CONBRACANN

2ª EDIÇÃO

CONGRESSO BRASILEIRO DE CANNABIS MEDICINAL

ORGANIZAÇÃO E REALIZAÇÃO

EAD PLUS

Educação em Saúde

CANABINOIDES E A PERDA DE PESO: QUAL É A RELAÇÃO?

ADRIANA GROSSO PhD

Atuante no mercado de Cannabis Medicinal como Medical Science Liaison (MSL). Graduação em Ciências Biológicas e com mestrado concluídos pela FFCLRP USP e PhD em Cardiologia pelo InCor FMUSP. Especialização em Pesquisa Clínica e Medical Affairs pela FCM Santa Casa de SP. Atuou na área acadêmica por mais de 20 anos. Docente do curso de especialização em Medicina Canabinoide - Abordagem baseada em evidências do HCFMUSP

REVIEW

Pathophysiology of obesity and its associated diseases

Xin Jin[a,d,e], Tingting Qiu[a], Li Li[a], Rilei Yu[a], Xiguang Chen[d], Changgui Li[b,*], Christopher G. Proud[c,*], Tao Jiang[a,*]

OBESIDADE é definida como um acúmulo anormal ou excessivo de gordura (World Health Organization, WHO) e tem sido considerada uma pandemia global

IMC da OBESIDADE = 30 kg/m2
IMC do SOBREPESO = 25 a 29.9 kg/m2

O valor standard de sobrepeso/obesidade são diferentes entre determinadas populações

Dragano NRVet al. Recent updates on obesity treatments: available drugs and future directions. Neuroscience 2020;437:215e39.
Ng M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980e2013: a systematic analysis for the global burden of disease study 2013. Lancet 2014;384:766e81.
Bluher M. Obesity: global epidemiology and pathogenesis. Nat Ver Endocrinol 2019;15:288e98.

Consultation WHOE. Appropriate body-mass index for Asian populationsand its implications for policy and intervention strategies. Lancet 2004;363:157e63.

OBESIDADE E DIFICULDADE NA PERDA DE PESO

- A principal justificativa para definir a obesidade como uma doença crônica (além dos riscos à saúde diretamente atribuíveis ao excesso de peso corporal) é a ***fisiopatologia distinta em pessoas com obesidade que resulta em poderosos mecanismos homeostáticos que impedem a perda de peso e promovem ganho de peso***

- Esses mecanismos biológicos alterados em pessoas com obesidade explicam por que as **intervenções comportamentais ou médicas de curto prazo frequentemente não são suficientes** para resultar em perda de peso em longo prazo. Embora as tentativas de promover uma alimentação saudável e mais atividade física sejam importantes para a prevenção da obesidade em nível social, essas recomendações não são suficientes para reduzir o IMC em indivíduos que já vivem com um peso corporal elevado

OBESIDADE: BALANÇO DE ENERGIA POSITIVO E POSSÍVEIS CAUSAS

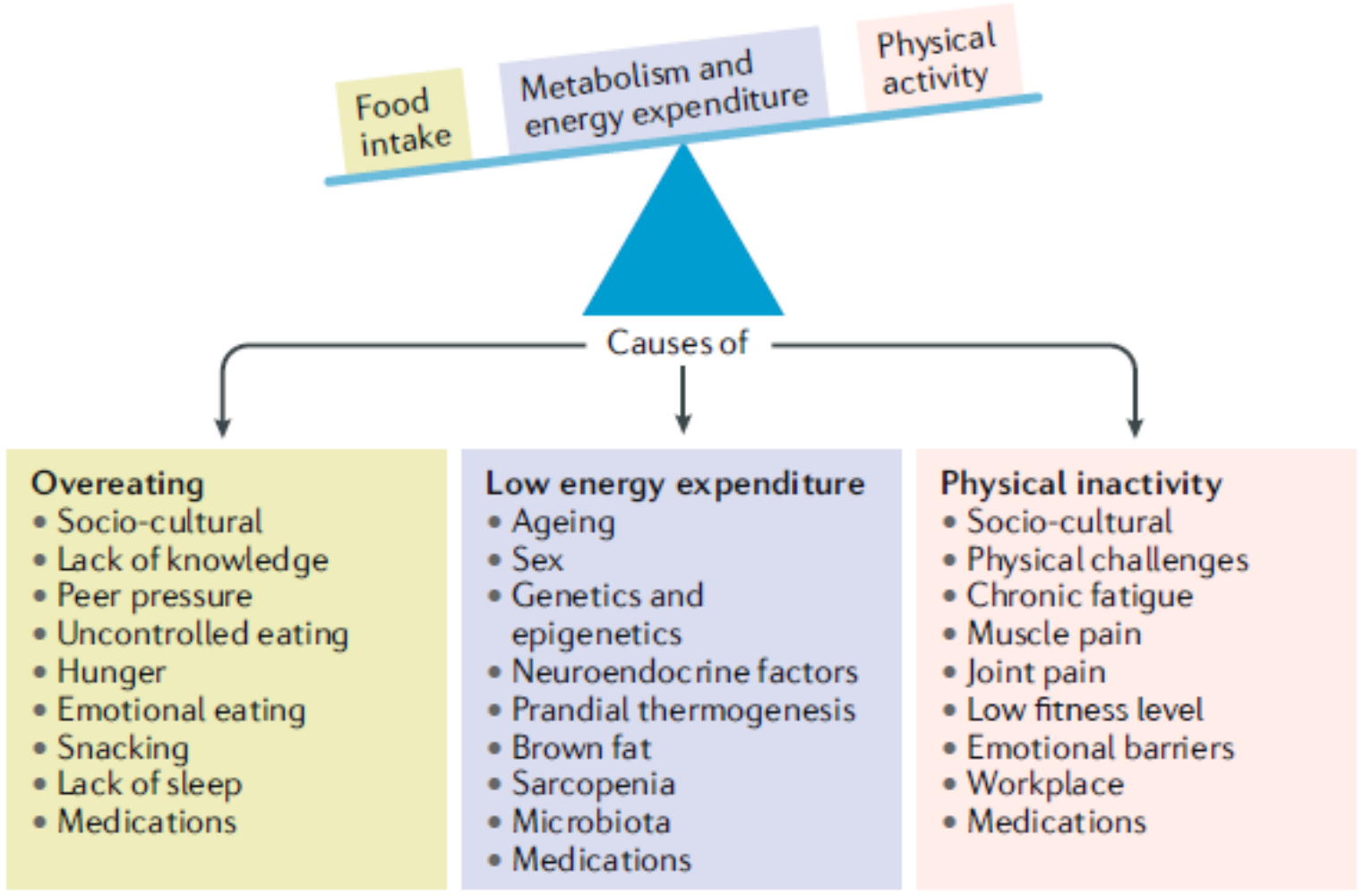


Fig. 1 | **Factors that can influence the chronic positive energy balance, thus subsequently causing obesity.** Weight gain can result from a combination of increased energy intake, low physical activity and reduced energy expenditure. Adapted with permission from REF.[28], Wiley-VCH.

Natue Review
https://doi.org/10.1038/s41574-019-0176-8

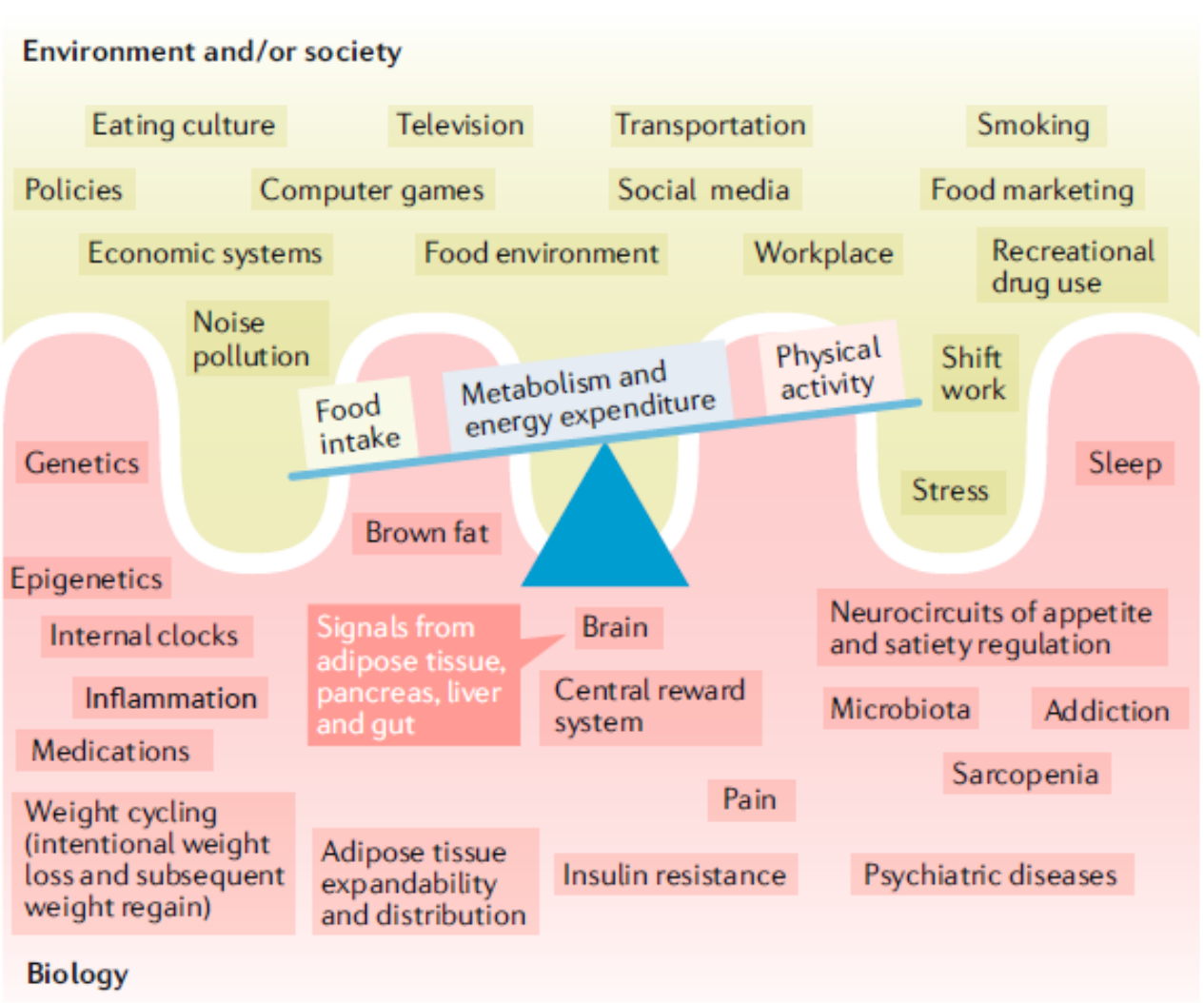


Fig. 2 | **Complex biological, environmental and societal factors contributing to obesity.** Individual factors (such as genetic background or the gut–brain–hormone axis) influence susceptibility to obesity, which may develop in an obesogenic environment (for example, influenced by eating culture, transportation and computerization).

AMBIENTE OBESOGÊNICO: FATORES SOCIAIS, AMBIENTAIS E BIOLÓGICOS DA SOCIEDADE MODERNA

Nature Review
https://doi.org/10.1038/s41574-019-0176-8

PREVALÊNCIA POR PAÍS

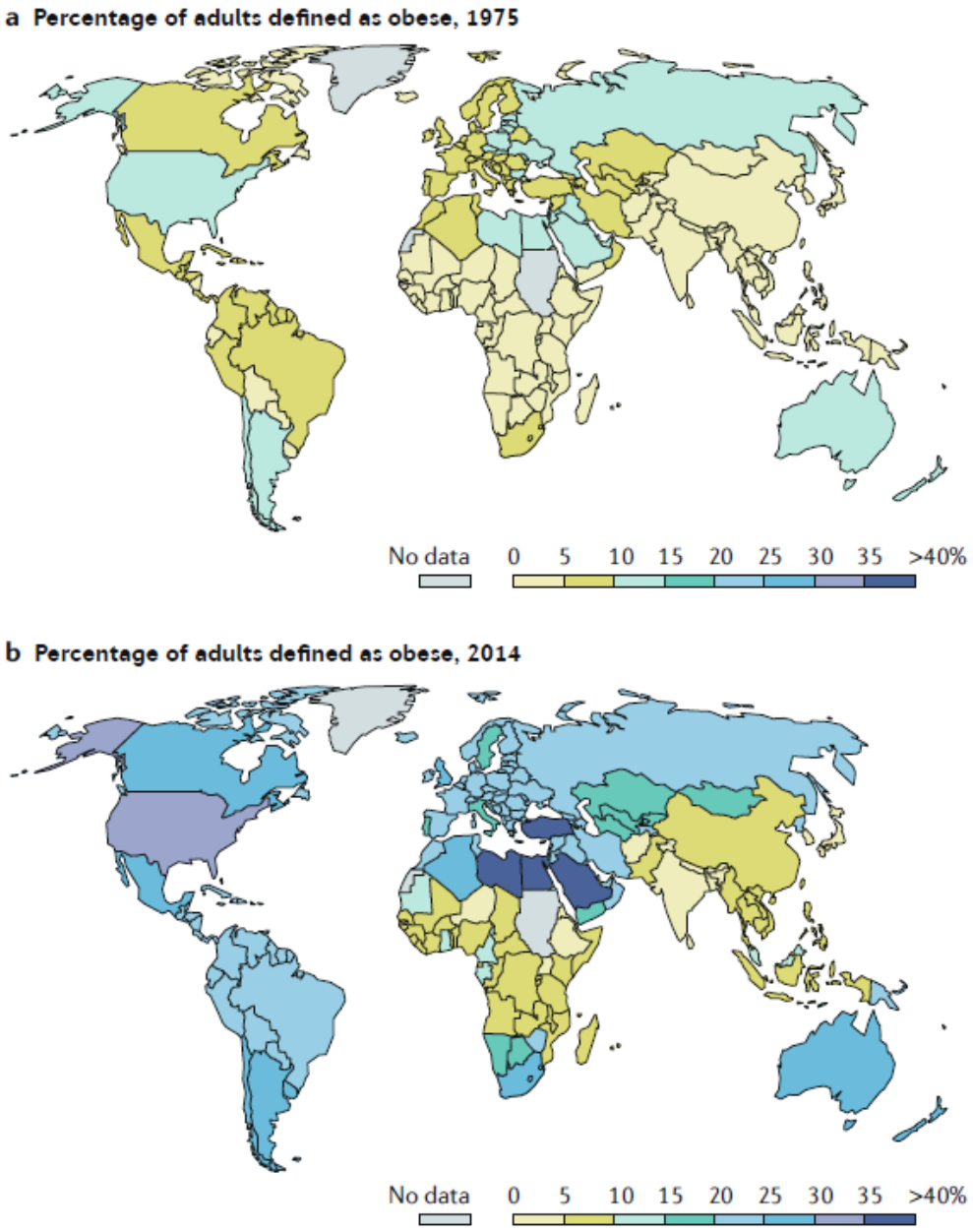


Fig. 4 | **Increase in prevalence of obesity over time.** Percentage of adults defined as obese by country in 1975 (part **a**) and 2014 (part **b**). The number of adults with obesity increased substantially between 1975 and 2014. Data from the WHO, Global Health Observatory.

