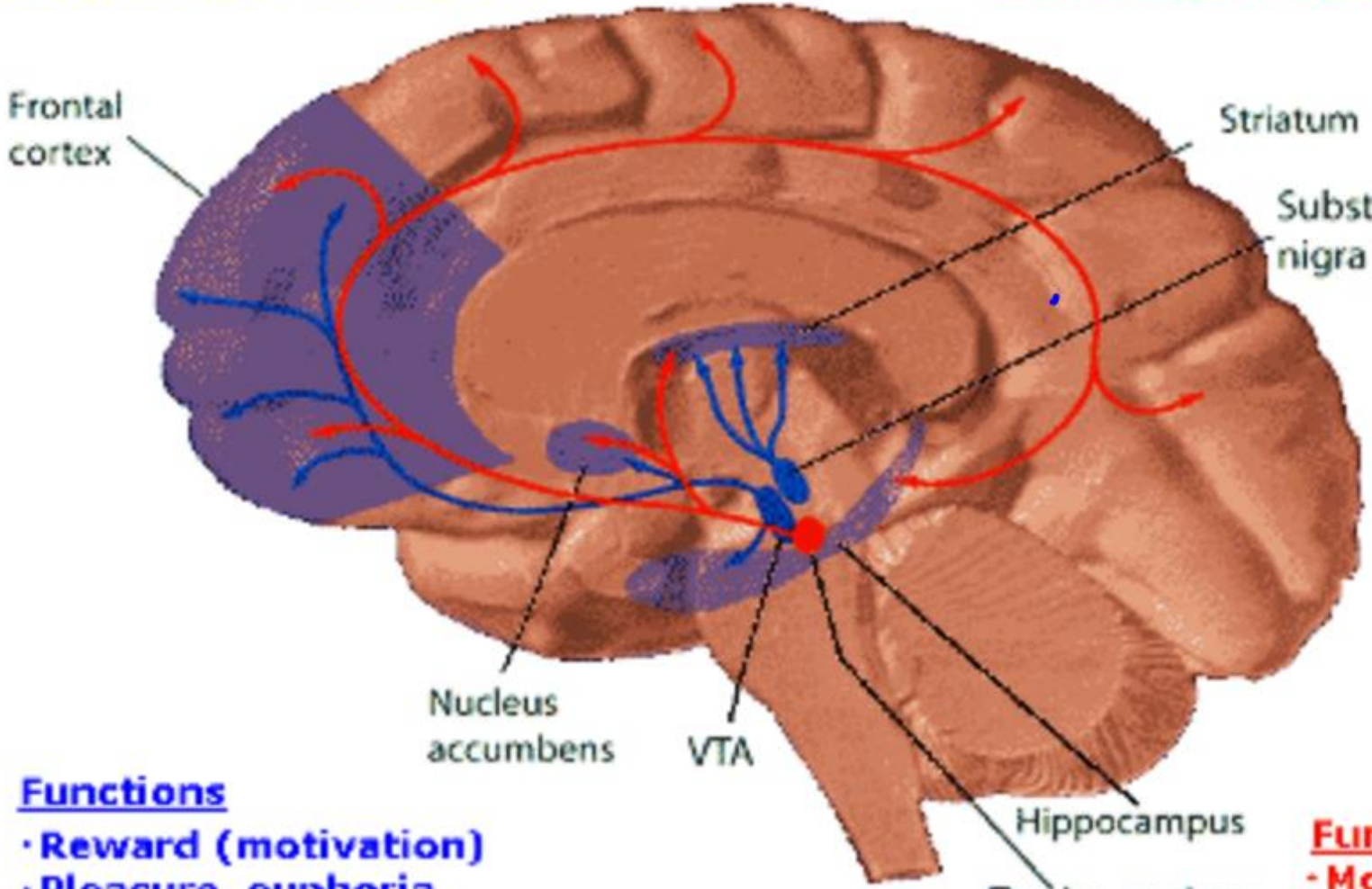
- Stress = a situation with demands that cannot be met by personal resources
- 28% of employees in 15 EU member countries suffer from work-related stress (survey responses 2002)
  - Reported causes:
    - Lack of control, e.g. regarding planning (35%), work duration (55%), time pressure (29%)
    - Monotony
    - Mobbing
    - Job insecurity
  - Reported effects:
    - Heart problems (Men:16%, women: 22%)
    - Absenteeism (50-60%)
    - Estimated costs 20 billion Euro



Human anxiety and addiction circuits. The BNST is a central node in both anxiety and addiction neurocircuitry. (left) The BNST is centrally located to influence human anxiety responses, with connections to multiple limbic and brainstem regions that mediate defensive response to threat, including the amygdala, anterior insula, hippocampus, hypothalamus, and periaqueductal gray (adapted from Grupe and Nitschke, 2013). (right) The BNST is engaged during the negative emotional stage of withdrawal and interacts with the amygdala and ventral striatum, including the shell of the nucleus accumbens and ventral tegmental area, to mediate negative reinforcement (adapted from Koob and Volkow, 2010). AI, anterior insula; Amyg, amygdala; BNST, bed nucleus of the stria terminalis; Hy, hypothalamus; PAG, periaqueductal gray; VS, ventral striatum.

Dopamine Pathways

Serotonin Pathways



Functions

- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

Functions

- Mood
- Memory processing
- Sleep
- Cognition

Questions to be Addressed

- 1) Is there stress in the modern world as we know it?
- **2) Does stress lead to obesity and/or marijuana?**
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- 6) Should we *as physicians* be concerned?

Blood Sugar Levels & Stress

- **Stress May Be Linked To Higher Risk Of Diabetes, CV Disease**.
- The New York Times (4/22/2013, Section D4, Nicholas Bakalar) reports that, according to research published online in **JCEM**
- 1) stress may be linked to a higher risk of diabetes and cardiovascular disease.
- 2) Investigators "measured the cortisol content in hair samples corresponding to roughly three months of growth from 283 older men and women, average age 75."
- 3) Additionally, the researchers "gathered self-reported data about coronary heart disease, stroke, peripheral artery disease, Type 2 diabetes, lung disease, cancer and osteoporosis."
- 4) The investigators found that, "compared with those in the lowest quartile for cortisol, those in the highest quartile had about three times the risk for cardiovascular disease and diabetes.“

- Laura Manenschijn and Elisabeth van Rossum. **High Long-Term Cortisol Levels, Measured in Scalp Hair, are Associated with a History of Cardiovascular Disease**. *Journal of Clinical Endocrinology & Metabolism*, May 2013

Stress and Marijuana

- A 2014 study from Vanderbilt University published in Neuron in 2014 (Ramikie T and Patel S) found that smoking marijuana can increase the presence of naturally-occurring brain chemicals called endocannabinoids, which are reduced as a result of chronic stress. Some researchers think that a reduction of endocannabinoids could be a major cause of anxiety disorders.

- A recent Canadian study found that within 90 days of using prescribed medical cannabis for anxiety and pain, 40% of patients were able to stop using benzodiazepines — a commonly prescribed anxiety drug with a number of side effects, including a high potential for abuse.

- Studies also suggest that marijuana could be an effective treatment for PTSD. Since marijuana is known to play a direct role in memory extinction, some experts believe that it could help PTSD sufferers forget bad memories and negative experiences.

Stress and Obesity

- Many pathways connect stress and obesity, two highly prevalent problems facing society today. First, stress interferes with cognitive processes such as executive function and self-regulation. Second, stress can affect behavior by inducing overeating and consumption of foods that are high in calories, fat, or sugar; by decreasing physical activity; and by shortening sleep. Third, stress triggers physiological changes in the hypothalamic-pituitary-adrenal axis, reward processing in the brain, and possibly the gut microbiome. Finally, stress can stimulate production of biochemical hormones and peptides such as leptin, ghrelin, and neuropeptide Y. Obesity itself can be a stressful state due to the high prevalence of weight stigma. This article therefore traces the contribution of weight stigma to stress and obesogenic processes, ultimately describing a vicious cycle of stress to obesity to stigma to stress. Current obesity prevention efforts focus solely on eating and exercise; the evidence reviewed in this article points to stress as an important but currently overlooked public policy target.

