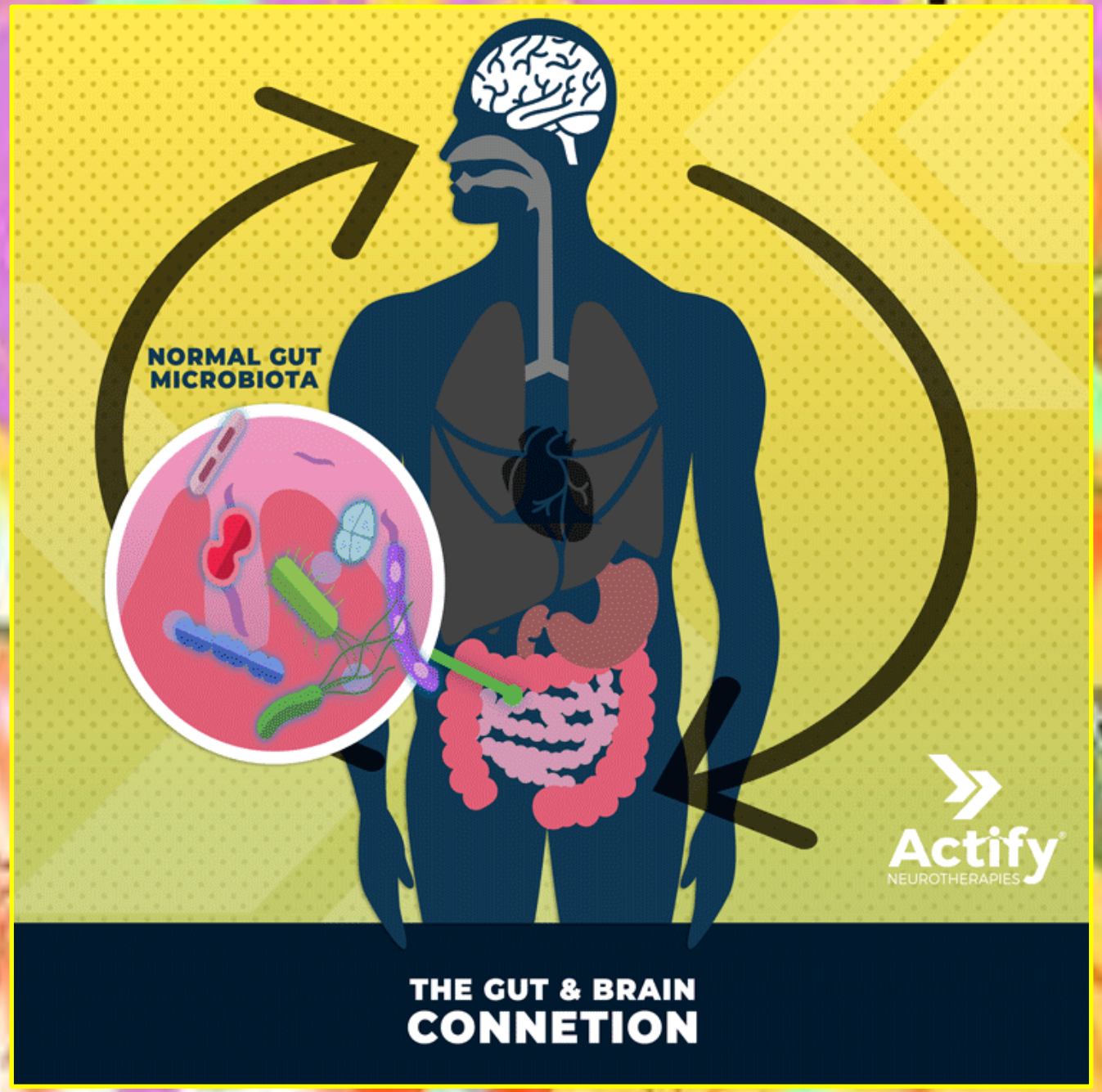
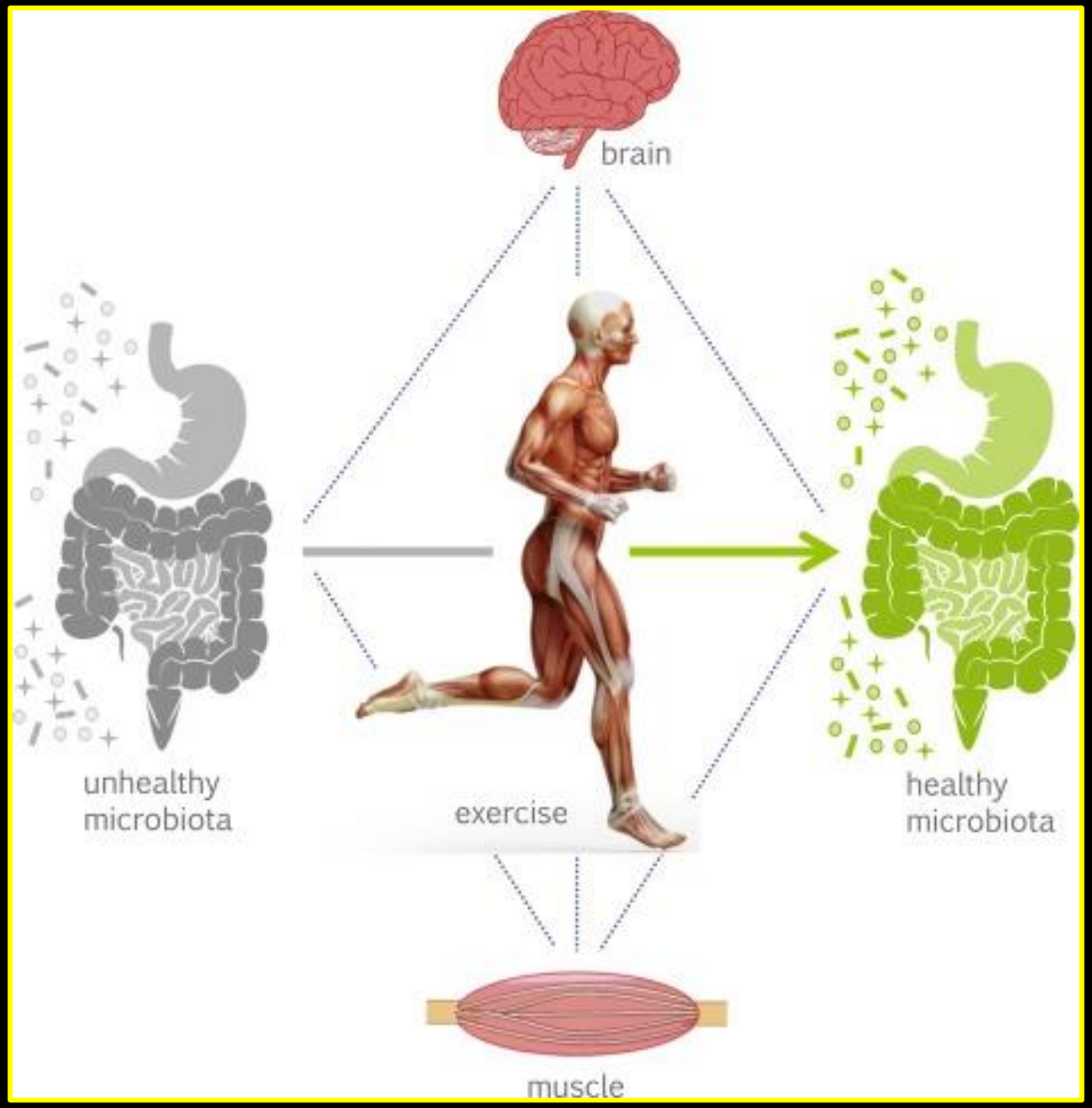