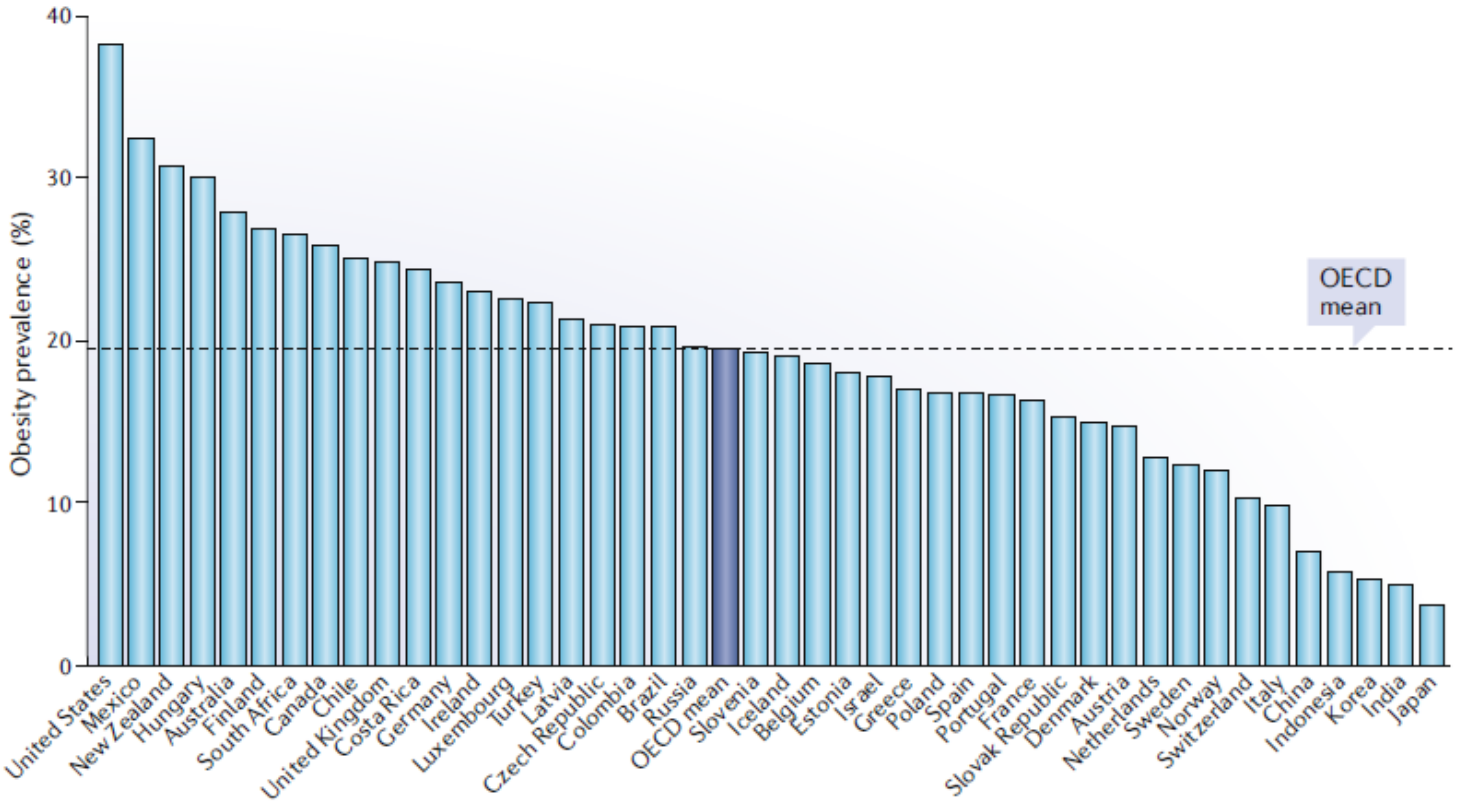


Fig. 3 | **Worldwide prevalence of obesity.** Prevalence of obesity (BMI ≥30 kg/m²) varies between selected countries (Organisation for Economic Cooperation and Development (OECD), 2017; percentage of adults with obesity from measured data). In 2015, across OECD countries, the mean prevalence of obesity in adults was 19.5% (dotted line) and ranged from <6% in Japan to >30% in the United States. Adapted with permission from REF.[40], the OECD.

Nature Review
https://doi.org/10.1038/s41574-019-0176-8

PREVALÊNCIA NOS EUA segundo dados de NHANES - National Health and Nutrition Examination Survey

An official website of the United States government

Prevalence of Overweight and Obesity

Adults

Age-adjusted percentage of US adults with overweight, obesity, and severe obesity by sex, 2017–2018 NHANES Data[2]

	All (Men and Women)	Men	Women
Overweight	30.7	34.1	27.5
Obesity (including severe obesity)	42.4	43.0	41.9
Severe obesity	9.2	6.9	11.5

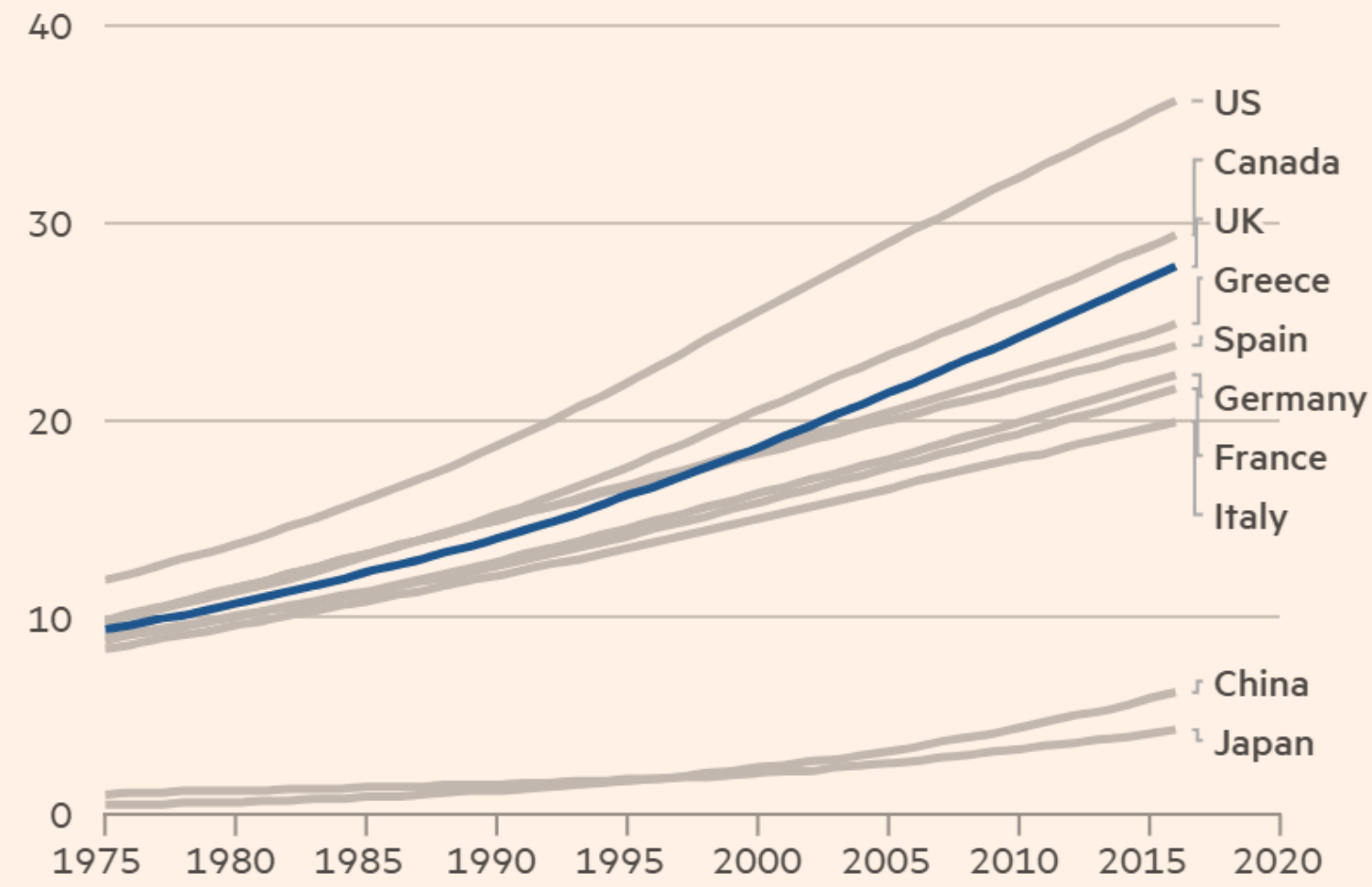
As shown in the above table

- Nearly 1 in 3 adults (30.7%) are overweight.
- More than 1 in 3 men (34.1%) and more than 1 in 4 women (27.5%) are overweight.
- More than 2 in 5 adults (42.4%) have obesity (including severe obesity).
- About 1 in 11 adults (9.2%) have severe obesity.
- The percentage of men who are overweight (34.1%) is higher than the percentage of women who are overweight (27.5%).
- The percentage of women who have severe obesity (11.5%) is higher than the percentage of men who have severe obesity (6.9%).

Britain has one of the worst obesity rates in Europe. Why?

Eri Sugiura in London OCTOBER 13 2023

Prevalence of obesity (BMI ≥ 30), among adults, 1975-2016 (%)



FINANCIAL TIMES

Source: WHO Global Health Observatory

Check for updates

OPEN

Time trends and projected obesity epidemic in Brazilian adults between 2006 and 2030

José Matheus Estivaleti[1], Juan Guzman-Habinger[2], Javiera Lobos[3], Catarina Machado Azeredo[4], Rafael Claro[5], Gerson Ferrari[6], Fernando Adami[7] & Leandro F. M. Rezende[1]✉

The prevalence of obesity increased from 11.8% in 2006 to 20.3% in 2019

The projected prevalences by 2030 are estimated to be 68.1% for overweight, 29.6% for obesity, and 9.3% for obesity classes II and III. Women, black and other minority ethnicities, middle-aged adults, adults with ≤ 7 years of education, and in Northern and Midwestern capitals are estimated to have higher obesity prevalence by 2030

- We examined time trends and **projected** obesity epidemic in Brazilian adults between **2006 and 2030 by sex, race/skin color, educational attainment, and state capitals**
- Self-reported body weight and height of 730,309 adults (≥ 18 years) from the Vigitel study were **collected by telephone interview between 2006 and 2019**
- **A multinomial logistic regression model** was **used to predict the prevalence of body mass index (BMI) categories as a function of time by 2030**