- Tomiyama AJ, Stress and Obesity Annu Rev Psychol 70:703,2019

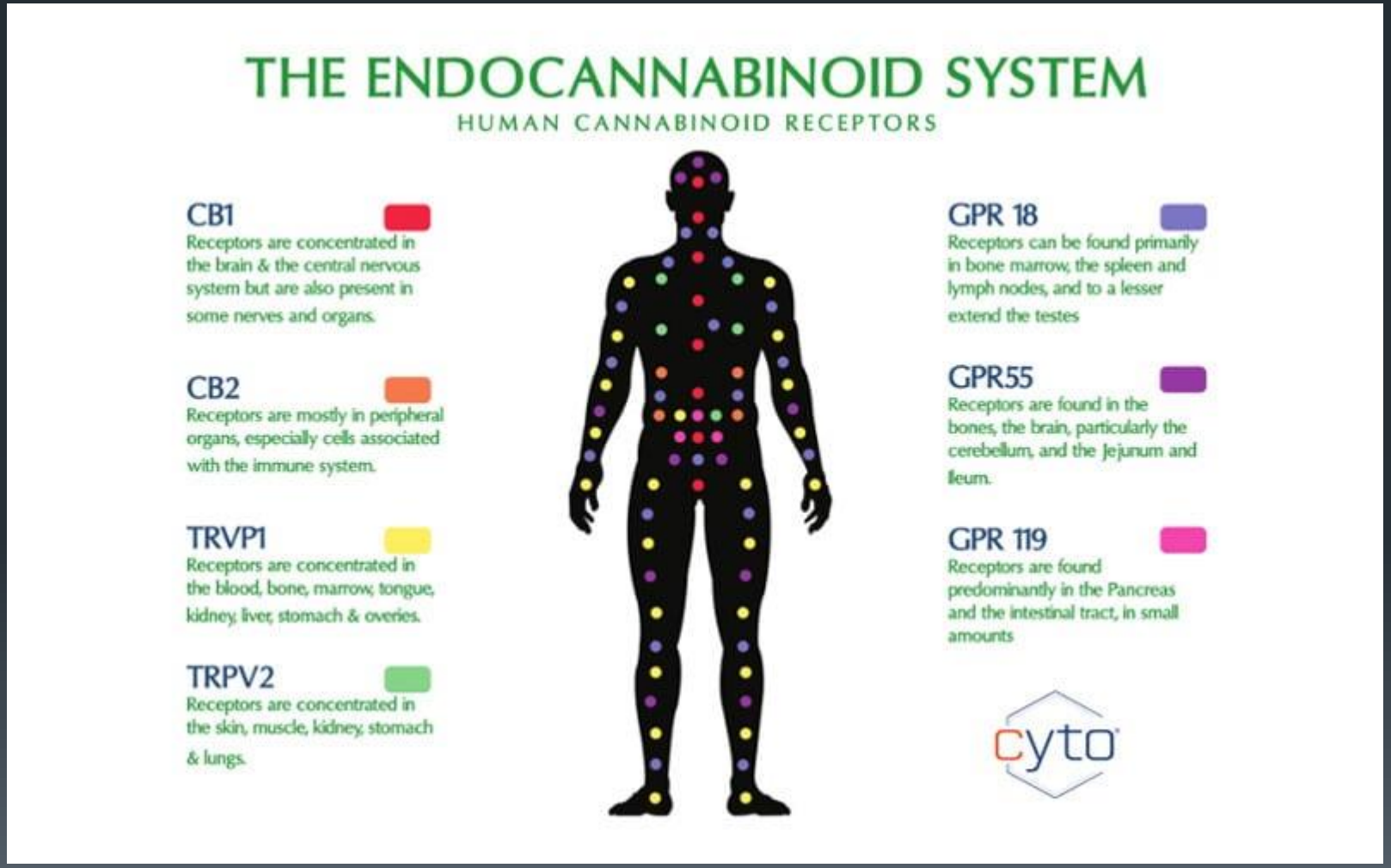
Obesity

- a horizontally challenging condition

Questions to be Addressed

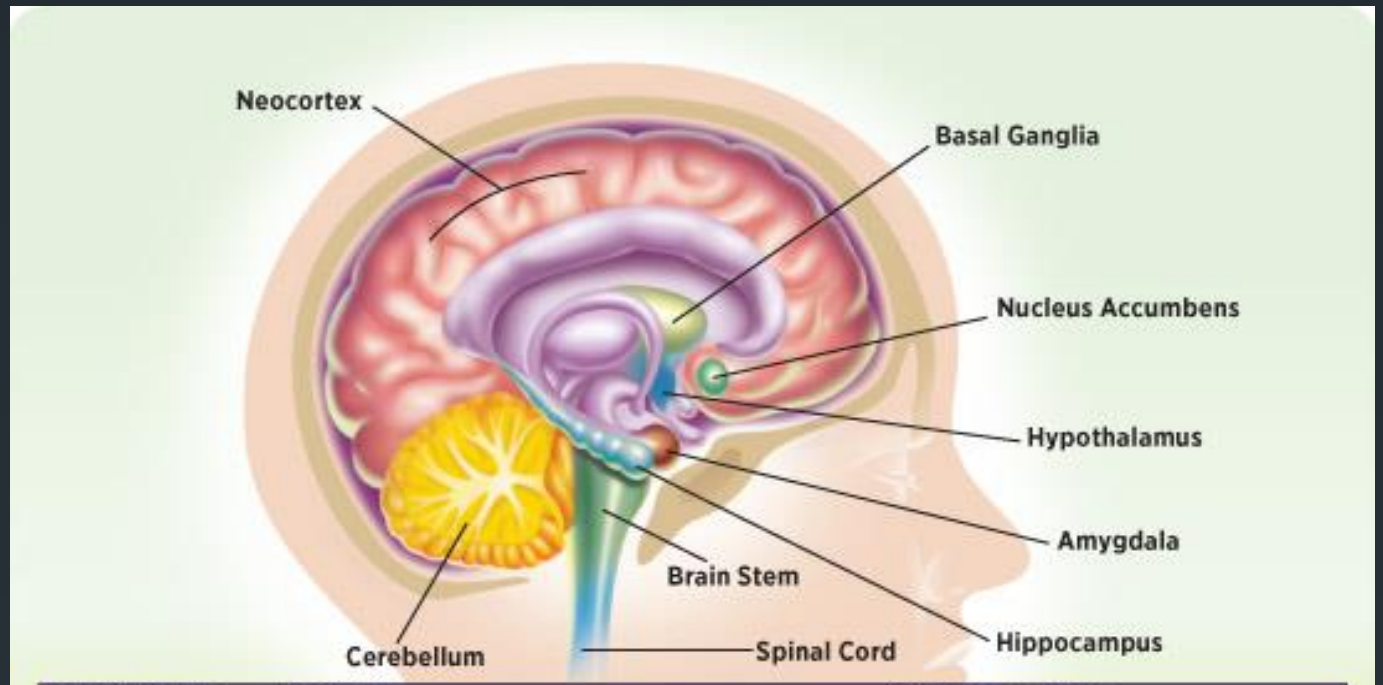
- 1) Is there stress in the modern world as we know it?
- 2) Does stress lead to obesity and/or marijuana?
- **3) Does marijuana lead to obesity? Does marijuana lead to diabetes?**
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- 6) Should we *as physicians* be concerned?

Experts have identified two key endocannabinoids so far:- anandamide (AEA) and 2-arachidonoylglycerol (2-AG).



Where in the brain do cannabinoids act?

What functions are affected?



Brain Structure	Regulates	THC Effect on User
Amygdala	emotions, fear, anxiety	panic/paranoia
Basal Ganglia	planning/starting a movement	slowed reaction time
Brain Stem	information between brain and spinal column	antinausea effects
Cerebellum	motor coordination, balance	impaired coordination
Hippocampus	learning new information	impaired memory
Hypothalamus	eating, sexual behavior	increased appetite
Neocortex	complex thinking, feeling, and movement	altered thinking, judgment, and sensation
Nucleus Accumbens	motivation and reward	euphoria (feeling good)
Spinal Cord	transmission of information between body and brain	altered pain sensitivity

THC and the “Munchies”

Marijuana “Munchies”

- A new study hints at a compelling metaphor for the way THC manipulates this natural system: it mimics sensations felt when we're deprived of food. As a final test, the researchers forced some mice to fast for 24 hours, \and found that this drove up levels of natural cannabinoids in the olfactory lobe. Not surprisingly, these starved mice showed greater scent sensitivity and ate much more too.

- Most intriguing, the genetically engineered mice with olfactory lobes that lacked cannabinoid receptors did not show increased scent sensitivity or appetite even when they were starved. This indicates that both THC and the natural cannabinoids that result from starvation are acting on the same neural pathway to allow us to smell and taste with greater sensitivity, and thus eat more. In other words, THC appears to give us the munchies by convincing our brains that we're starving.