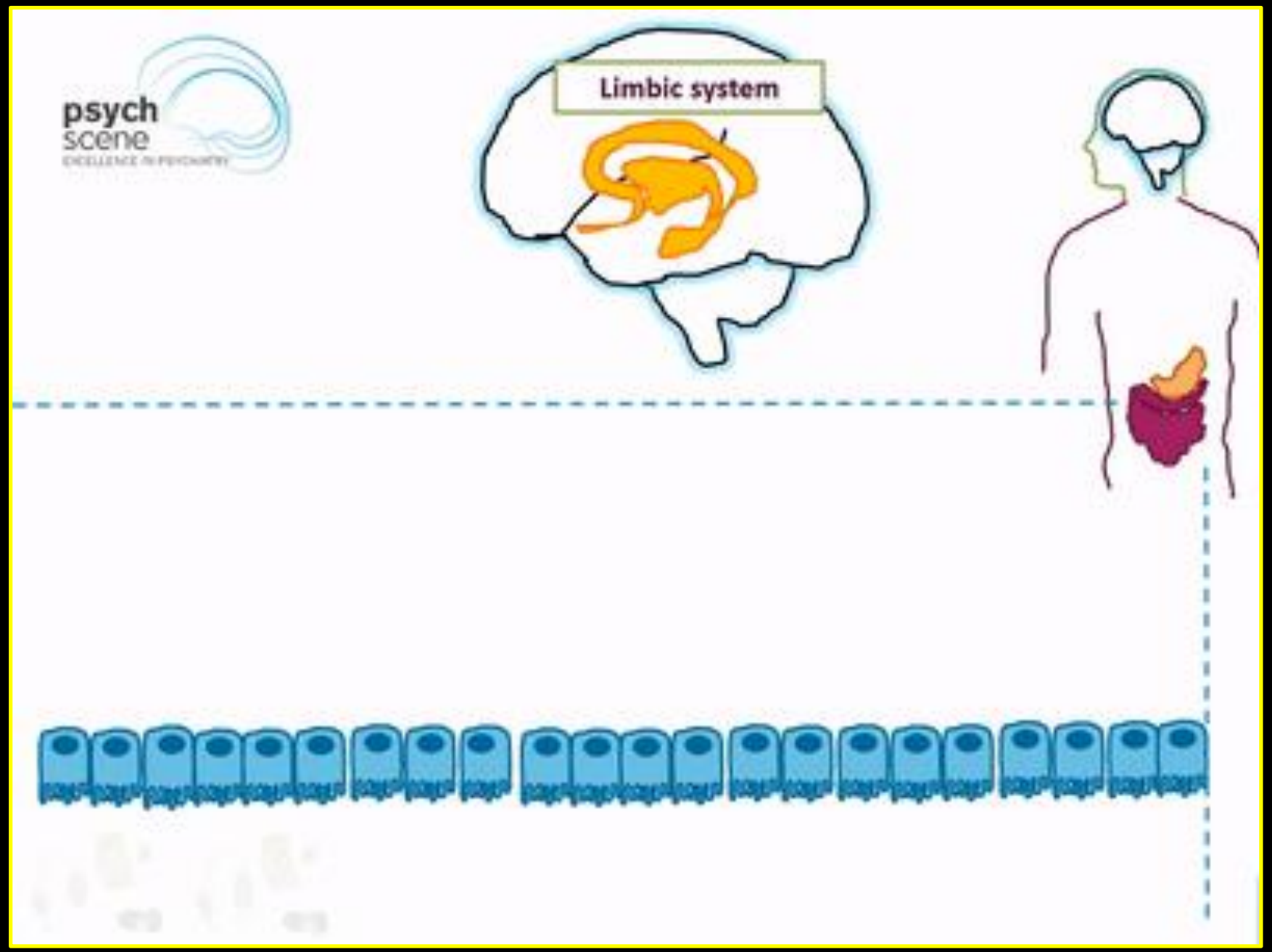
Eixo Intestino cérebro na saúde cognitiva