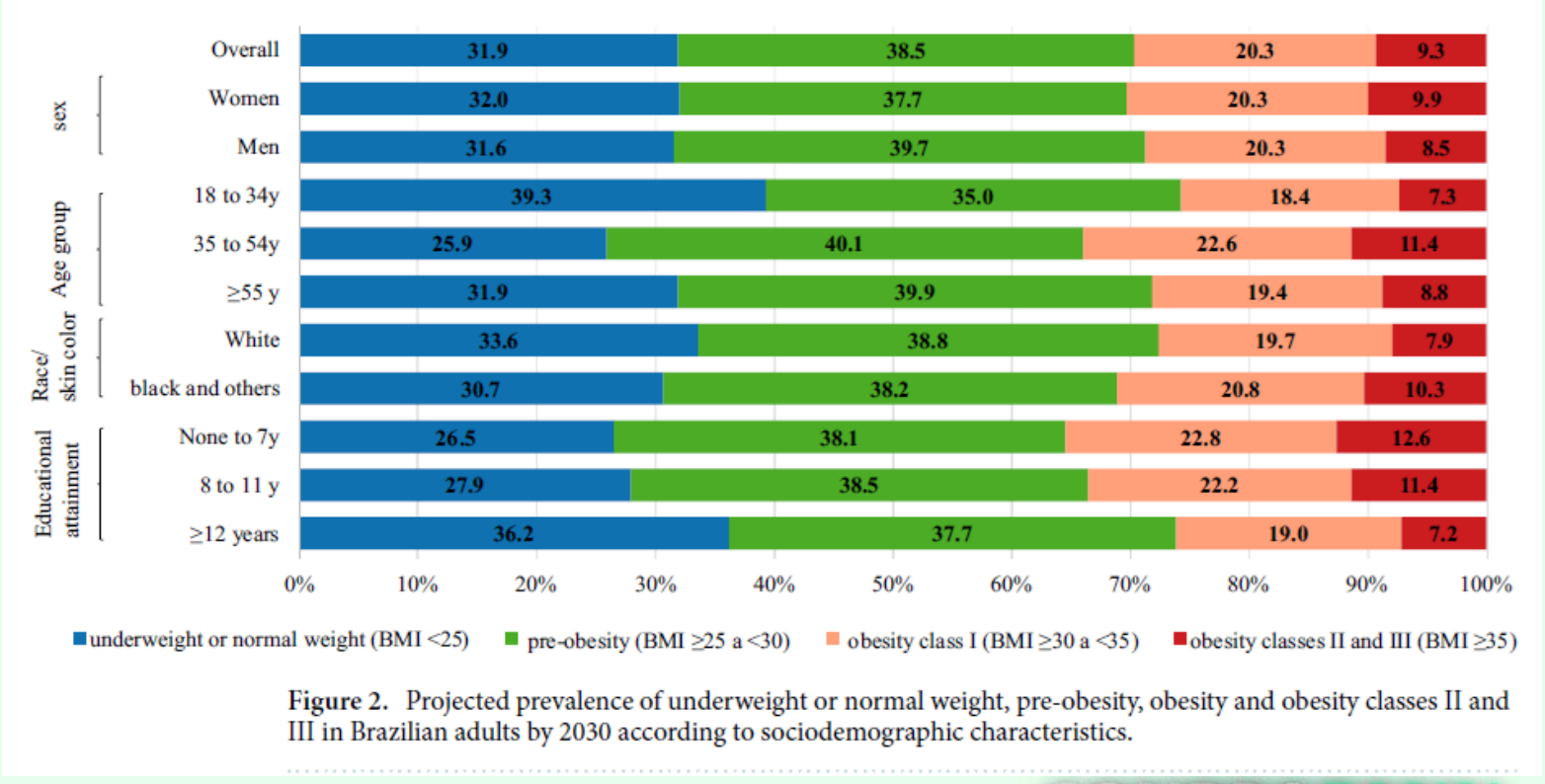
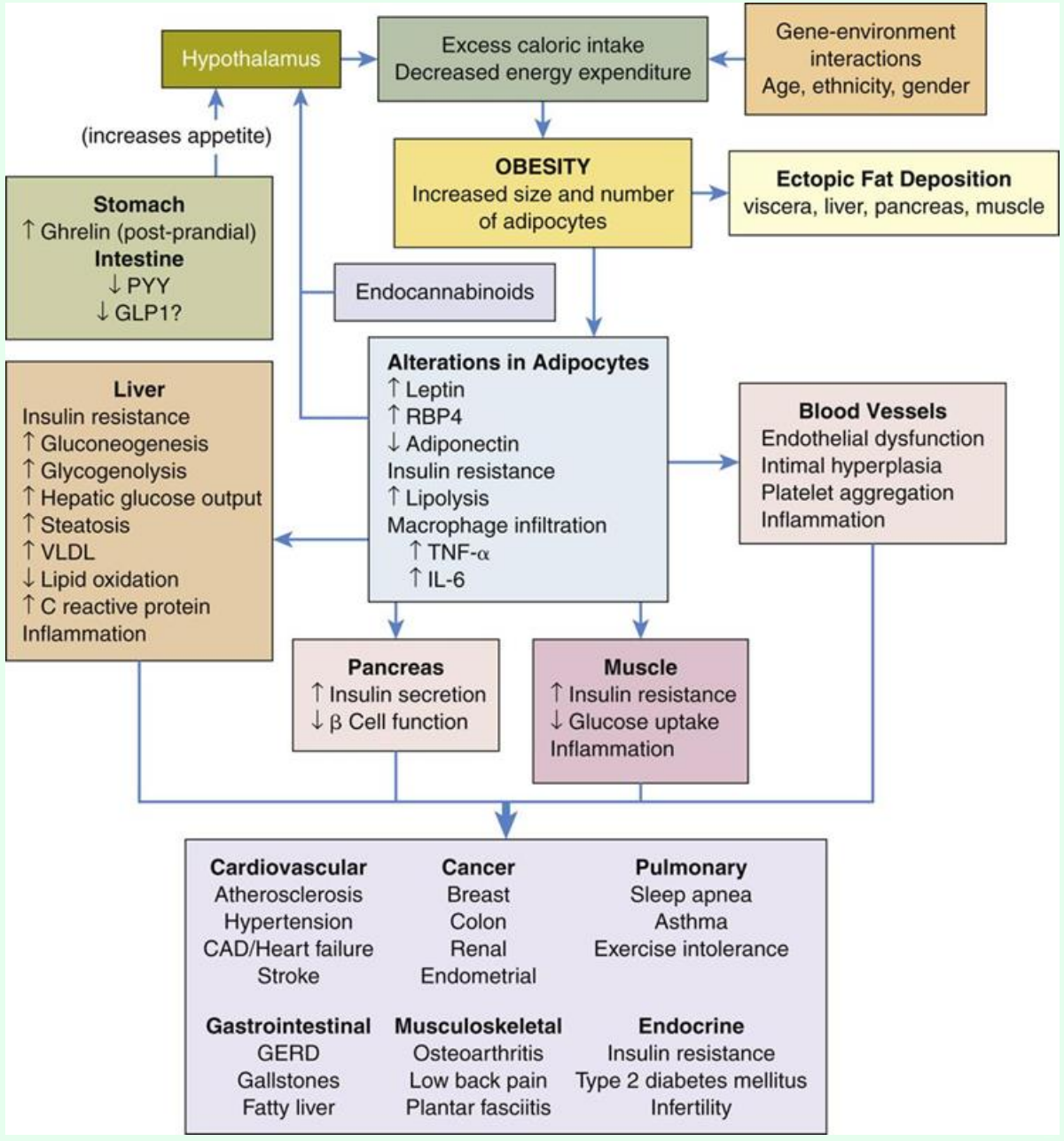


Figure 2. Projected prevalence of underweight or normal weight, pre-obesity, obesity and obesity classes II and III in Brazilian adults by 2030 according to sociodemographic characteristics.

Obesity is a disease that can cause premature disability and death by increasing the risk of cardiometabolic diseases, osteoarthritis, dementia, depression and some types of cancers



https://ukdiss.com/examples/obesity-pathophysiology-complications.php

FISIOPATOLOGIA: OBESIDADE E INFLAMAÇÃO

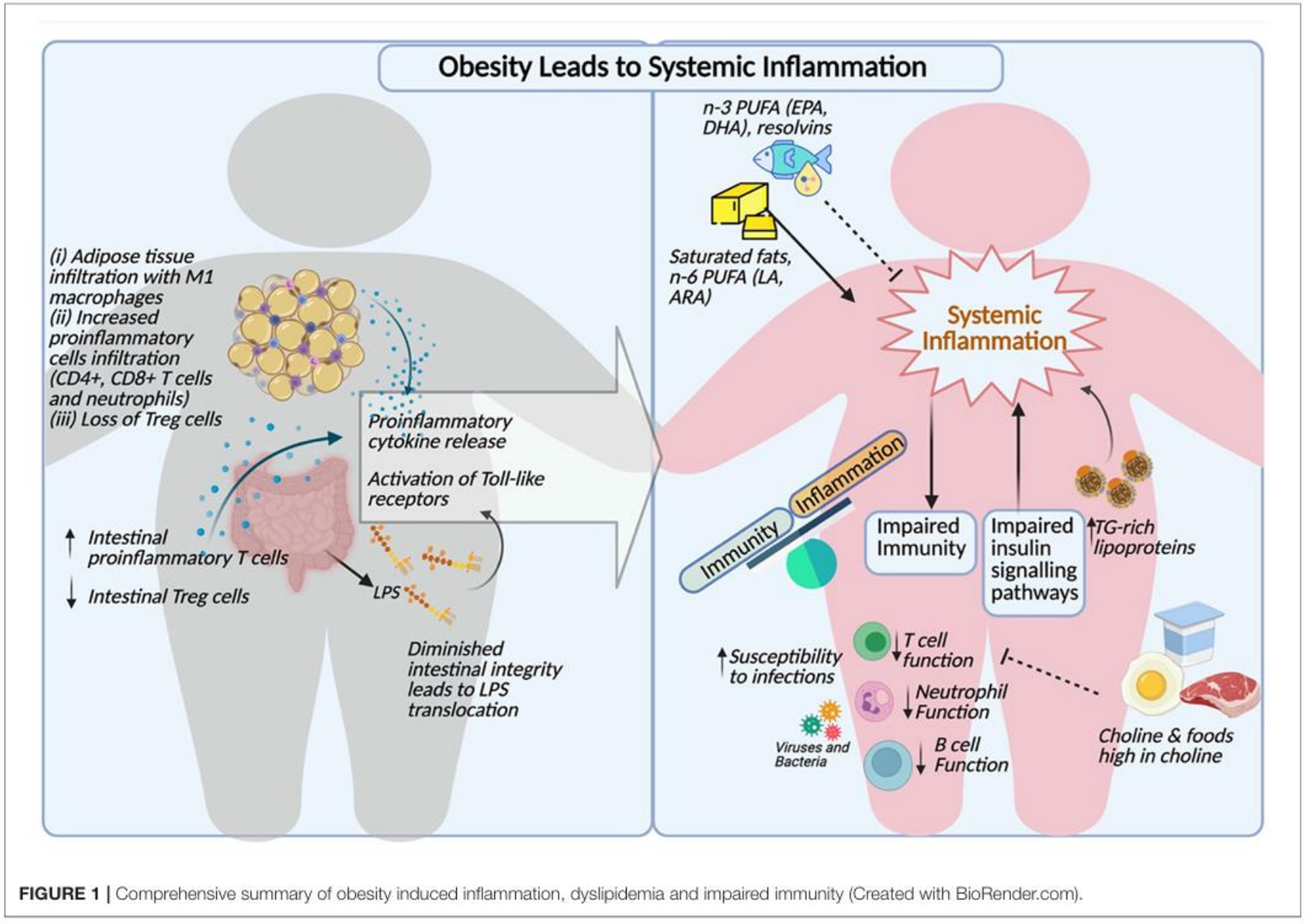
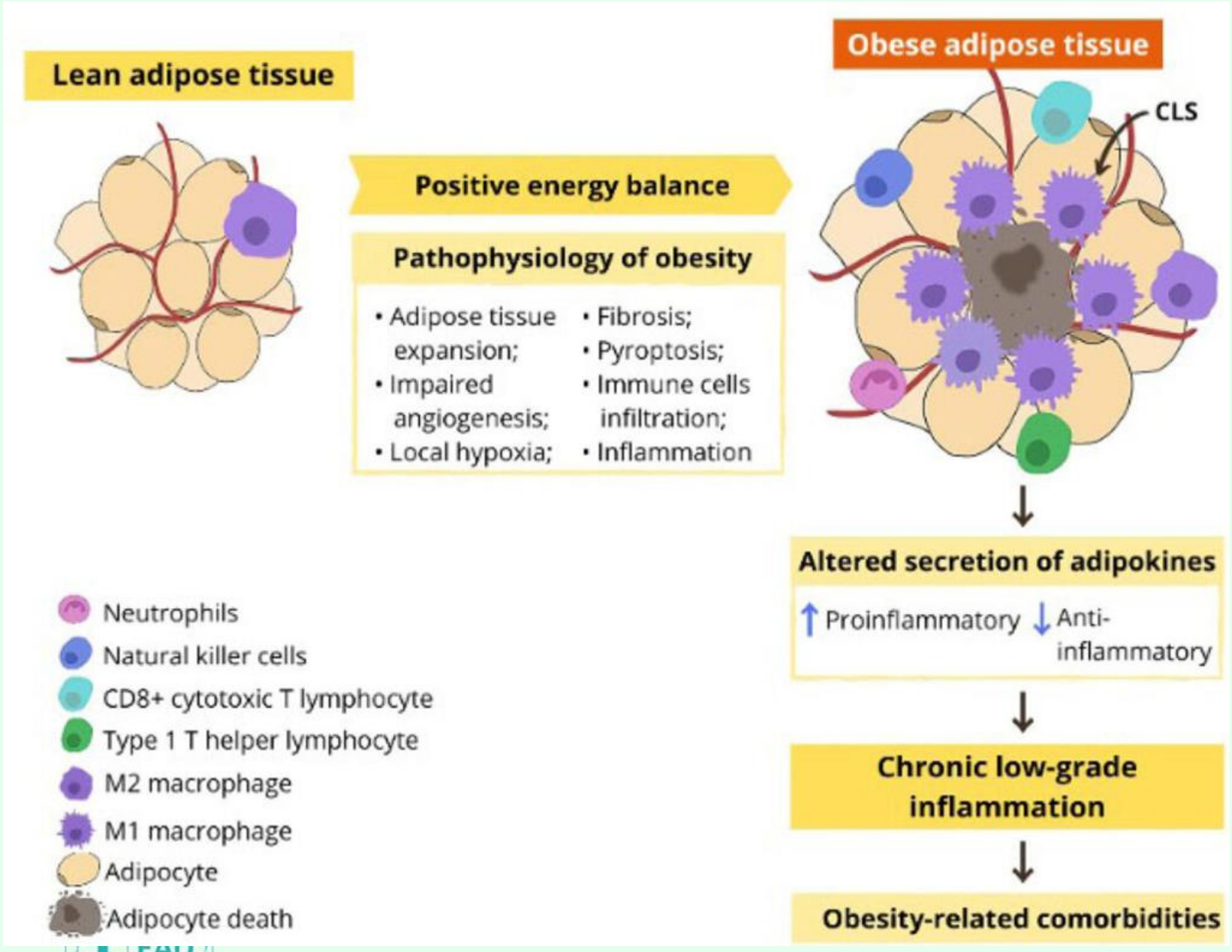