The endocannabinoid system controls food intake via olfactory processes Edgar Soria-Gómez, Luigi Bellocchio, …Giovanni Marsicano *Nature Neuroscience* volume 17, pages407–415 (2014)

The Prevalence of Obesity may be Lower in Cannabis Users than in Nonusers.

- The adjusted prevalences of obesity in the NESARC and the NCS-R were 22.0% and 25.3%, respectively, among participants reporting no use of cannabis in the past 12 months and 14.3% and 17.2%, respectively, among participants reporting the use of cannabis at least 3 days per week. These differences were not accounted for by tobacco smoking status. Additionally, after adjustment for sex and age, the use of cannabis was associated with body mass index differences in both samples.

- Obesity and Cannabis Use: Results From 2 Representative National Surveys
- Yann Le Strat, Bernard Le Foll American Journal of Epidemiology, Volume 174, Issue 8, 15 October 2011, Pages 929–933, https://doi.org/10.1093/aje/kwr200

At a mean age of 50, compared with those who never used marijuana, **those who were current users had a 66% increased risk of having prediabetes** (hazard ratio [HR], 1.66; 95% CI, 1.15 – 2.38) and those who were heavy users had a 38% nonsignificant increased risk of prediabetes (HR, 1.38; 95% CI, 0.96 – 1.97), after adjustment for age, sex, race, smoking, alcohol, education, study center, systolic blood pressure, C-reactive protein, physical activity, use of illicit drugs, BMI, BMI^2, and waist circumference.

There was no association between marijuana use and diabetes, however.

Individuals who reported a high lifetime use of marijuana when they were young adults were more likely to develop prediabetes by the time they were 50 years old (HR, 1.40; 95% CI, 1.13 – 1.72, $P < .01$), but they were not more likely to develop diabetes (HR, 1.16; 95% CI, 0.77 – 1.74, $P = .32$), after adjustment for the same confounders. Bancks M, *Diabetologia* 2015. Published online September 13, 2015.

Fetal Exposure to Cannabis and Childhood Metabolic Outcomes: The Healthy Start Study

- Approximately 15% of the women had detectable levels of any cannabinoid, indicating fetal exposure to cannabis. Exposed offspring had higher fat mass (1.0 kg; 95% CI, 0.3-1.7), fat-free mass (1.2 kg; 95% CI, 0.4-2.0), adiposity (2.6%; 95% CI, 0.1-5.2), and fasting glucose (5.6 mg/dL; 95% CI, 0.8-10.3) compared with nonexposed offspring

- We provide novel evidence to suggest an association between **fetal exposure to cannabis with increased adiposity and fasting glucose in childhood**, a finding that should be validated in other cohorts. Brianna F Moore, Katherine A Sauder, Allison L B Shapiro, Tessa Crume, Gregory L Kinney, Dana Dabelea

- https://doi.org/10.1210/clinem/dgac101 *Journal of Clinical Endocrinology & Metabolism*, Volume 107, Issue 7, July 2022, Pages e2862–e2869,

Questions to be Addressed

- 1) Is there stress in the modern world as we know it?
- 2) Does stress lead to obesity and/or marijuana?
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- **4) Does obesity lead to pre-diabetes and/or frank diabetes?**
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- 6) Should we *as physicians* be concerned?

A recent study suggests that insulin resistance in particular regions of the brain that control overeating and the homeostatic setpoint are involved in visceral adiposity.

Stephanie Kullmann, PhD, Diabetes Care, March 20, 2015
[a postdoctoral fellow at the Institute for Diabetes Research and Metabolic Diseases, Helmholtz Center Munich, University of Tübingen, Germany]

Entry criteria

25 lean, 10 overweight, and 13 obese students from the University of Tubingen.

Screened to rule out neurologic, psychiatric, and eating disorders, and given glucose tolerance tests to rule out diabetes.

Even though obese subjects showed evidence of peripheral insulin resistance, none had T2DM and all were considered healthy.

Study Design

Participants randomly received treatment on two separate days—intranasal insulin one day, placebo the next.

Fifteen to 30 minutes after participants received treatment, they underwent MRI scans to measure cerebral blood flow (CBF).

They also rated desire for and liking of pictures of high-caloric savory and sweet food 60 minutes after receiving treatment.

Results

- Blood flow to the hypothalamus decreased significantly in all participants who received intranasal insulin vs placebo (P<.001)
- Level of hypothalamic response correlated inversely with amounts of visceral adipose tissue, independent of other fat compartments (P adjusted = .015)
- Only lean participants experienced insulin-induced decreases in CBF in the prefrontal cortex (*binary* effect.) This prefrontal cortex response to insulin correlated negatively with peripheral insulin resistance, (P<.001) and positively with food disinhibition (P=.004), and food craving (P=.007)

Possible Take Home Points

- Research shows that **insulin resistance** affects not just peripheral organs but certain areas of the brain in obese university students
- Participants with large amounts of **visceral fat** were particularly vulnerable to developing **hypothalamic insulin resistance**, and may have an **altered homeostatic setpoint** that makes it difficult for them to lose weight
- **Peripheral insulin resistance** was linked **to insulin resistance of the prefrontal cortex**, which **controls** many behaviors, including inhibitory control of **eating**
- Participants with peripheral **insulin resistance** and prefrontal insulin resistance had **difficulties with food cravings and control** over their eating

The Diabetes Epidemic *So Far…*

CDC: More than 100 Million U.S. Adults Have Diabetes

The prevalence of diagnosed diabetes greatly varies by region, race and age, according to a new report from the Centers of Disease Control and Prevention.

Stefanie Valentic

Jul 20, 2017

More About: Wellness

Prevalence of the Metabolic Syndrome ("***Pre-Diabetes***")

Prevalence of Prediabetes

- An estimated 33.9% of U.S. adults aged 18 years or older (84.1 million people) had prediabetes in 2015, based on their fasting glucose or A1C level. Nearly half (48.3%) of adults aged 65 years or older had prediabetes (Table 3) (Methods).
- Among adults with prediabetes, 11.6% reported being told by a health professional that they had this condition (Table 3).
- Age-adjusted data for 2011–2014 indicated that more men (36.6%) than women (29.3%) had prediabetes. Prevalence of prediabetes was similar among racial and ethnic groups (see Table 3a in the Appendix for more details).

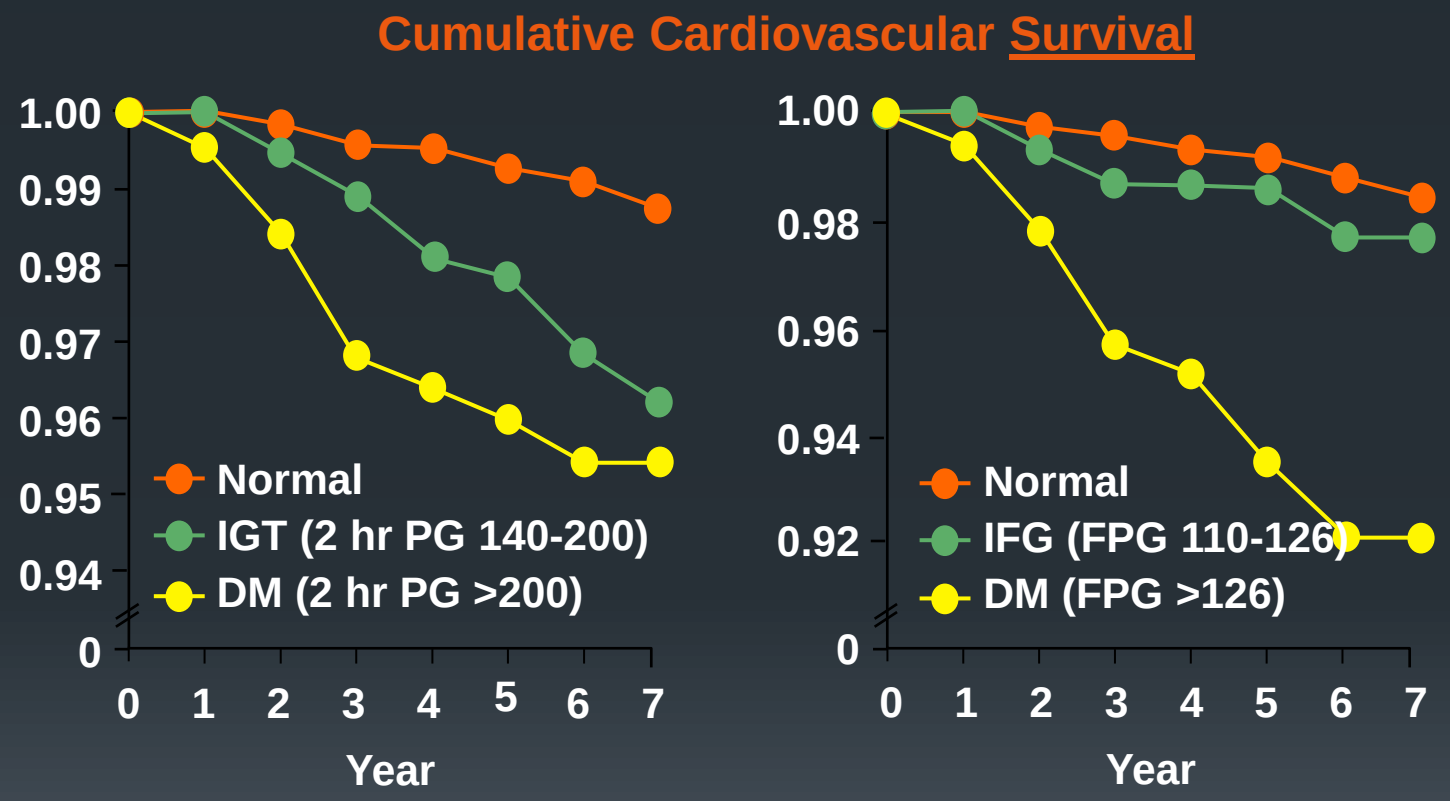
Table 3. Estimated number, percentage, and awareness of prediabetes among adults aged ≥18 years, United States, 2015