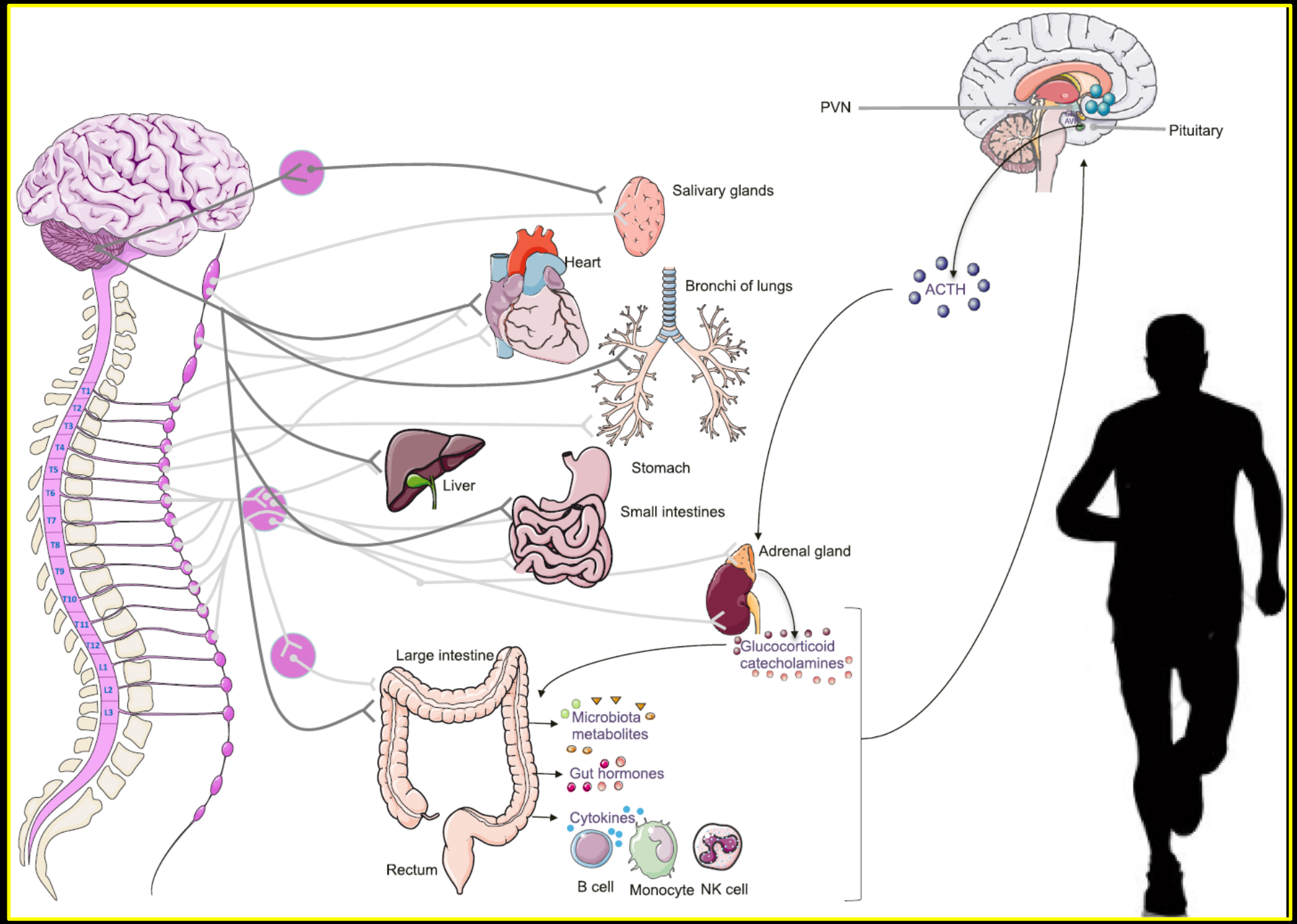
Prof. Dr. Bruno Zylbergeld
Microbiologista