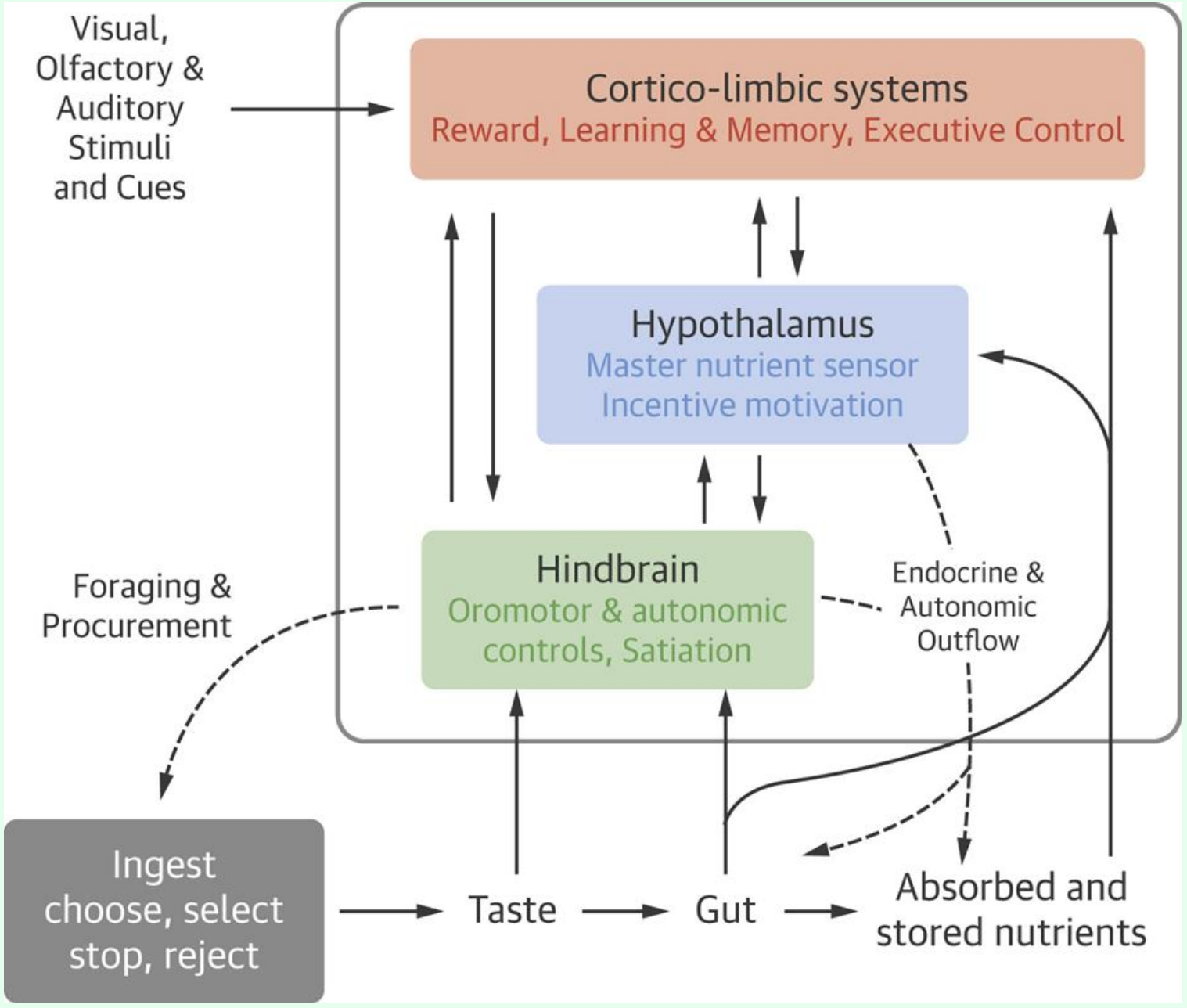
FIGURE 1 | Comprehensive summary of obesity induced inflammation, dyslipidemia and impaired immunity (Created with BioRender.com).



FISIOPATOLOGIA: OBESIDADE E INFLAMAÇÃO

Nature Review
https://doi.org/10.1038/s41574-019-0176-8

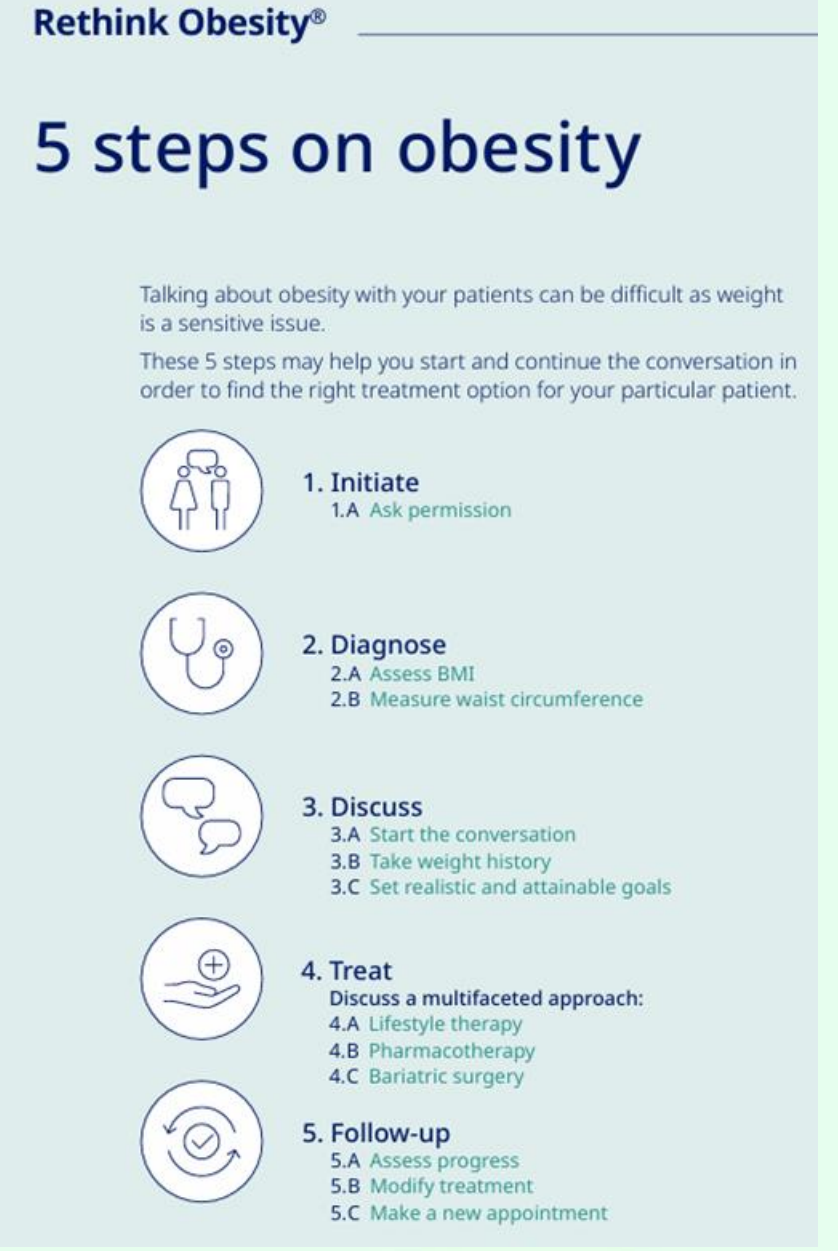
OBESIDADE E MECANISMOS NEUROENDÓCRINOS



Nature Review
https://doi.org/10.1038/s41574-019-0176-8

OBESIDADE: PENSANDO NO TRATAMENTO.....

"Following weight loss, endocrine adaptations lead to increased appetite and decreased satiety leading to persistent increase in hunger, harder resistance in continued weight loss and final weight regain."[1]



Rethink Obesity®

5 steps on obesity

Talking about obesity with your patients can be difficult as weight is a sensitive issue.

These 5 steps may help you start and continue the conversation in order to find the right treatment option for your particular patient.

1. Initiate
   - 1.A Ask permission

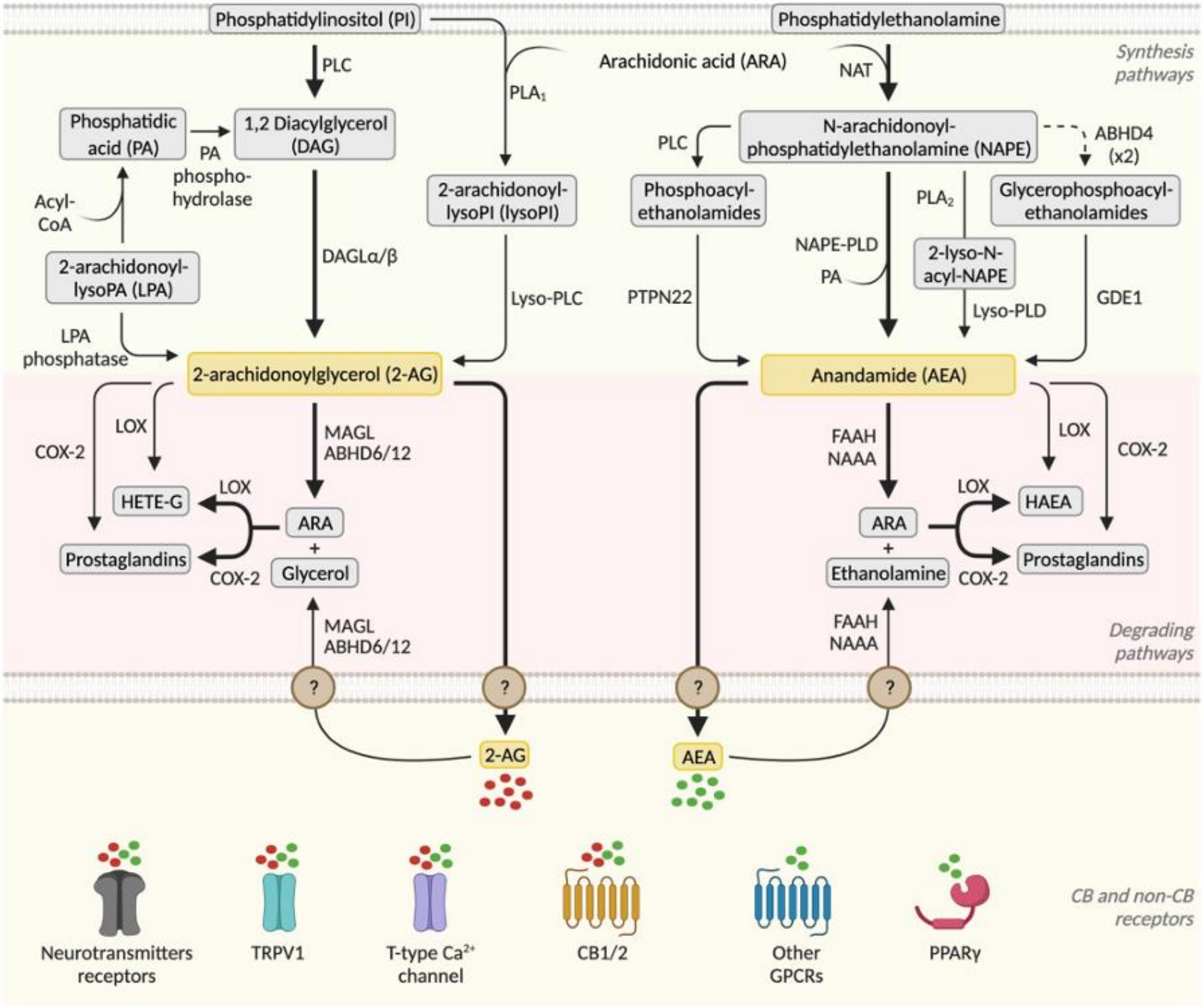
2. Diagnose
   - 2.A Assess BMI
   - 2.B Measure waist circumference

3. Discuss
   - 3.A Start the conversation
   - 3.B Take weight history
   - 3.C Set realistic and attainable goals

4. Treat
   Discuss a multifaceted approach:
   - 4.A Lifestyle therapy
   - 4.B Pharmacotherapy
   - 4.C Bariatric surgery

5. Follow-up
   - 5.A Assess progress
   - 5.B Modify treatment
   - 5.C Make a new appointment

CANABINOIDES E A PERDA DE PESO: QUAL É A RELAÇÃO???



The endocannabinoid system (ECS) is involved in various processes, including brain plasticity, learning and memory, neuronal development, nociception, inflammation, appetite regulation, digestion, metabolism, energy balance, motility, and regulation of stress and emotions

HOMEOSTASIS

CONBRACANN
2ª EDIÇÃO

Mol. Life Sci. 78, 7469–7490 (2021).
https://doi.org/10.1007/s00018-021-04002-6

Randomized Controlled Trial > JAMA. 2006 Feb 15;295(7):761-75. doi: 10.1001/jama.295.7.761.

Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial

F Xavier Pi-Sunyer [1], Louis J Aronne, Hassan M Heshmati, Jeanne Devin, Julio Rosenstock; RIO-North America Study Group

Randomized, double-blind, placebo controlled trial of 3045 obese (body mass index 30) or overweight (body mass index 27 and treated or untreated hypertension or dyslipidemia) adult patients at 64 US and 8 Canadian clinical research centers from August 2001 to April 2004

Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study

*Luc F Van Gaal, Aila M Rissanen, André J Scheen, Olivier Ziegler, Stephan Rössner, for the RIO-Europe Study Group**

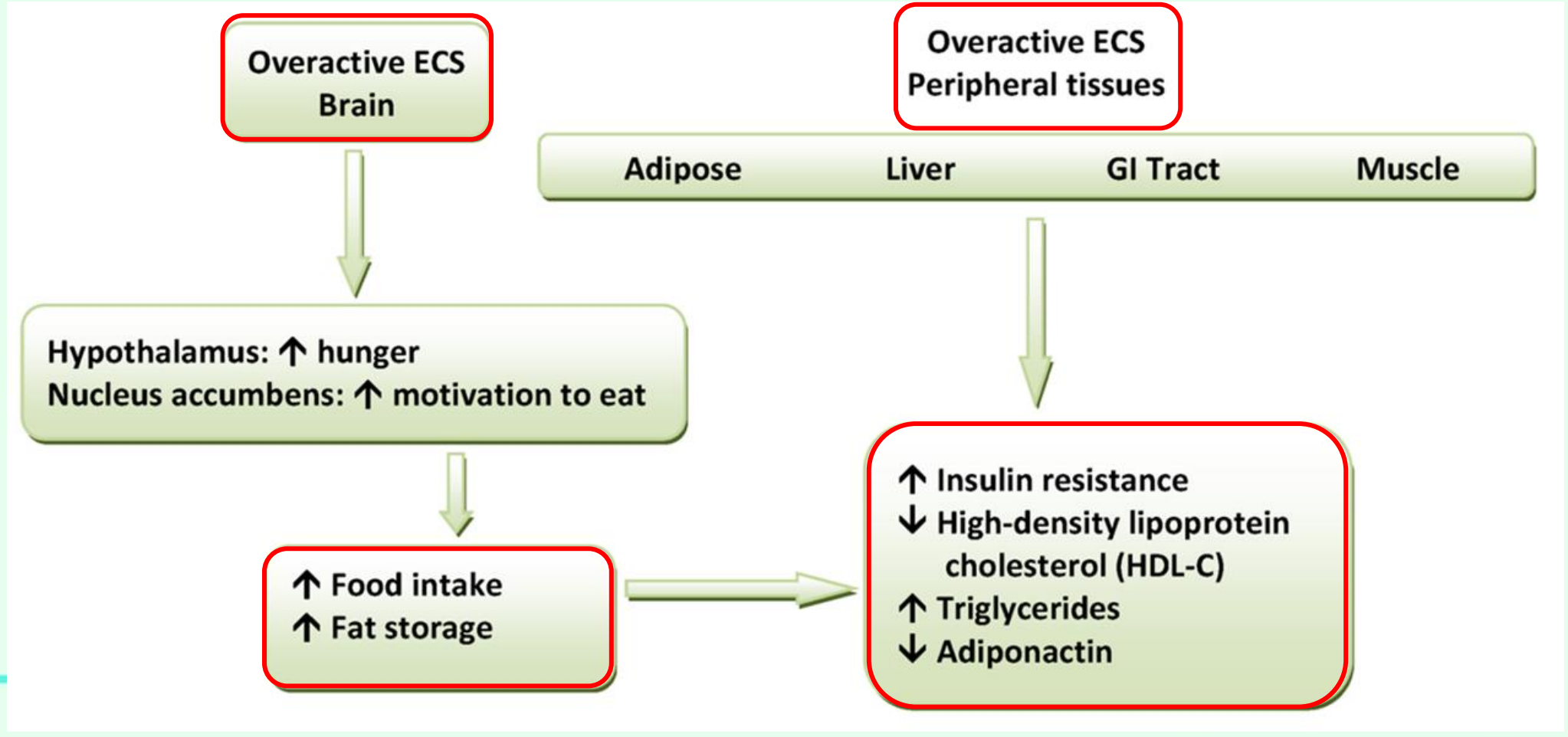
- Rimonabant (Acomplia), a selective cannabinoid-1 receptor blocker, may reduce body weight and improve cardiometabolic risk factors in patients who are overweight or obese

- To compare the efficacy and safety of rimonabant with placebo each in conjunction with diet and exercise for sustained changes in weight and cardiometabolic risk factors over 2 years

Randomized Controlled Trial > JAMA. 2006 Feb 15;295(7):761-75. doi: 10.1001/jama.295.7.761.

Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial

F Xavier Pi-Sunyer [1], Louis J Aronne, Hassan M Heshmati, Jeanne Devin, Julio Rosenstock; RIO-North America Study Group

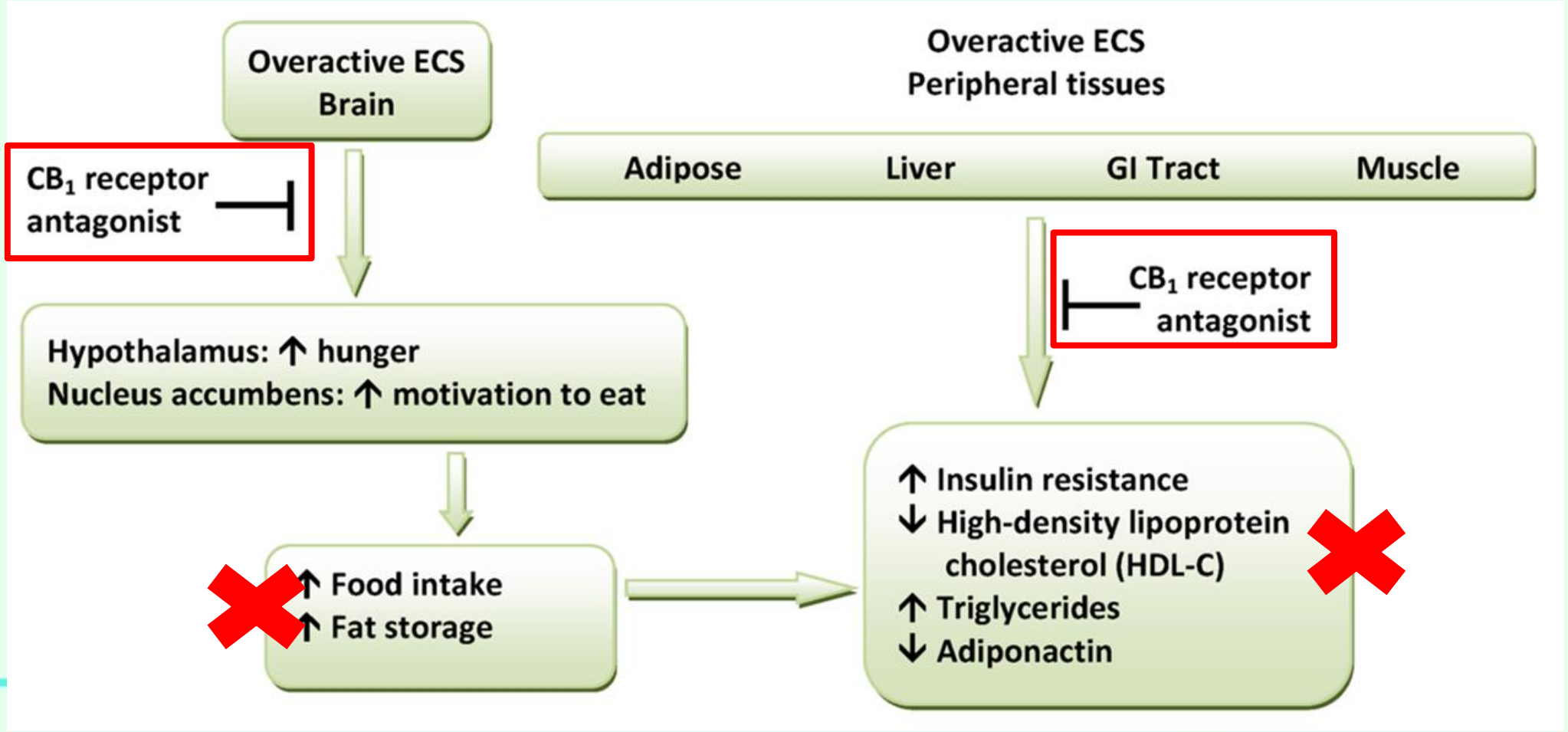


EAD PLUS
Educação em Saúde

Randomized Controlled Trial > JAMA. 2006 Feb 15;295(7):761-75. doi: 10.1001/jama.295.7.761.

Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial

F Xavier Pi-Sunyer [1], Louis J Aronne, Hassan M Heshmati, Jeanne Devin, Julio Rosenstock; RIO-North America Study Group

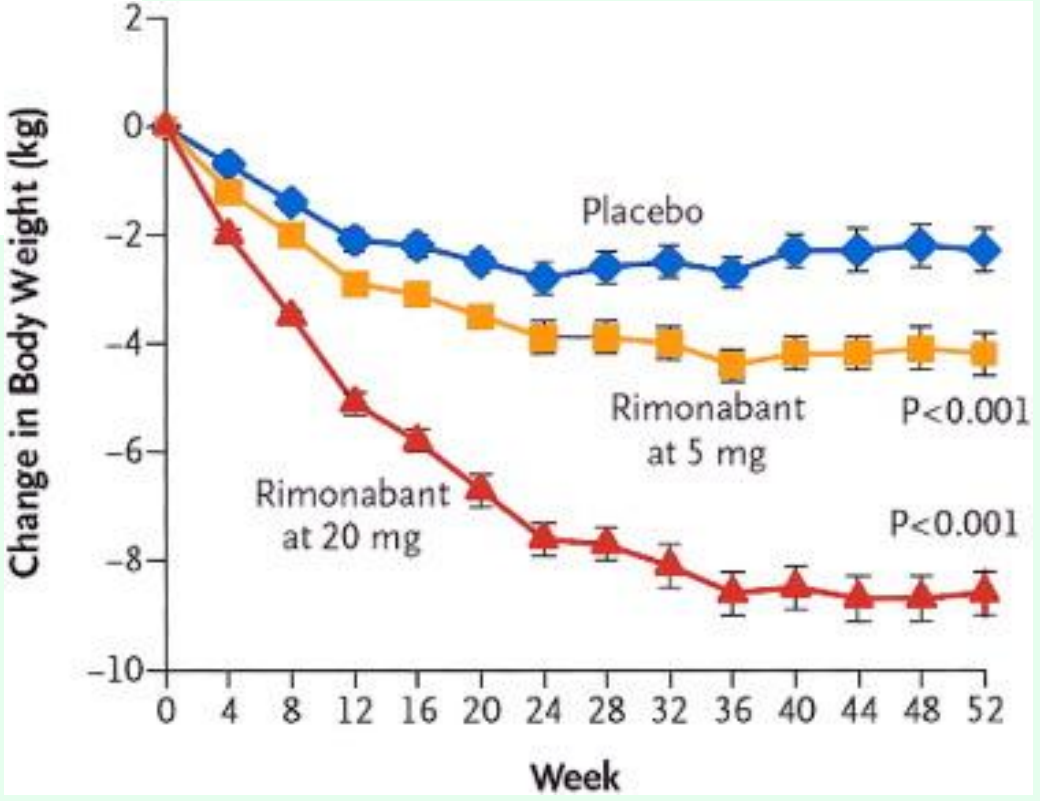


EAD PLUS
Educação em Saúde

Randomized Controlled Trial > JAMA. 2006 Feb 15;295(7):761-75. doi: 10.1001/jama.295.7.761.

Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial

F Xavier Pi-Sunyer [1], Louis J Aronne, Hassan M Heshmati, Jeanne Devin, Julio Rosenstock; RIO-North America Study Group



Randomized Controlled Trial > JAMA. 2006 Feb 15;295(7):761-75. doi: 10.1001/jama.295.7.761.

Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial

F Xavier Pi-Sunyer [1], Louis J Aronne, Hassan M Heshmati, Jeanne Devin, Julio Rosenstock;
RIO-North America Study Group

Besides the truly striking metabolic efficacy of rimonabant, reports appeared of a darker side to the weight-loss treatment: was it possible that the drug was producing not only the opposite of 'the munchies', but also the opposite of euphoria? Clinical trials reported nausea and dizziness, but also increased depression, anxiety and the specter of suicides