Characteristic	No. in millions (95% CI)[a]	Percentage (95% CI)[b]	Percentage aware of prediabetes (95% CI)[a,c]
Total	**84.1 (78.0–90.4)**	**33.9 (31.5–36.5)**	**11.6 (9.9–13.6)**
Age in years			
18–44	27.4 (24.5–30.6)	23.7 (21.1–26.4)	8.2 (5.8–11.5)
45–64	34.3 (31.5–37.2)	40.9 (37.5–44.3)	12.9 (10.2–16.1)
≥65	23.1 (21.1–25.1)	48.3 (44.2–52.5)	14.1 (10.5–18.6)
Sex			
Women	39.5 (36.0–43.3)	31.1 (28.3–34.0)	14.1 (11.3–17.6)
Men	44.5 (40.5–48.7)	36.9 (33.6–40.4)	9.4 (6.6–13.3)

CI = confidence interval.
[a] Numbers for subgroups may not add up to the total because of rounding.
[b] Data are crude, not age-adjusted.
[c] Among those with prediabetes.
Data source: 2011–2014 National Health and Nutrition Examination Survey and 2015 U.S. Census Bureau data.

THE FUNAGATA DIABETES STUDY

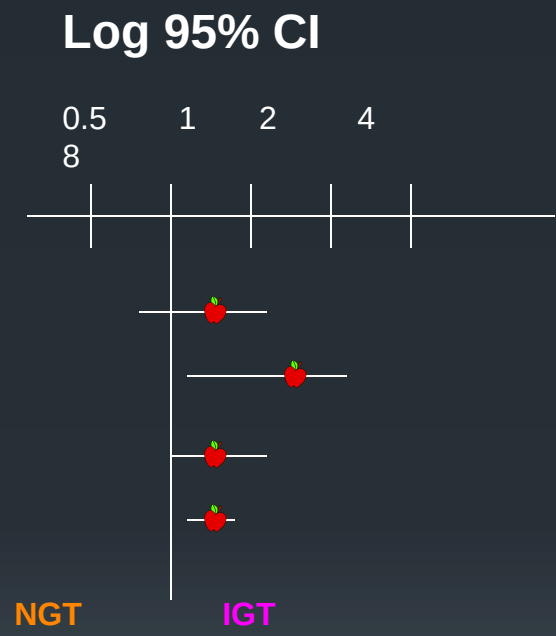
Impaired Glucose Tolerance is a CV Risk Factor[3b]



Tominaga M, et al. Impaired glucose tolerance is a risk factor for cardiovascular disease, ***but not impaired fasting glucose***. *Diabetes Care* 1999;22:920-4.

Cardiovascular Mortality in Normal Glucose Tolerance vs Impaired Glucose Tolerance[3b]

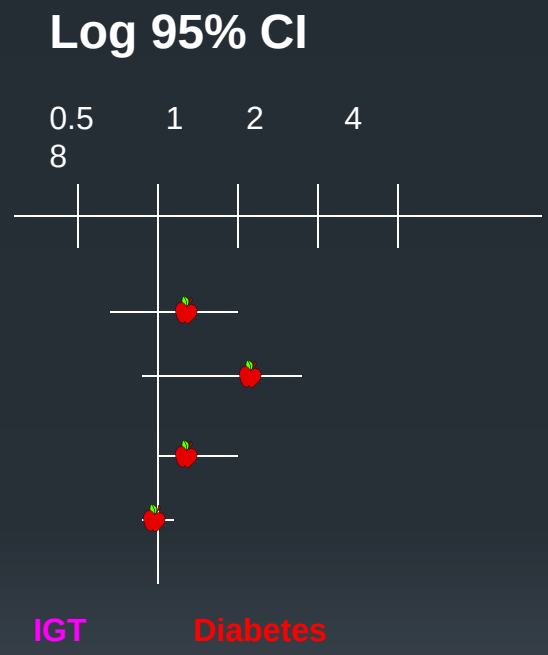
Study	Ratio	p value
Bedford Mortality Study (1982)[1]		
Males	1.42	ns
Females	**2.76**	**<0.05**
Paris Prospective Study (1993)[2]	1.6	ns
Malmohus County Study (1997)[3]	1.8	<0.01



1. Odds Ratio
2. Relative Risk
3. Age-Sex Adjusted Relative Risk **(minus SFU Pts)**

Cardiovascular Mortality in Impaired Glucose Tolerance vs Diabetics[3b]

Study	Ratio	p value
Bedford Mortality Study (1982)[1]		
Males	1.31	ns
Females	2.12	ns
Paris Prospective Study(1993)[2]	1.43	ns
Malmohus County Study(1997)[3]	1.0	ns



1. Odds Ratio
2. Relative Risk
3. Age-Sex Adjusted Relative Risk **(minus SFU Pts)**

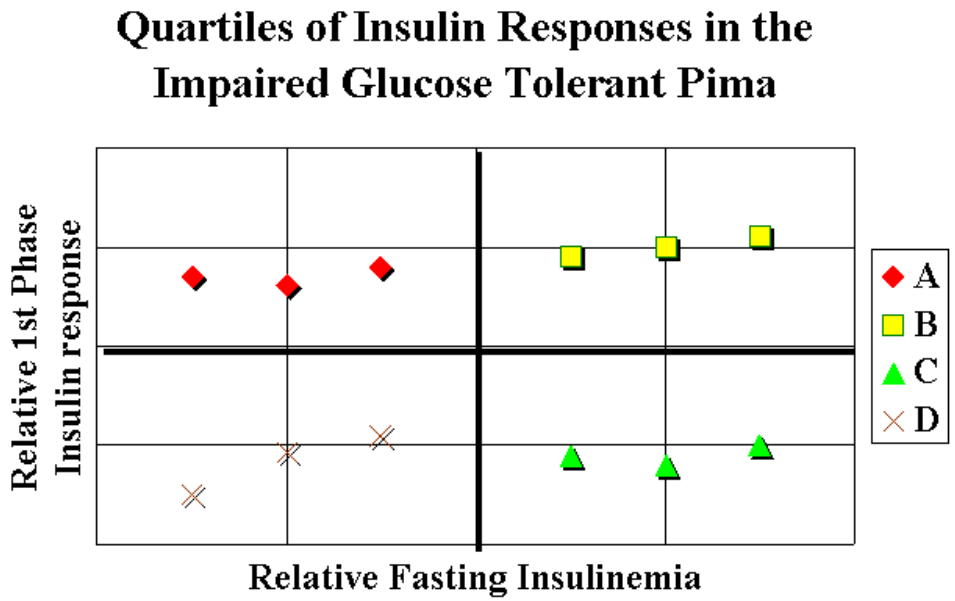
Obesity and Insulin Resistance:- The “Metabolic Syndrome”

- Most people who have metabolic syndrome have insulin resistance. The body makes insulin to move glucose (sugar) into cells for use as energy. ***Centripetal obesity, commonly found in people with metabolic syndrome, makes it more difficult for cells in the body to respond to insulin***. If the body can’t make enough insulin to override the resistance, the blood sugar level increases, causing type 2 diabetes. Metabolic syndrome may be a start of the development of type 2 diabetes.