O eixo intestino cérebro

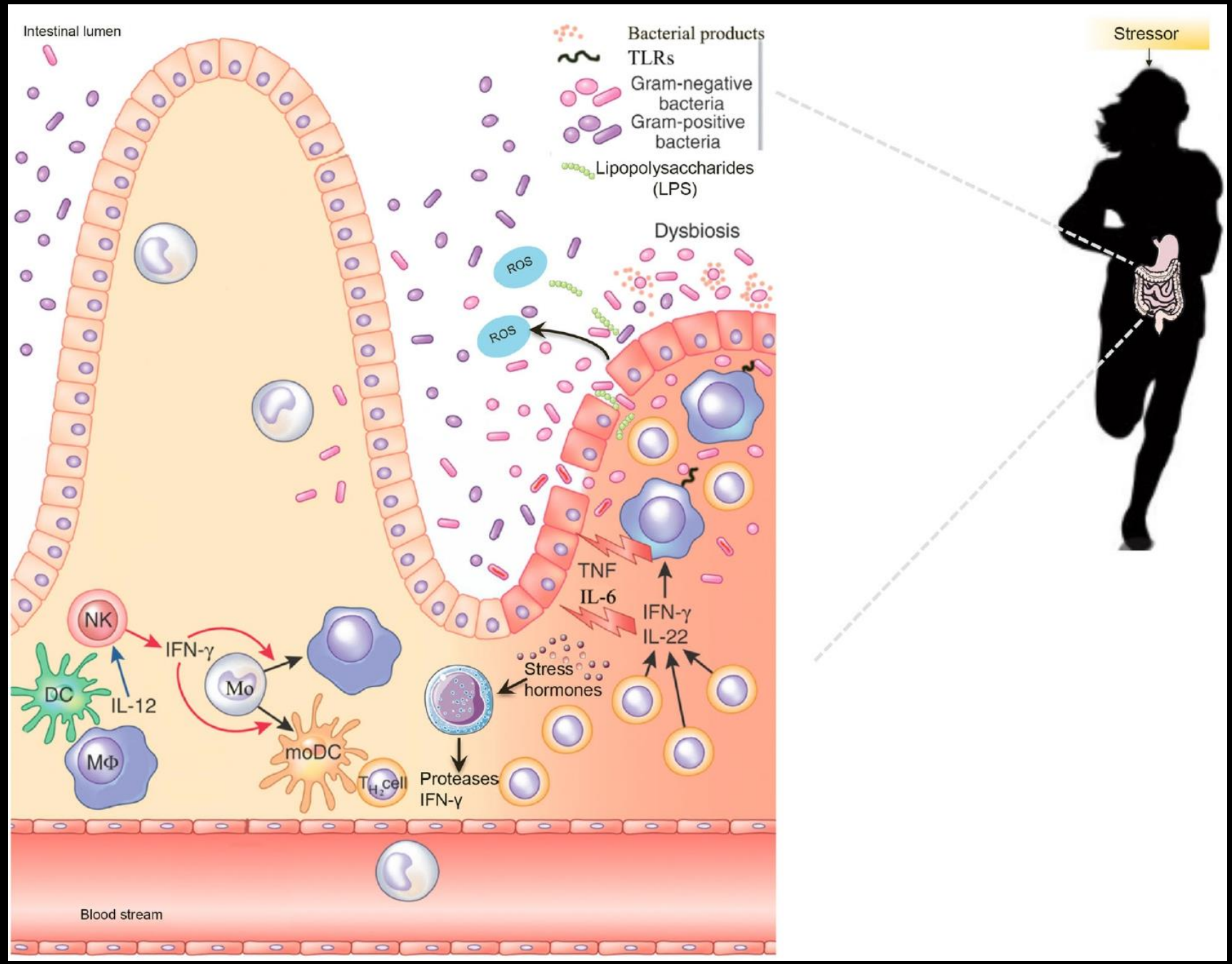


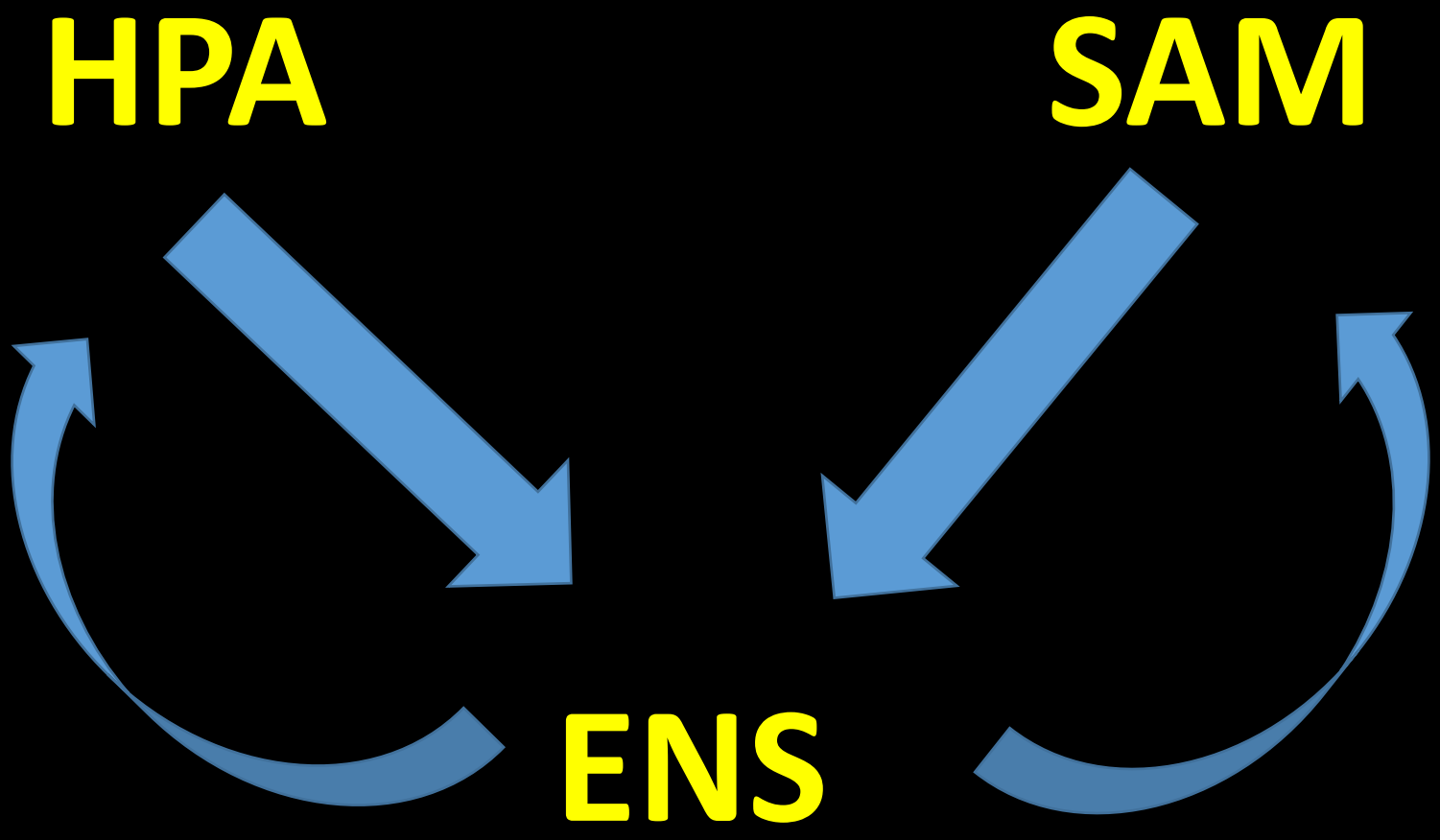

psych
scene
Limbic system

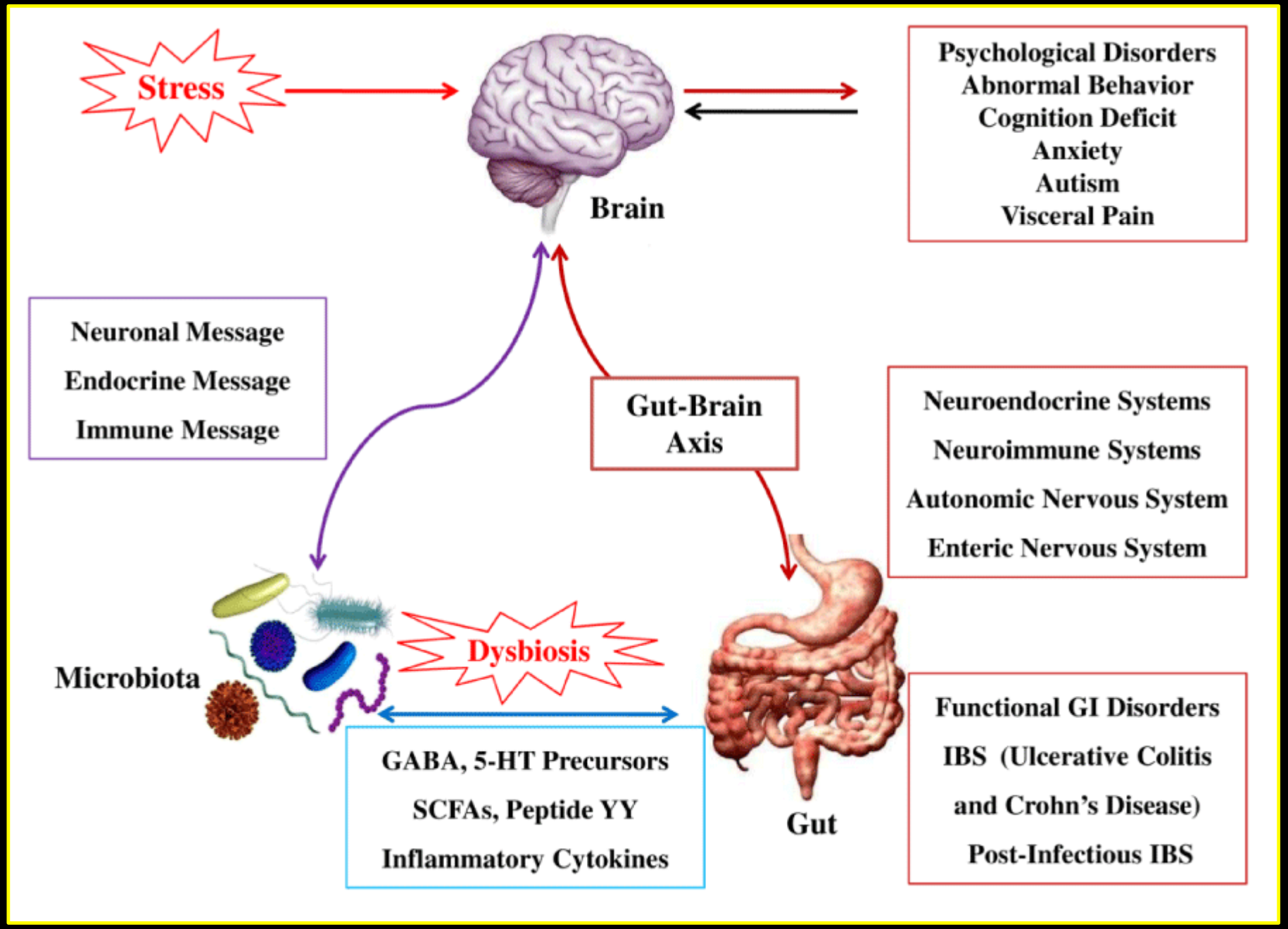
Via de mão dupla



Estresse causado por exercícios intensos e constantes



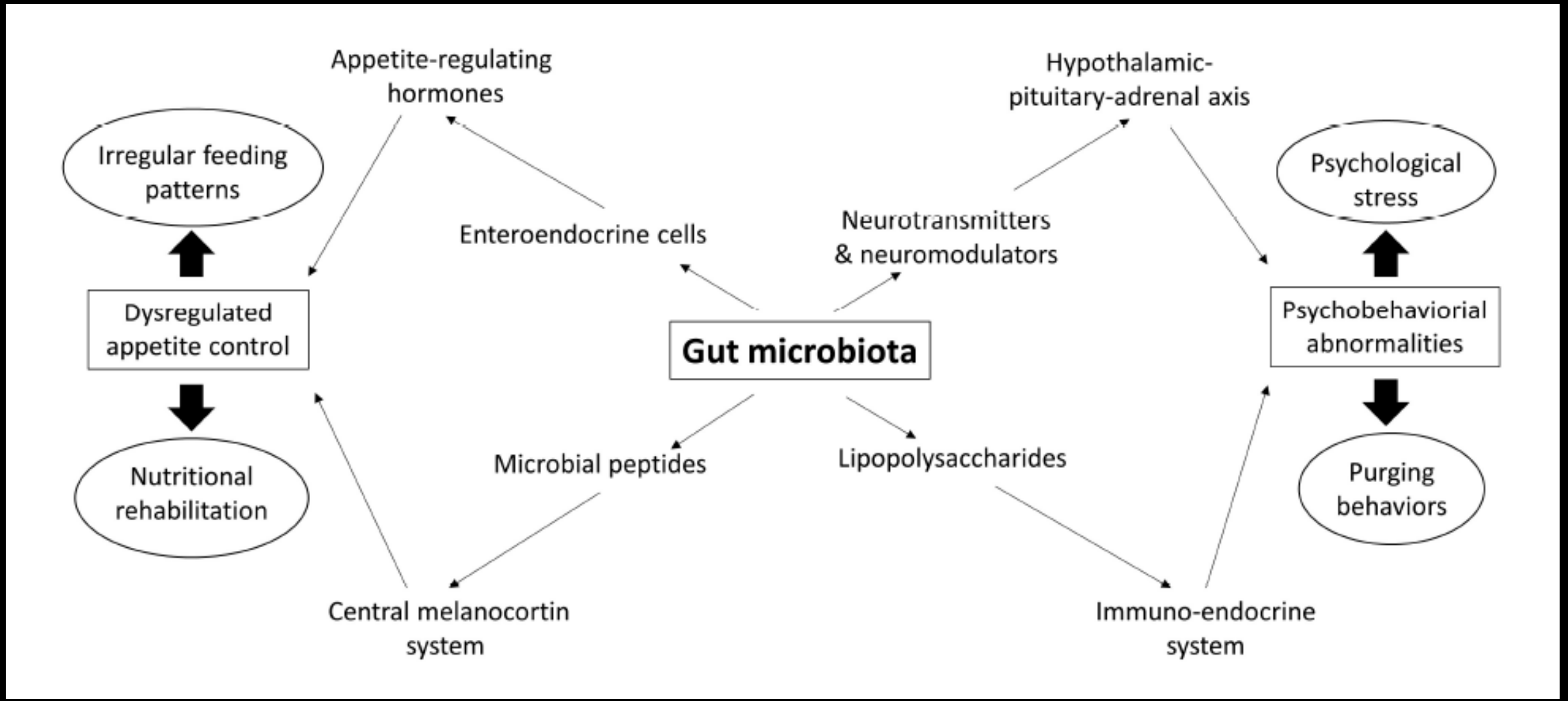

HPA
SAM
ENS


Stress
Brain
Psychological Disorders
Abnormal Behavior
Cognition Deficit
Anxiety
Autism
Visceral Pain
Neuronal Message
Endocrine Message
Immune Message
Gut-Brain Axis
Neuroendocrine Systems
Neuroimmune Systems
Autonomic Nervous System
Enteric Nervous System
Microbiota
Dysbiosis
GABA, 5-HT Precursors
SCFAs, Peptide YY
Inflammatory Cytokines
Gut
Functional GI Disorders
IBS (Ulcerative Colitis
and Crohn's Disease)
Post-Infectious IBS