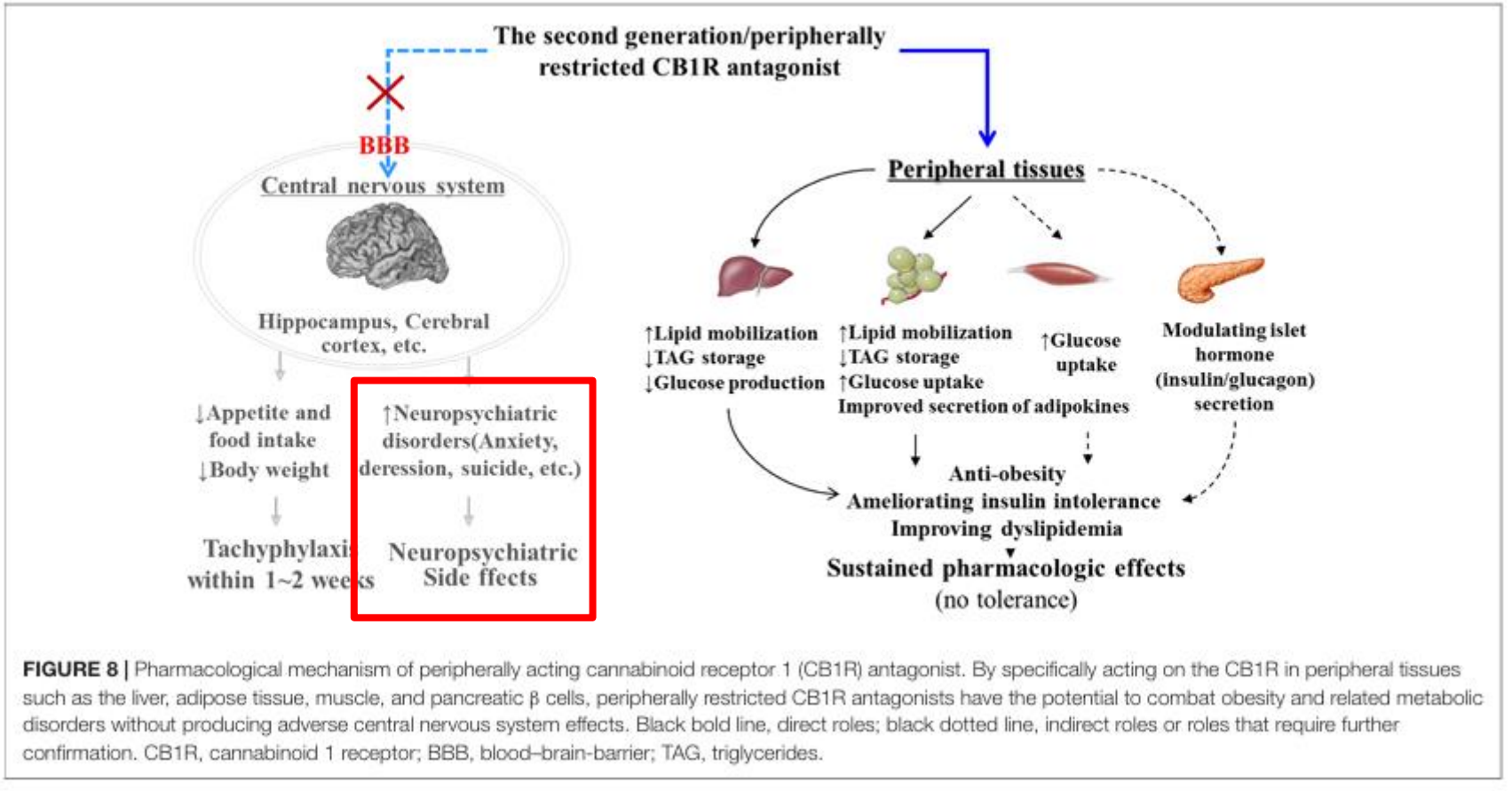
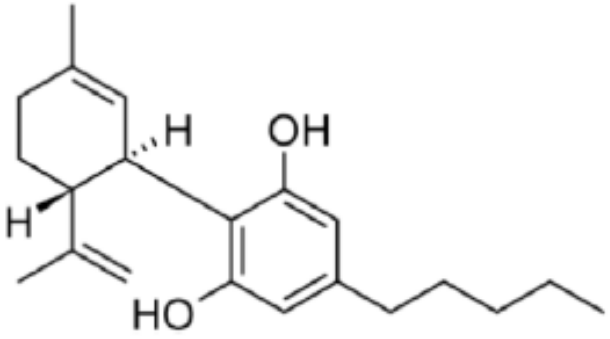
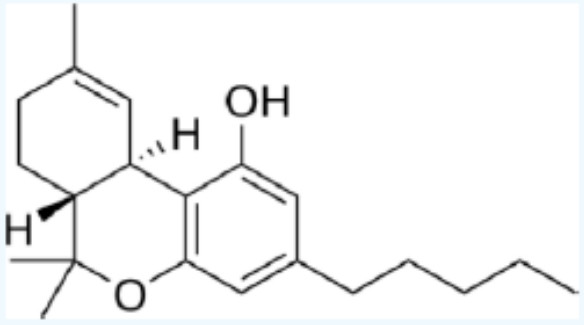
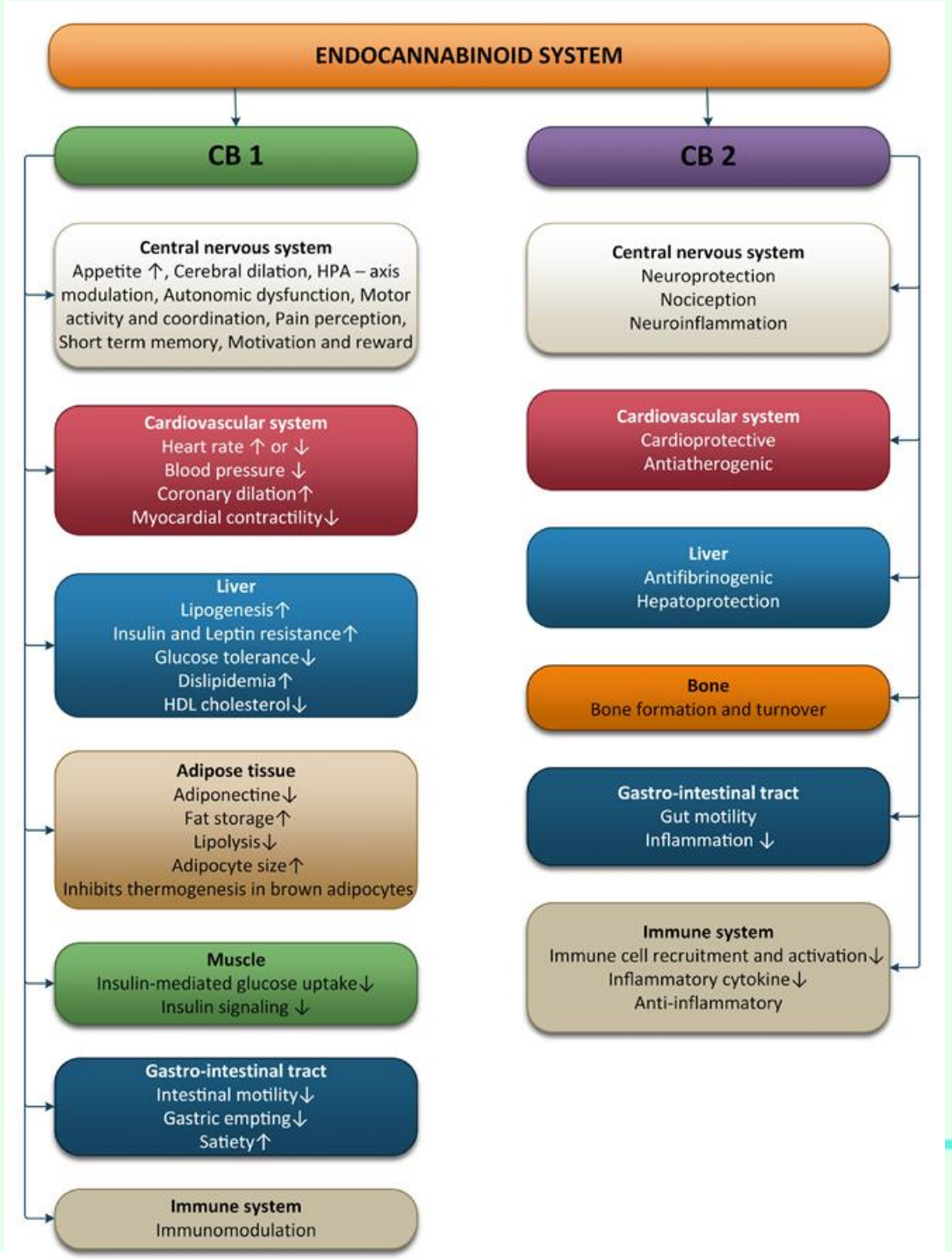
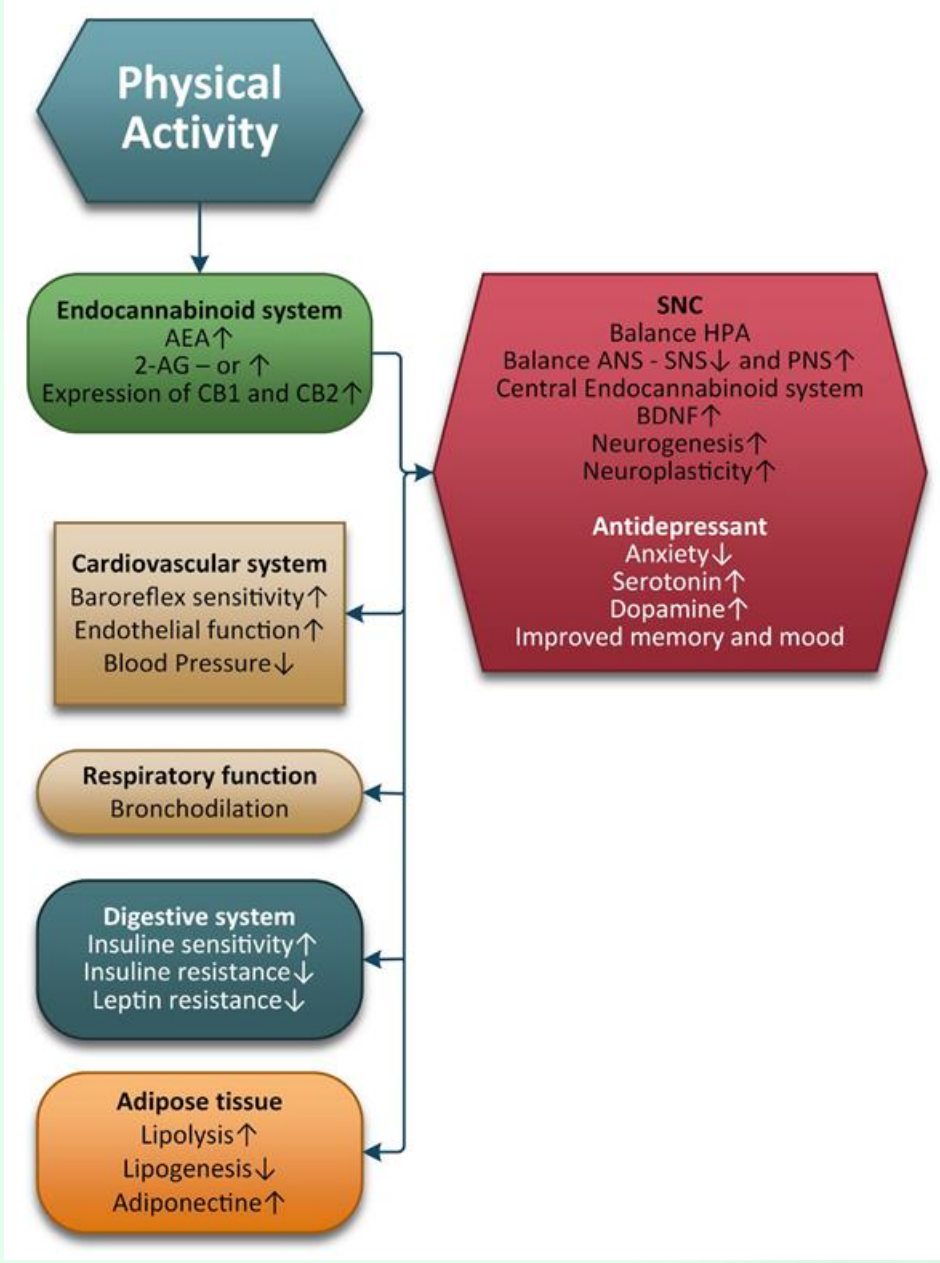


FIGURE 8 | Pharmacological mechanism of peripherally acting cannabinoid receptor 1 (CB1R) antagonist. By specifically acting on the CB1R in peripheral tissues such as the liver, adipose tissue, muscle, and pancreatic β cells, peripherally restricted CB1R antagonists have the potential to combat obesity and related metabolic disorders without producing adverse central nervous system effects. Black bold line, direct roles; black dotted line, indirect roles or roles that require further confirmation. CB1R, cannabinoid 1 receptor; BBB, blood–brain-barrier; TAG, triglycerides.

Table 1. Mechanisms of action of the most common phytocannabinoids.

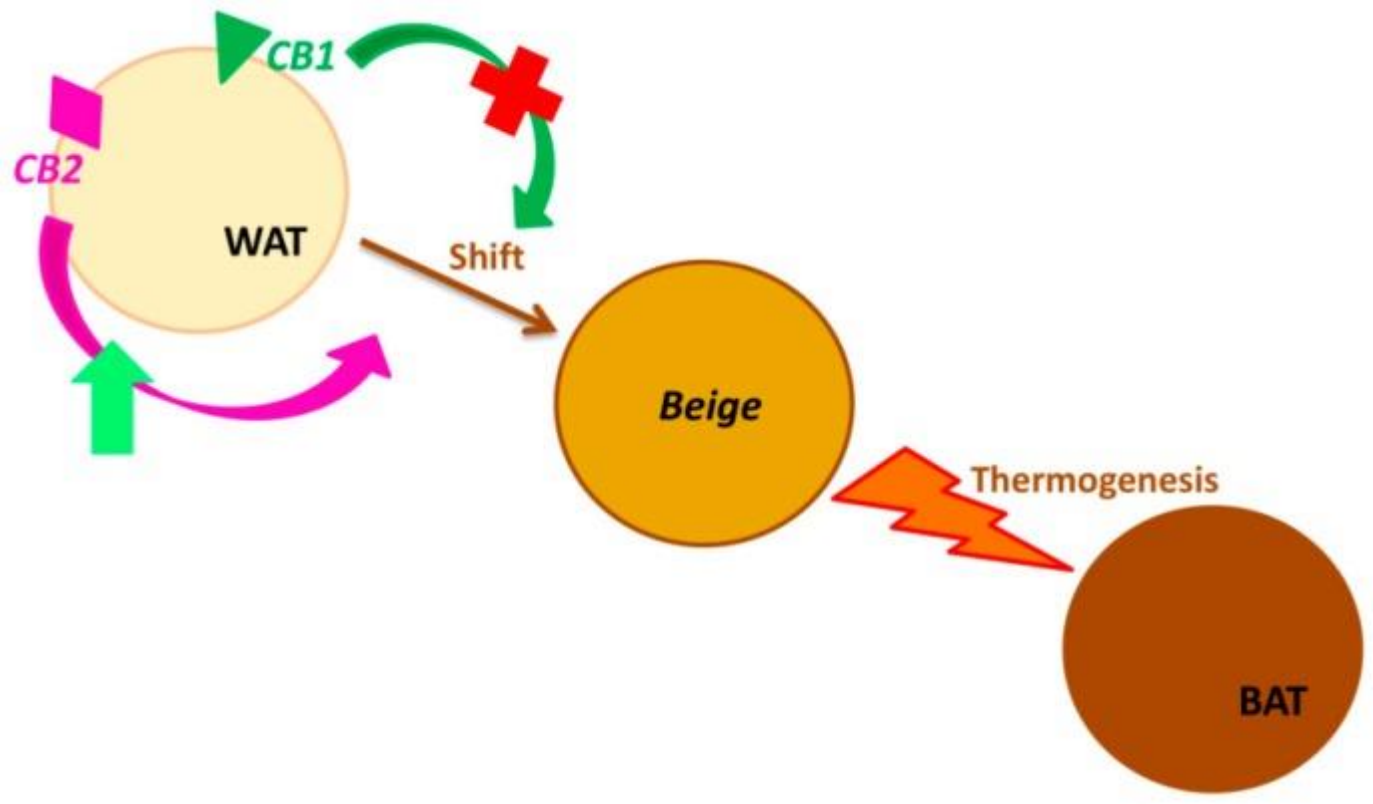
Phytocannabinoid	Molecular structure	Mechanism of action
CBD		• Non-psychoactive;[36–39] • CB_1 receptor negative allosteric modulator;[40–42] • CB_2 receptor partial agonist;[40–42] • AEA and 2-AG uptake inhibitor;[35] • GPR55 antagonist;[44,45] • TRPA1, TRPV1, TRPV2 agonist, TRPM8 antagonist;[48,49] • PPARγ weak/partial agonist;[53,54] • $5\text{-}HT_{1A}$ receptor weak agonist.[55]
Δ^9-THC		• Psychoactive;[33] • CB_1 receptor and CB_2 receptor partial agonist;[65,66] • GPR18, PPARγ, PPARα agonist;[67–69] • TRPV2, TRPV3, TRPA1, and TRPV4 agonist.[70]