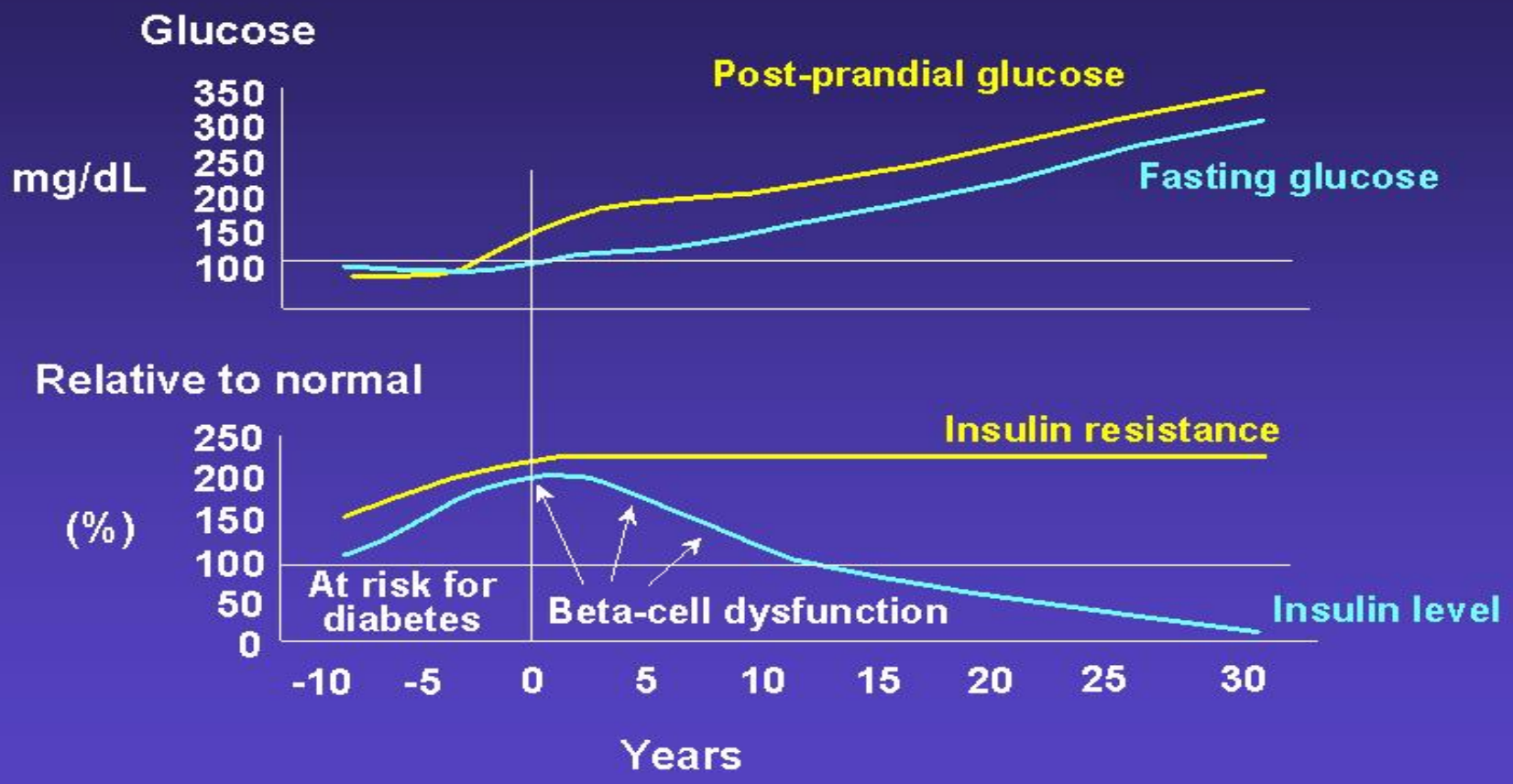
- Because the population of the U.S. is aging, and because metabolic syndrome is more likely the older you are, the American Heart Association (AHA) has estimated that ***the metabolic syndrome soon will become the main risk factor for cardiovascular disease*****, ahead of cigarette smoking**. Experts also think that increasing rates of obesity are related to the increasing rates of metabolic syndrome.

Who progresses to Type 2 from *Pre*-Diabetes?

Who Progresses to Type 2 DM?