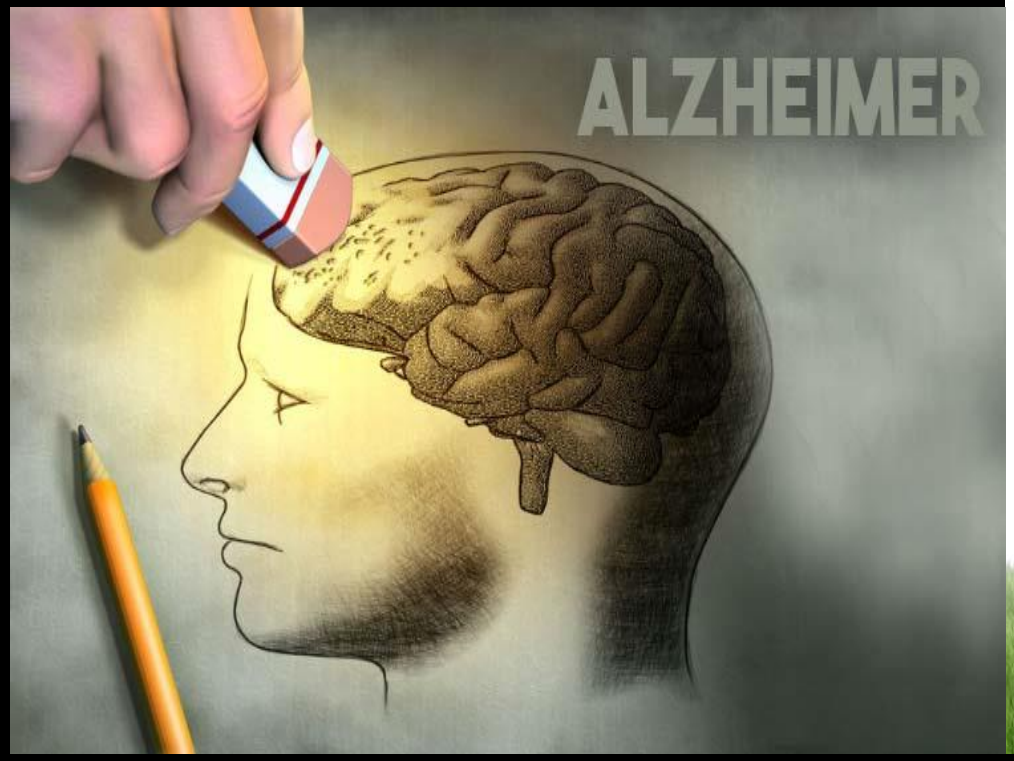
IBDs e IBSs

IBDs

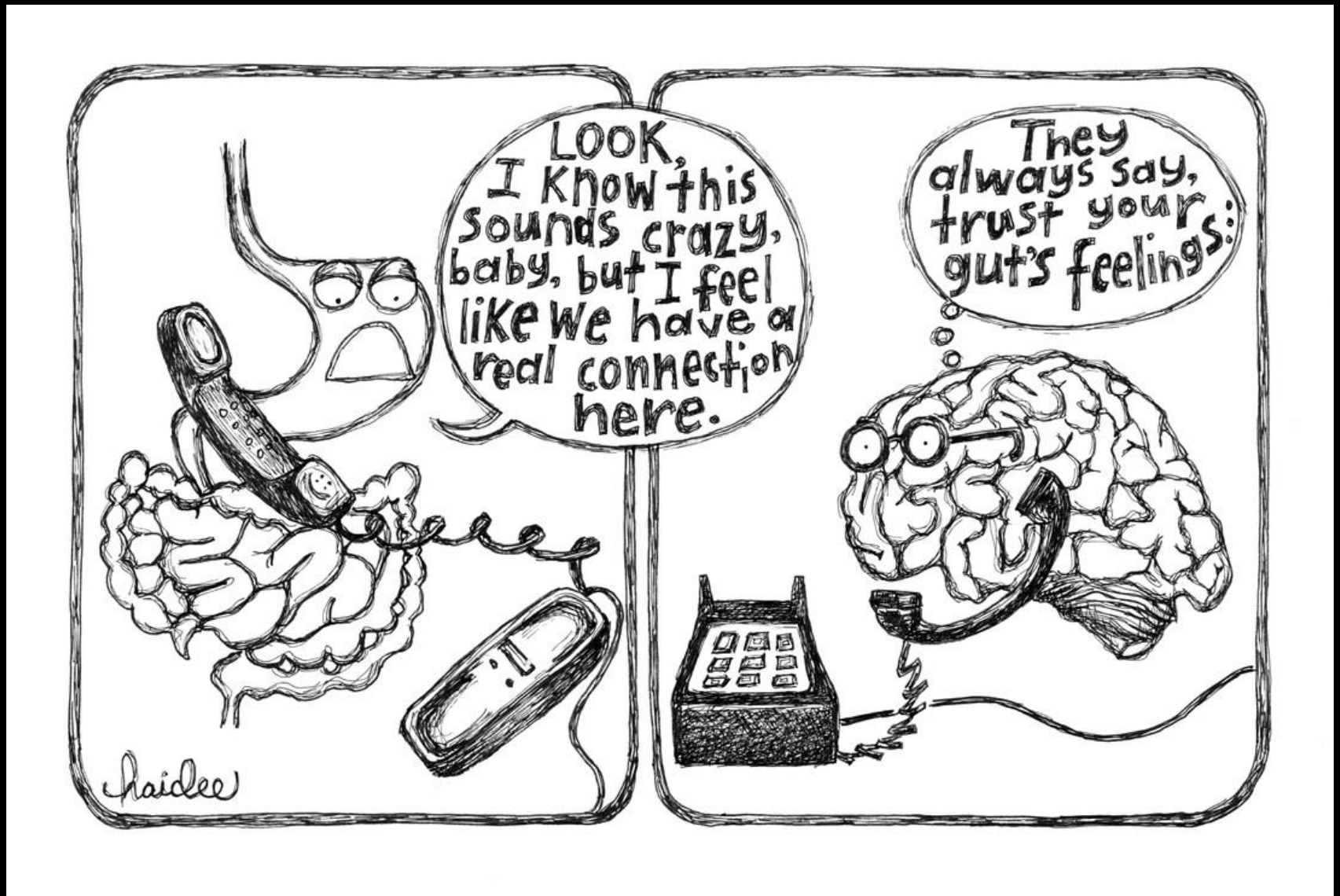
IBSs

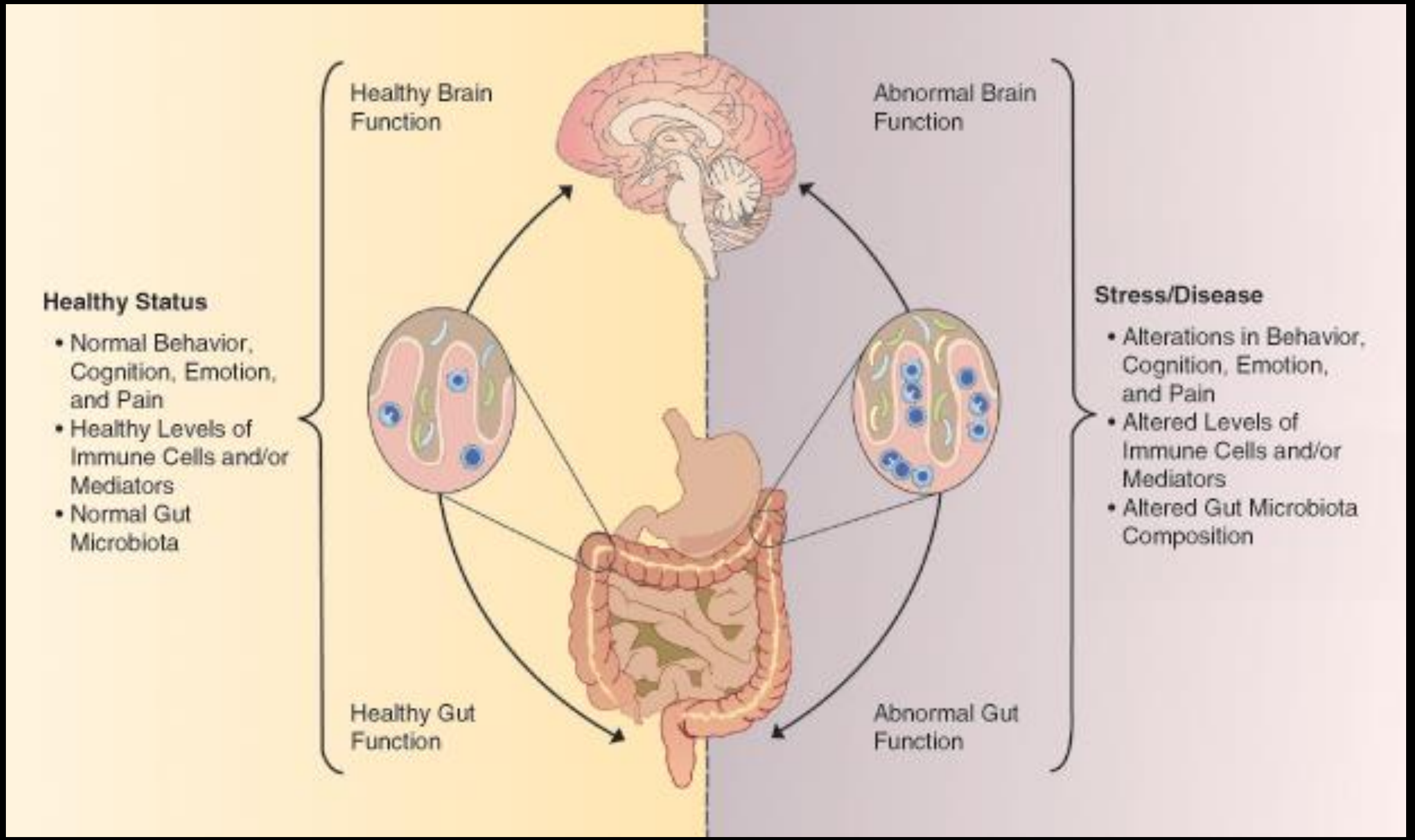

Appetite-regulating hormones
Hypothalamic-pituitary-adrenal axis
Irregular feeding patterns
Psychological stress
Enteroendocrine cells
Neurotransmitters & neuromodulators
Dysregulated appetite control
Gut microbiota
Psychobehaviorial abnormalities
Nutritional rehabilitation
Microbial peptides
Lipopolysaccharides
Purging behaviors
Central melanocortin system
Immuno-endocrine system