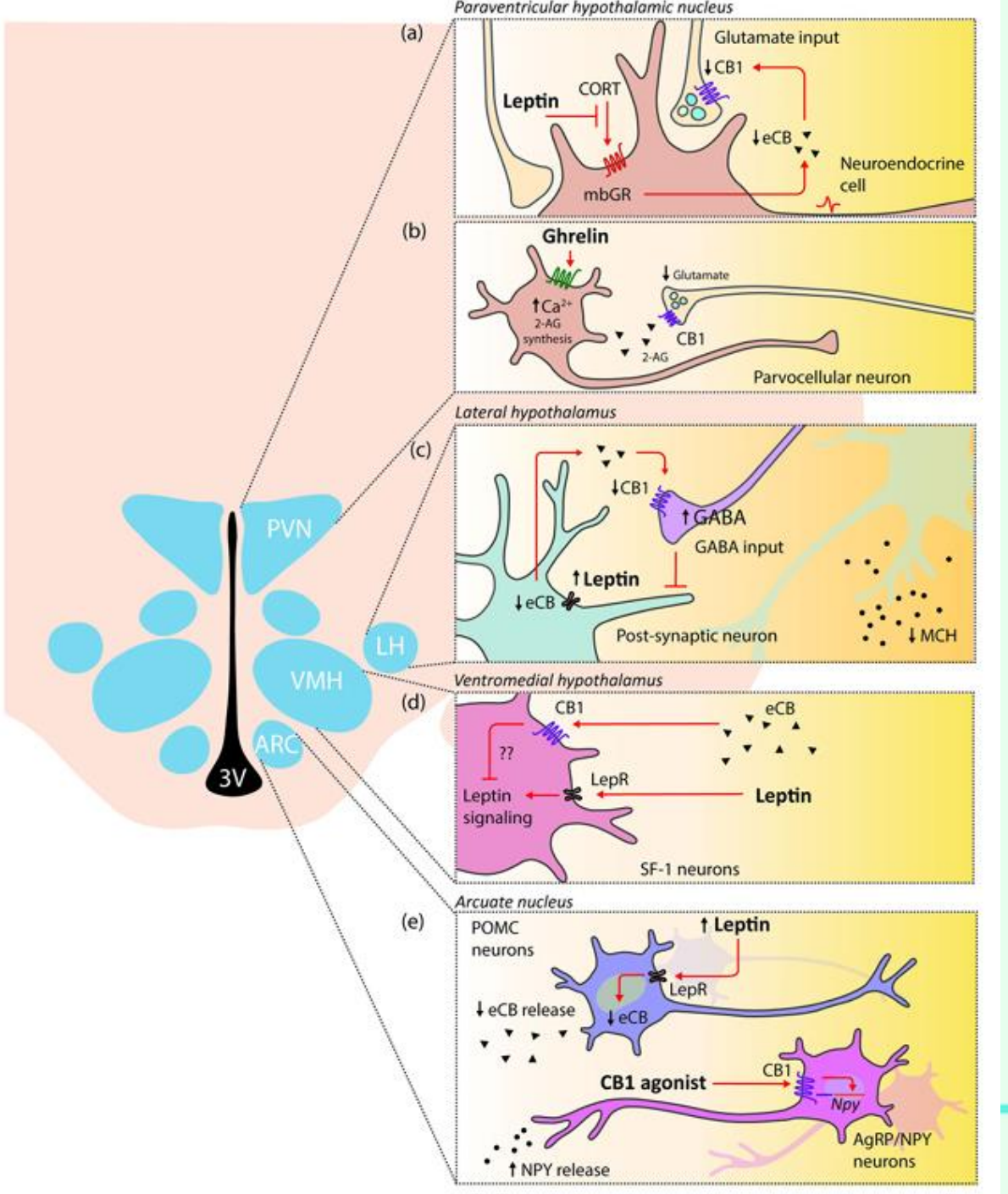




Int. J. Mol. Sci. 2023, 24(3), 1989; https://doi.org/10.3390/ijms24031989

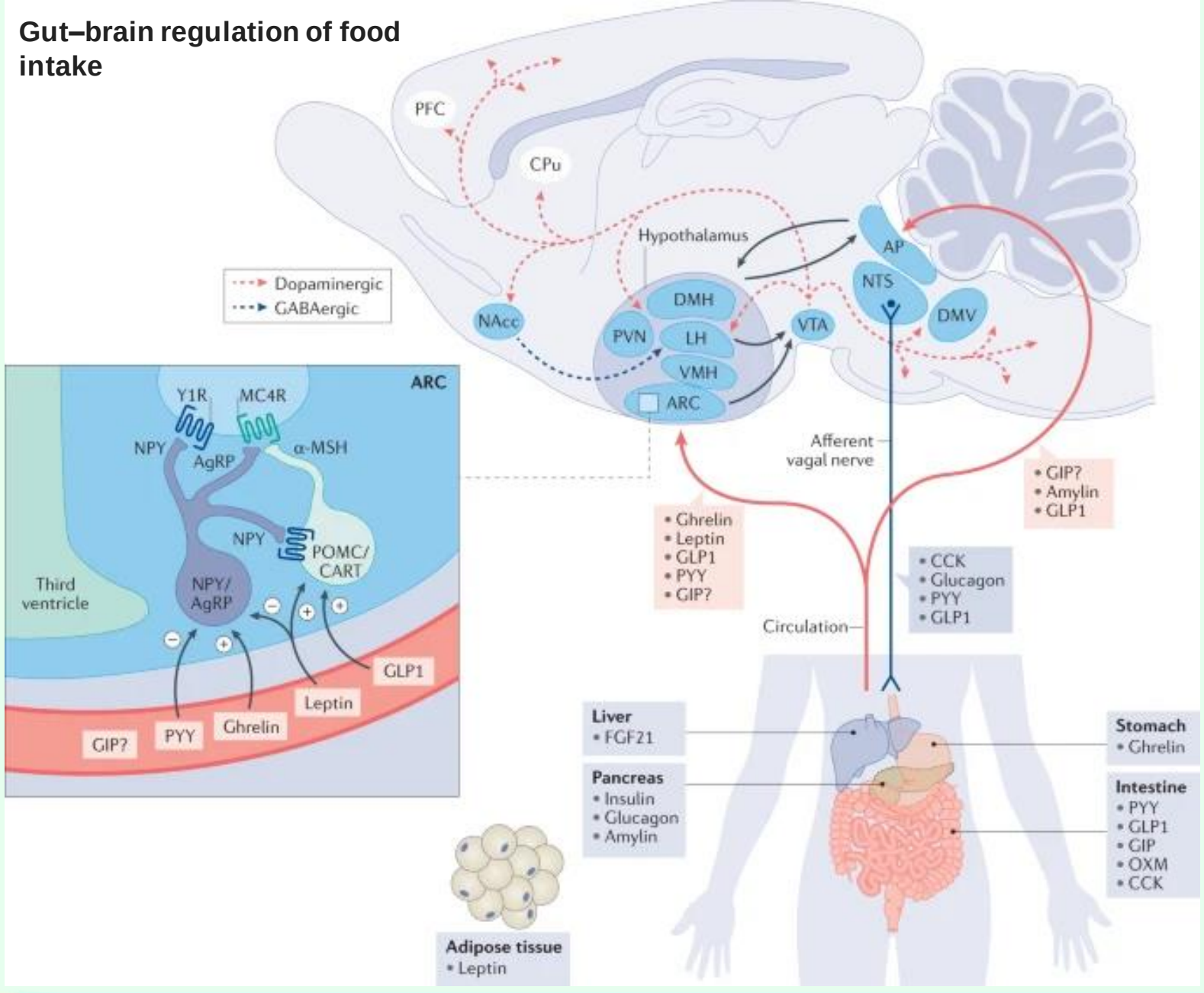
Cannabinoid receptors (CB1 and CB2) in Browning. (Browning is the process by which the white adipose tissue's physiology and morphology switch from white (WAT) towards brown phenotype (BAT), through the intermediate beige phenotype. CB2 receptor stimulation enhances this transformation, triggering the thermogenesis. Analogously, the blockade of CB1 receptor induces the same adipocyte's phenotype change).





Interactions of leptin and ghrelin with the endocannabinoid system (ECS) in hypothalamic neurons

Gut–brain regulation of food intake



Peripheral hormones integrate in central control of homeostatic and hedonic eating behaviour

D9-Tetrahydrocannabivarin (THCV) is a neutral CB1 antagonist producing hypophagia and body weight reduction in lean mice

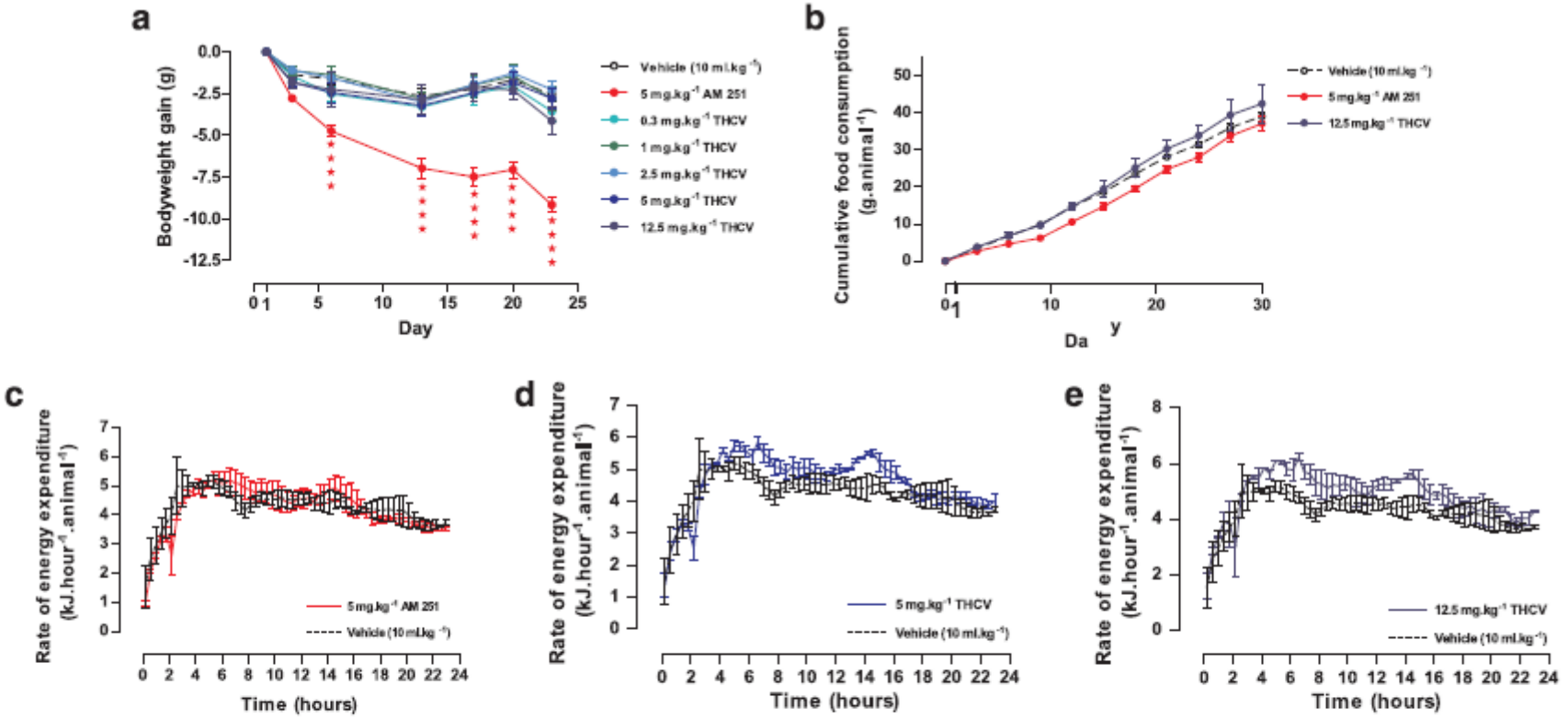


Figure 1. Effect of THCV on body weight gain, cumulative food intake and energy expenditure in DIO mice (study 1). (**a**) Body weight gain in the dose–response study, $n = 9$ mice per treatment. (**b**) Cumulative food intake in mice given AM251 or THCV (12.5 mg kg^{-1} p.o.), $n = 3$ groups of three mice per treatment (other dose levels of THCV excluded from graph for sake of clarity since identical to controls). However, all treatments were included in the one-way ANOVA statistical analysis. (**c**) Twenty-four-hour energy expenditure after 9 days treatment in DIO mice given AM251, (**d**) THCV (5 mg kg^{-1}) or (**e**) THCV (12.5 mg kg^{-1} p.o.) in study 1, $n = 3$ groups of three mice per treatment. ****$P < 0.0001$ as compared to vehicle treated animals.