Natural History of Type 2 Diabetes

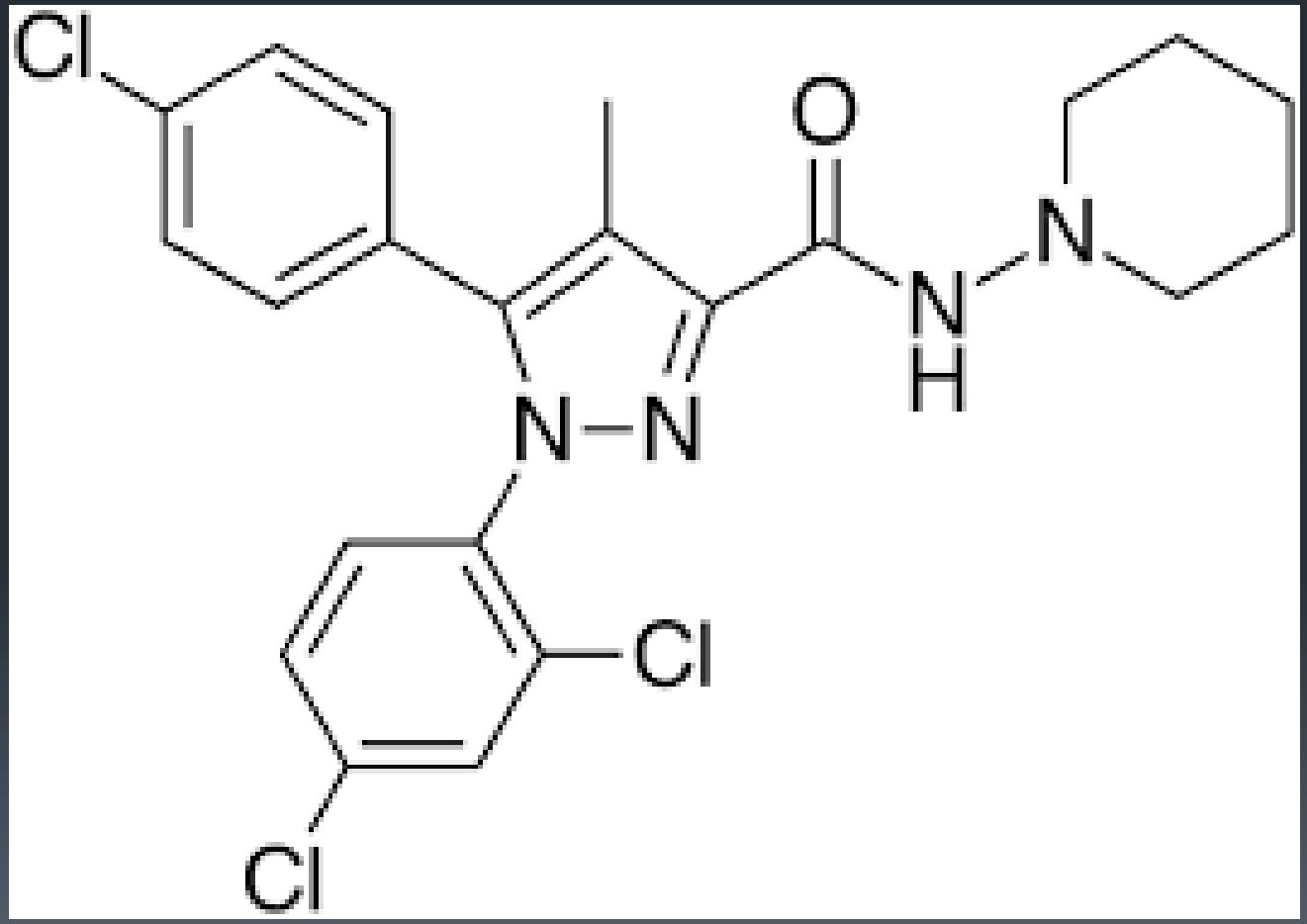


R.M. Bergenstal, International Diabetes Center

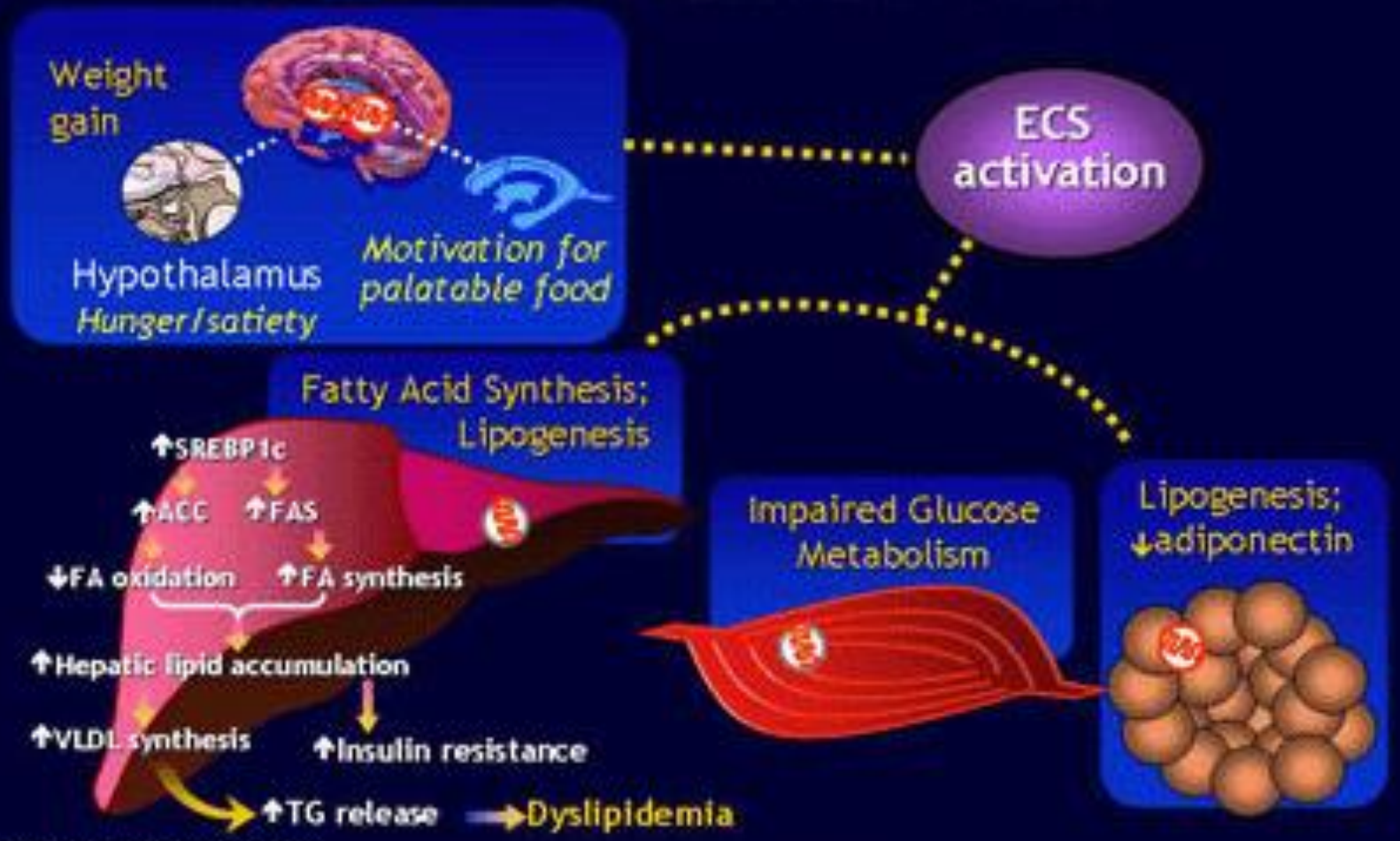
Questions to be Addressed

- 1) Is there stress in the modern world as we know it?
- 2) Does stress lead to obesity and/or marijuana?
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- **5) Does *specifically* blocking the effects of marijuana improve obesity and diabetes?**
- 6) Should we *as physicians* be concerned?

Introducing “rimonabant” – a cannabinoid receptor inhibitor developed by Sanofi



ECS: A Possible "Vertical Integrator" of Cardiometabolic Risk



ECS=endocannabinoid system.

Bensaid M et al. *Mol Pharmacol*. 2003;63:908-914; Osei-Hyiaman D et al. *J Clin Invest* 2005;115:1298-1305; Pagotto U et al. *Endocr Rev*. 2006;27:73-100.

Rimonabant: RIO program summary

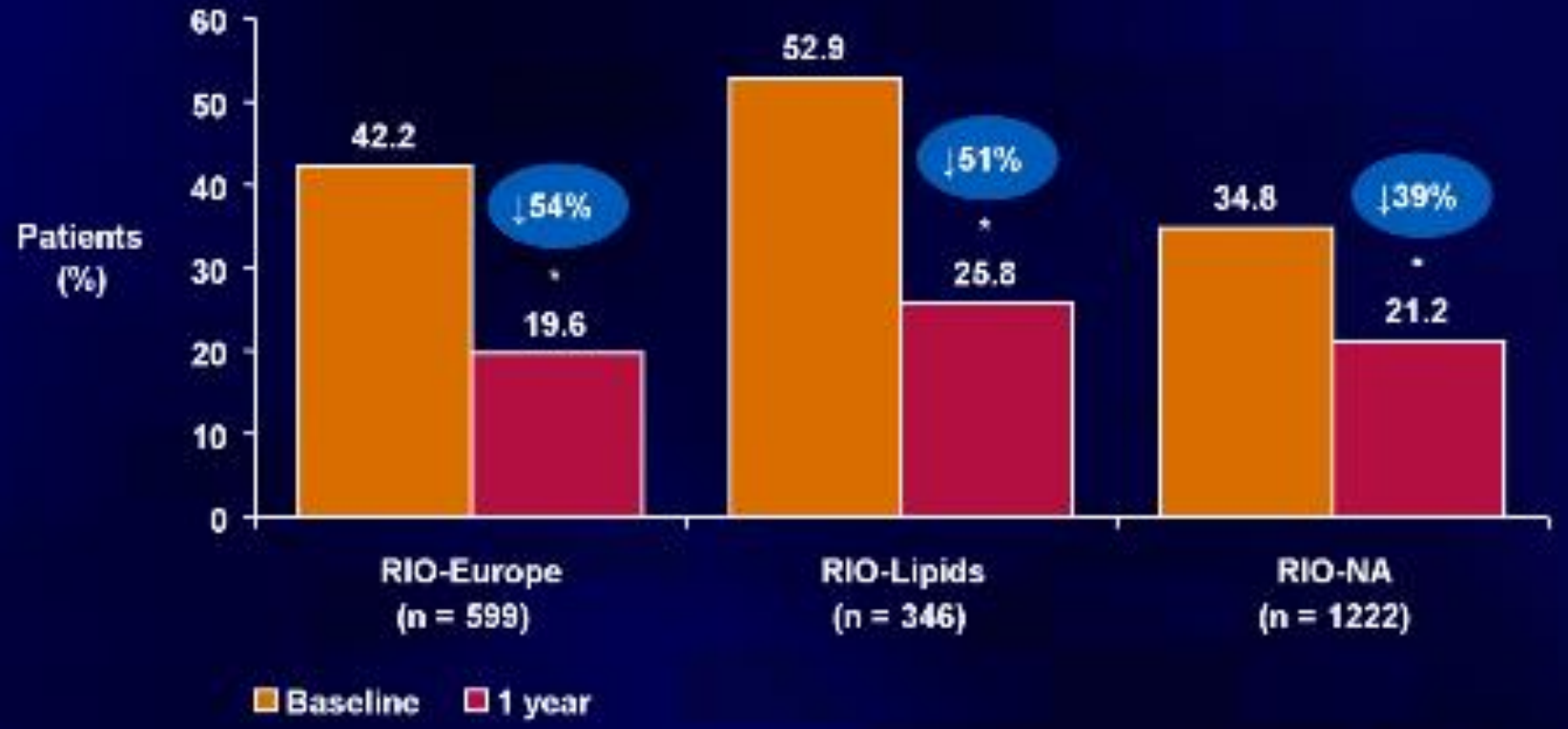
- Over 1 year, rimonabant 20 mg combined with diet demonstrated:
  - Significant decreases in weight and waist circumference
  - Weight loss: 14.0–15.3 lbs absolute change, 10.4–12.0 lbs placebo-corrected change
  - Favorable changes in cardiometabolic risk factor profile

Van Gaal LF et al. *Lancet*. 2006;365:1389-97.
Després J-P et al. *N Engl J Med*. 2005;353:2121-34.
Pi-Sunyer FX et al. *JAMA*. 2006;295:761-75.