O Mal de Alzheimer



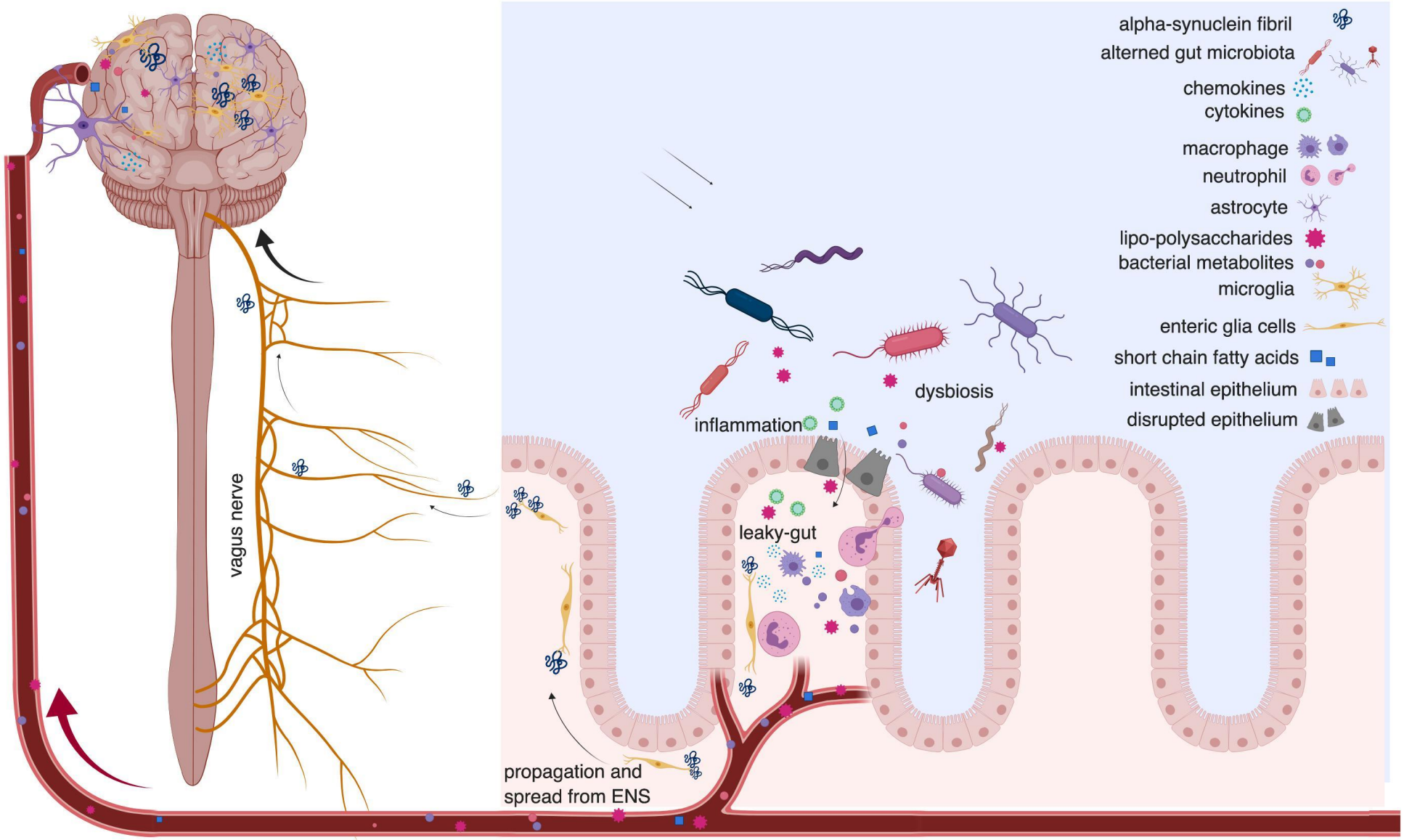
Microbiota e Alzheimer

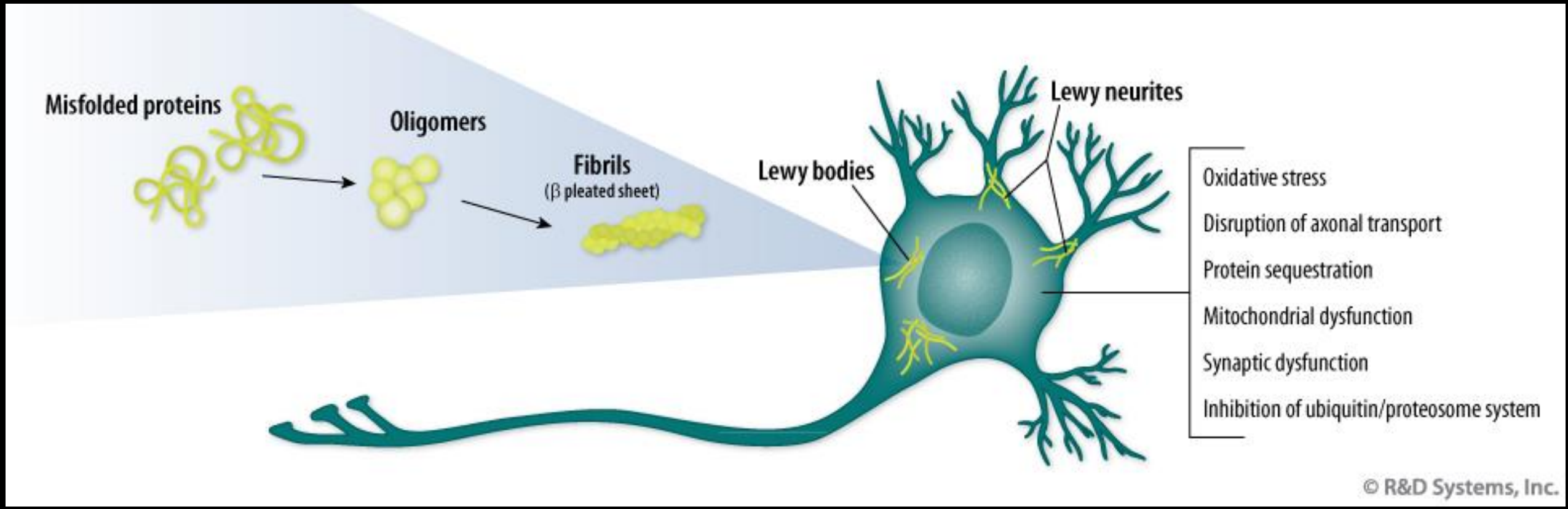



Healthy Status
• Normal Behavior, Cognition, Emotion, and Pain
• Healthy Levels of Immune Cells and/or Mediators
• Normal Gut Microbiota
Healthy Brain Function
Abnormal Brain Function
Stress/Disease
• Alterations in Behavior, Cognition, Emotion, and Pain
• Altered Levels of Immune Cells and/or Mediators
• Altered Gut Microbiota Composition
Healthy Gut Function
Abnormal Gut Function