THCV is a naturally occurring analog of THC. Unlike THC, which is psychoactive and an agonist at the CB1 and CB2 receptors, THCV is a non-psychoactive, neutral CB1 antagonist / reverse agonist and may act as agonist or antagonist at the CB2 receptors depending on its dose

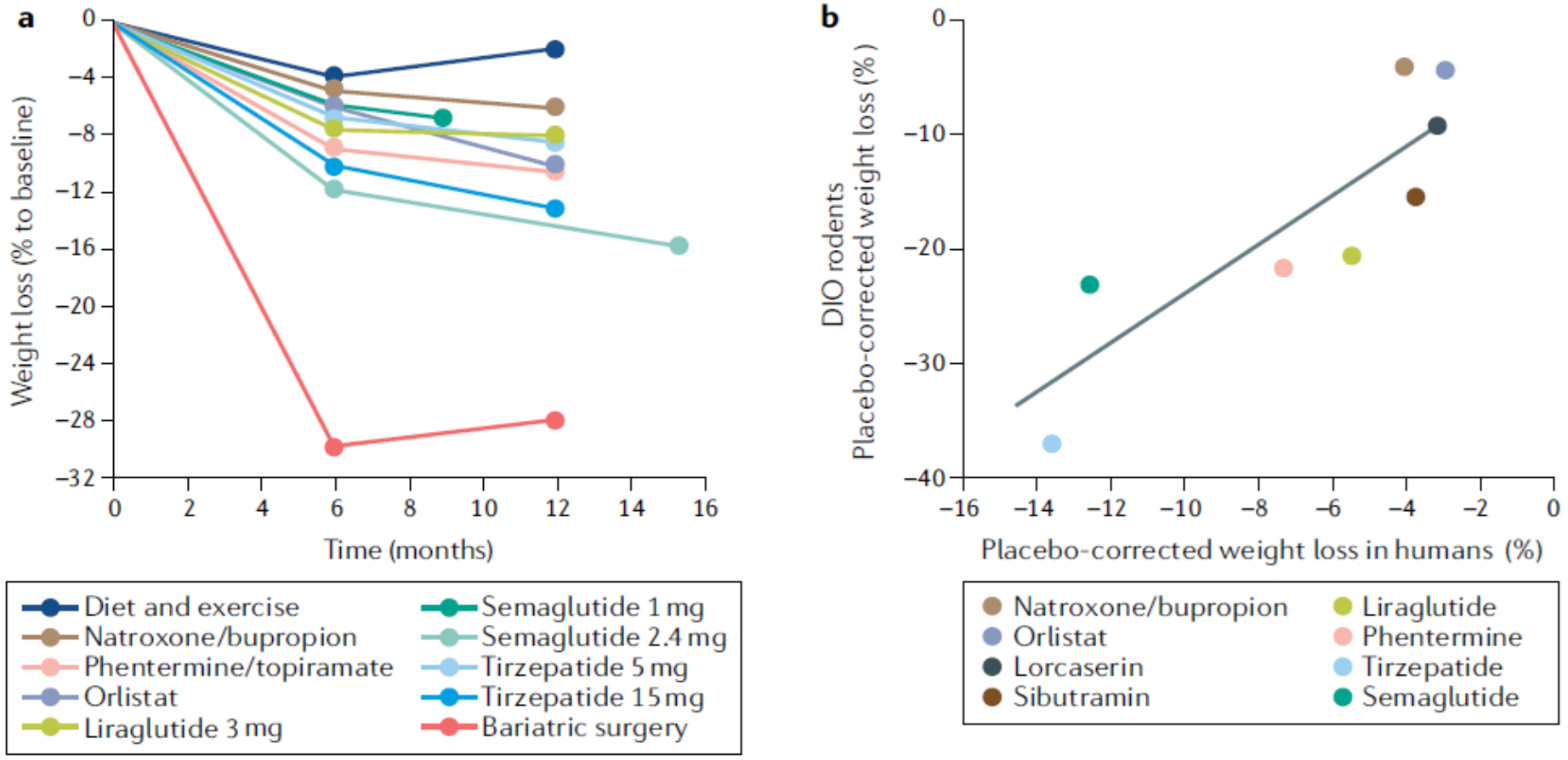


Fig. 3 | **Body weight loss by AOMs in humans and rodents.** Body weight loss achieved through lifestyle changes, currently approved anti-obesity medications (AOMs) and bariatric surgery (part **a**) and correlation of drug-induced body weight loss in rodents and humans (part **b**). Data in panel **a** refer to liraglutide 3 mg (REF.[176]), orlistat[289], naltrexone/bupropion[292], phentermine/topiramate[291], semaglutide 1 mg (REF.[125]), semaglutide 2.4 mg (REF.[38]) and tirzepatide (5 and 15 mg)[126]. Data in panel **b** refer to naltrexone/bupropion[39,295], orlistat[39,296], lorcaserin[39,297], sibutramine[154,298], liraglutide[39,299], phentermine[121,145], semaglutide[38,123] and tirzepatide[122,127].

Pure Δ^9-tetrahydrocannabivarin and a Cannabis sativa extract with high content in Δ^9-tetrahydrocannabivarin inhibit nitrite production in murine peritoneal macrophages

Barbara Romano [1], Ester Pagano [2], Pierangelo Orlando [3], Raffaele Capasso [2], Maria Grazia Cascio [4], Roger Pertwee [4], Vincenzo Di Marzo [5], Angelo A Izzo [2], Francesca Borrelli [6]

Article

Effect of THC, CBD, THCV, CBC and CBN Cannabinoids on β-Cells Exposed to High Glucose—High Lipids

Esmaeel Ghasemi Gojani, Bo Wang, Dong-Ping Li, Olga Kovalchuk and Igor Kovalchuk *

Cannabis sativa as a Treatment for Obesity: From Anti-Inflammatory Indirect Support to a Promising Metabolic Re-Establishment Target

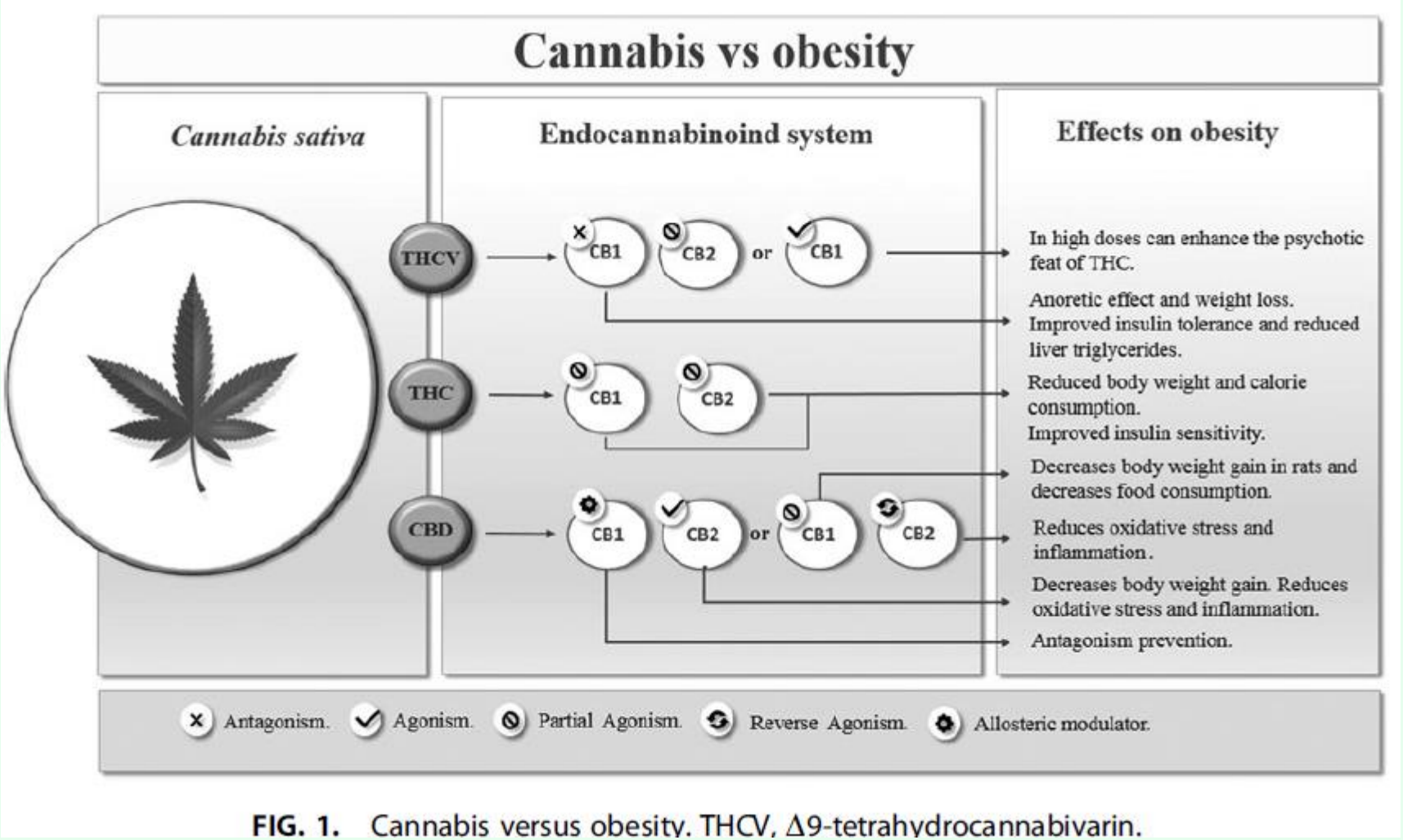


FIG. 1. Cannabis versus obesity. THCV, Δ9-tetrahydrocannabivarin.

Cells 2021, 10(12), 3396; https://doi.org/10.3390/cells10123396

Cannabis sativa as a Treatment for Obesity: From Anti-Inflammatory Indirect Support to a Promising Metabolic Re-Establishment Target

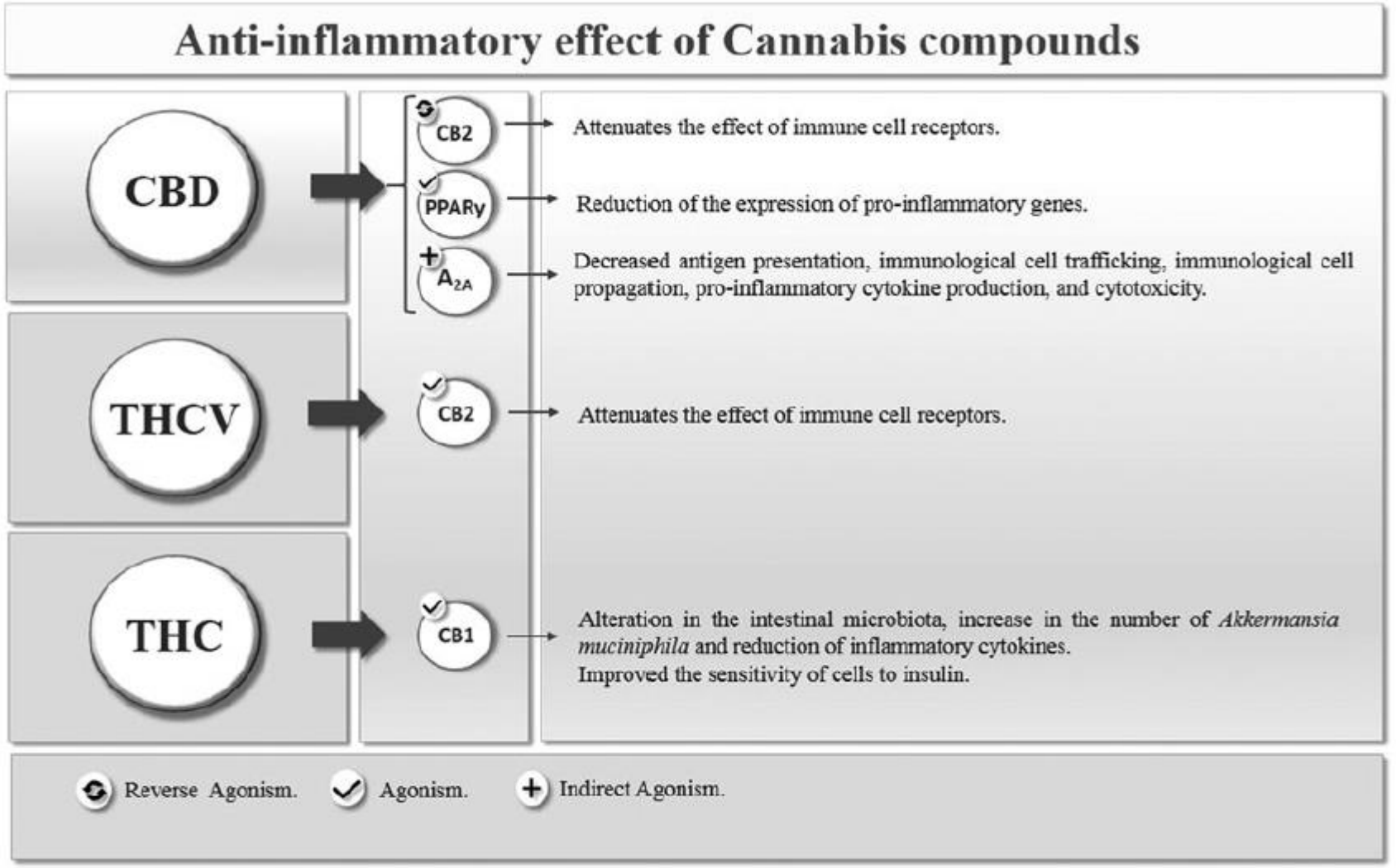


FIG. 2. Anti-inflammatory effect of cannabis compounds.

Cells 2021, 10(12), 3396; https://doi.org/10.3390/cells10123396

PÓS-GRADUAÇÃO EM
CANNABIS MEDICINAL

O maior programa de especialização
lato sensu de Medicina Endocanabinoide

- ✓ 100% online
- ✓ Reconhecido pelo MEC
- ✓ Professores renomados

EAD PLUS
Educação em Saúde

CONBRACANN

2ª EDIÇÃO

+55 (11) 91122-0533

atendimento@eadplus.com.br

ORGANIZAÇÃO E REALIZAÇÃO

EAD PLUS

Educação em Saúde