VBWG

Significant decrease in metabolic syndrome

Rimonabant 20 mg

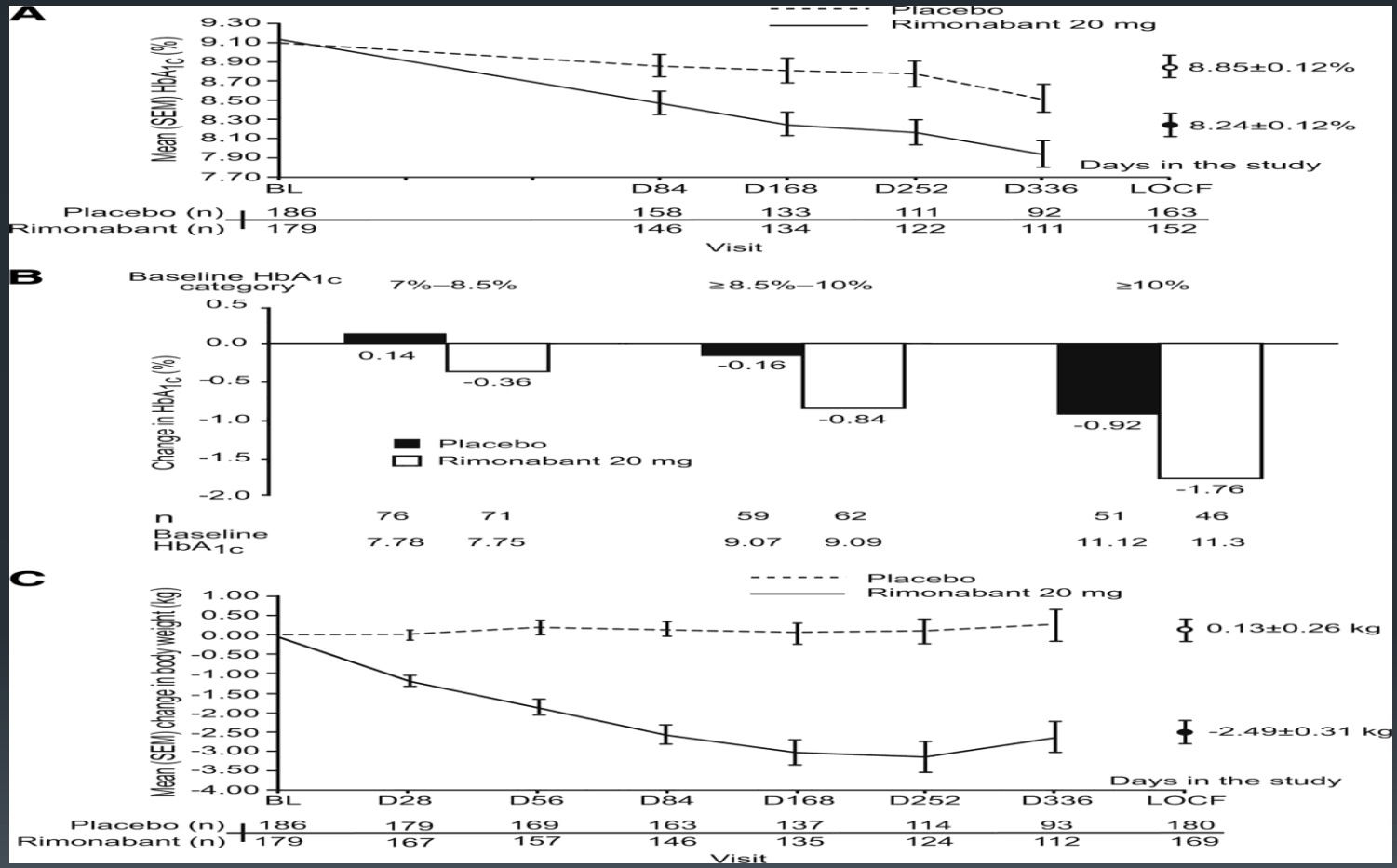


ATP III criteria
*P < 0.001 vs placebo

Van Gaal LF et al. *Lancet*. 2005.
Després J-P et al. *N Engl J Med*. 2005.
Pi-Sunyer FX et al. *JAMA*. 2006.

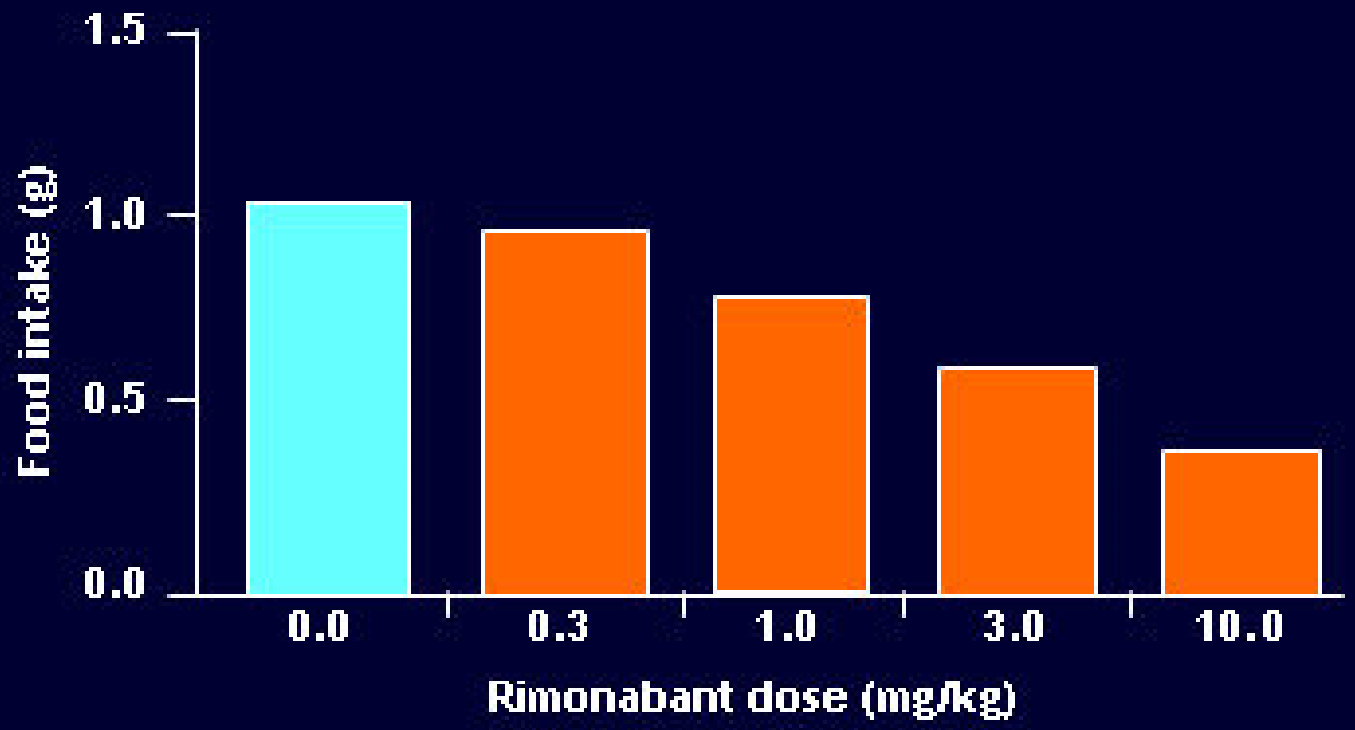
From: **Effect of Rimonabant on Glycemic Control in Insulin-Treated Type 2 Diabetes: The ARPEGGIO Trial**

Diabetes Care. 2009;33(3):605-607. doi:10.2337/dc09-0455

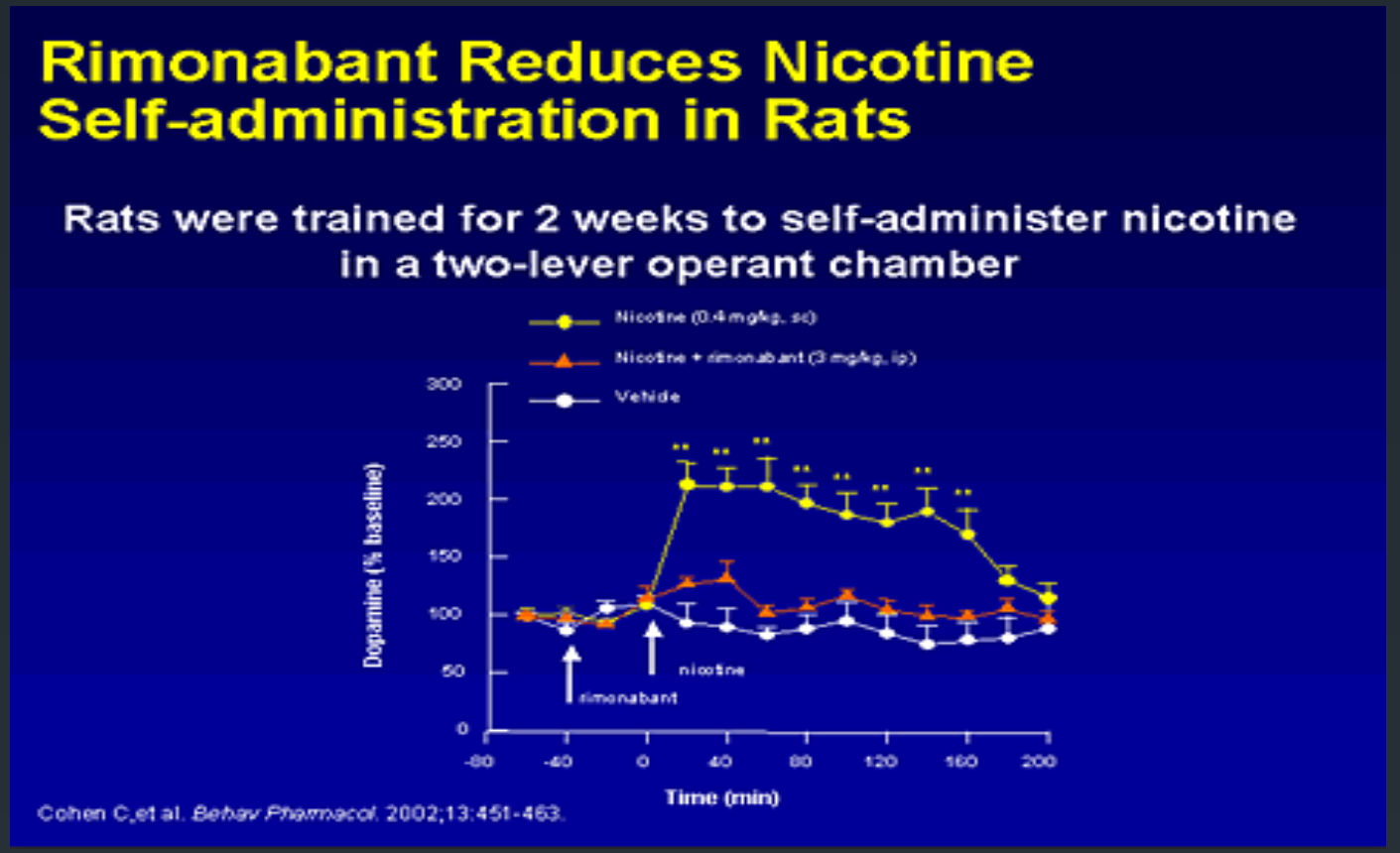


A: Change in A1C over time. B: Change in A1C according to baseline level. C: change in body weight over time.

CB1 Blockade Produces a Dose-Related Reduction in Food Intake in Mice



Wiley J L et al. *Br J Pharmacol*. 2005;145:293-300.



SR141716 (1-3 mg/kg) blocked nicotine-induced dopamine release in the shell of the nucleus accumbens (NAc) and the bed nucleus of the stria terminalis. To investigate whether SR141716 would block the dopamine-releasing effects of another drug of abuse, we extended the neurochemical study to the effect of ethanol, consumption of which in rodents is reduced by SR141716. Dopamine release induced by ethanol in the NAc was also reduced by SR141716 (3 mg/kg). These results suggest that activation of the endogenous cannabinoid system may participate in the motivational and dopamine-releasing effects of nicotine and ethanol. Thus, SR141716 may be effective in reduction of alcohol consumption….

C Cohen[1], G Perrault, C Voltz, R Steinberg, P SoubriéBehav Pharmacol 13:461-463, 2002

Rimonabant *also*:-

1) Reduced resumption of cocaine-seeking behaviors in recovering cocaine addicts

2) Reduced resumption of EtOH-seeking behaviors in recovering alcoholics

3) Reduced resumption of morphine-seeking behaviors in recovering heroin addicts

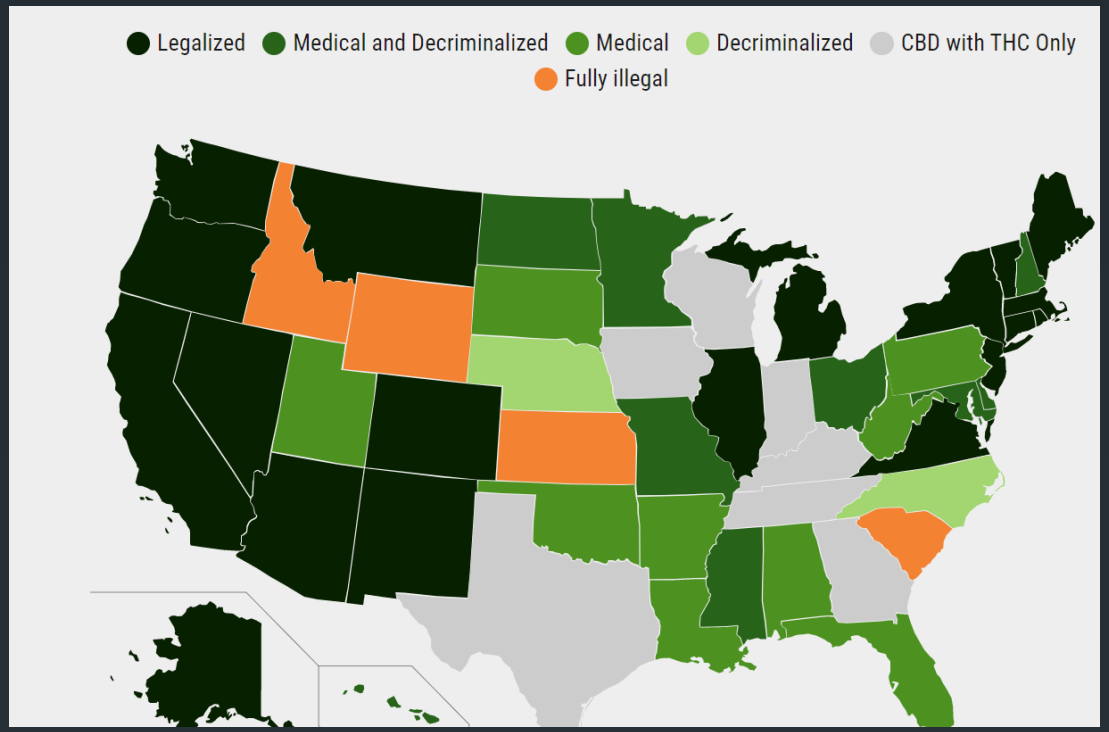
Side Effects

Depression
Nausea
Anxiety
Unpredictable mood swings
Insomnia

Suicides

Marijuana,
More Metabolic Syndrome
(More Prediabetes….)
Recommendations?

The Prediabetes Epidemic *So Far….*



CDC: More than 100 Million U.S. Adults Have Diabetes

The prevalence of diagnosed diabetes greatly varies by region, race and age, according to a new report from the Centers of Disease Control and Prevention.

Stefanie Valentic

Jul 20, 2017

Questions to be Addressed

- **1)** Is there stress in the modern world as we know it?
- 2) Does stress lead to obesity and/or marijuana?
- 3) Does marijuana lead to obesity? Does marijuana lead to diabetes?
- 4) Does obesity lead to pre-diabetes and/or frank diabetes?
- 5) Does *specifically* blocking the effects of marijuana improve diabetes and obesity?
- **6) Should we *as physicians* be concerned?**

Thank you!
Any questions?