Brain

Gut


vagus nerve
inflammation
dysbiosis
leaky-gut
propagation and
spread from ENS
alpha-synuclein fibril
alterned gut microbiota
chemokines
cytokines
macrophage
neutrophil
astrocyte
lipo-polysaccharides
bacterial metabolites
microglia
enteric glia cells
short chain fatty acids
intestinal epithelium
disrupted epithelium

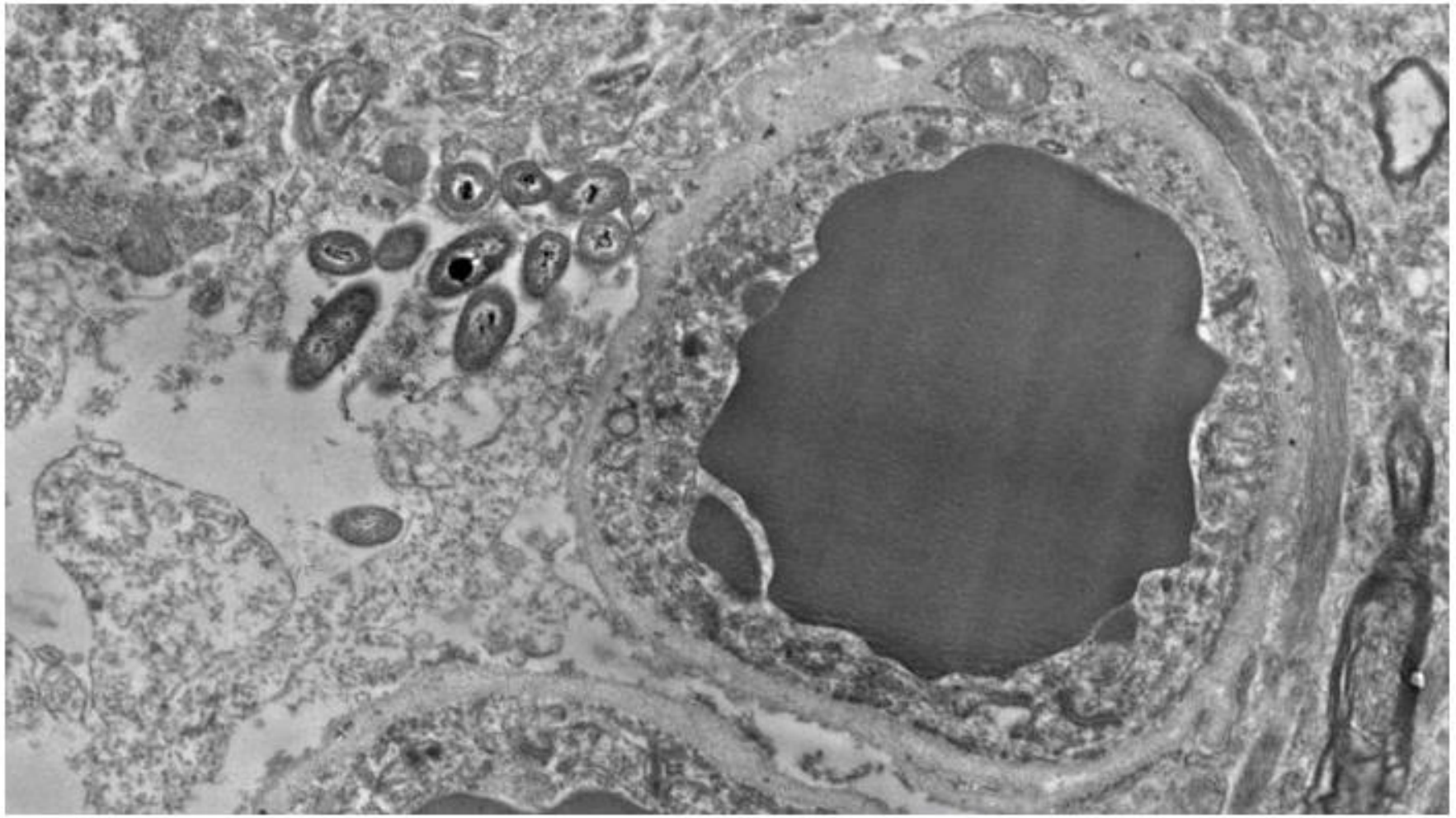

Misfolded proteins
Oligomers
Fibrils
(β pleated sheet)
Lewy bodies
Lewy neurites
Oxidative stress
Disruption of axonal transport
Protein sequestration
Mitochondrial dysfunction
Synaptic dysfunction
Inhibition of ubiquitin/proteosome system
© R&D Systems, Inc.

Suzana Herculano-Houzel

suzanahh@gmail.com

Zumbis do intestino chegam ao cérebro, o que pode explicar o parkinson

Doença pode ser causada por proteínas deformadas no intestino, dizem cientistas

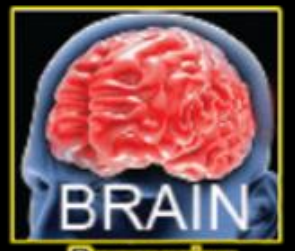


Images of human brain slices reveal bacteria, shown here to the left of a blood vessel—tantalizing but preliminary evidence of a "brain microbiome." ROSALINDA ROBERTS, COURTNEY WALKER, AND CHARLENE FARMER

Do gut bacteria make a second home in our brains?

By Kelly Servick | Nov. 9, 2018 , 2:45 PM

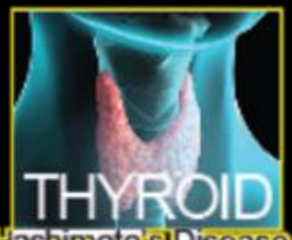
Acne
Rosacea
Eczema
Psoriasis



Depression
Anxiety
ADH Disorder
Dementia

Frequent Colds
Allergies

Food Sensitivities
Heartburn



Hashimoto's Disease
Hypothyroidism

Disbiose

Appetite
Metabolism

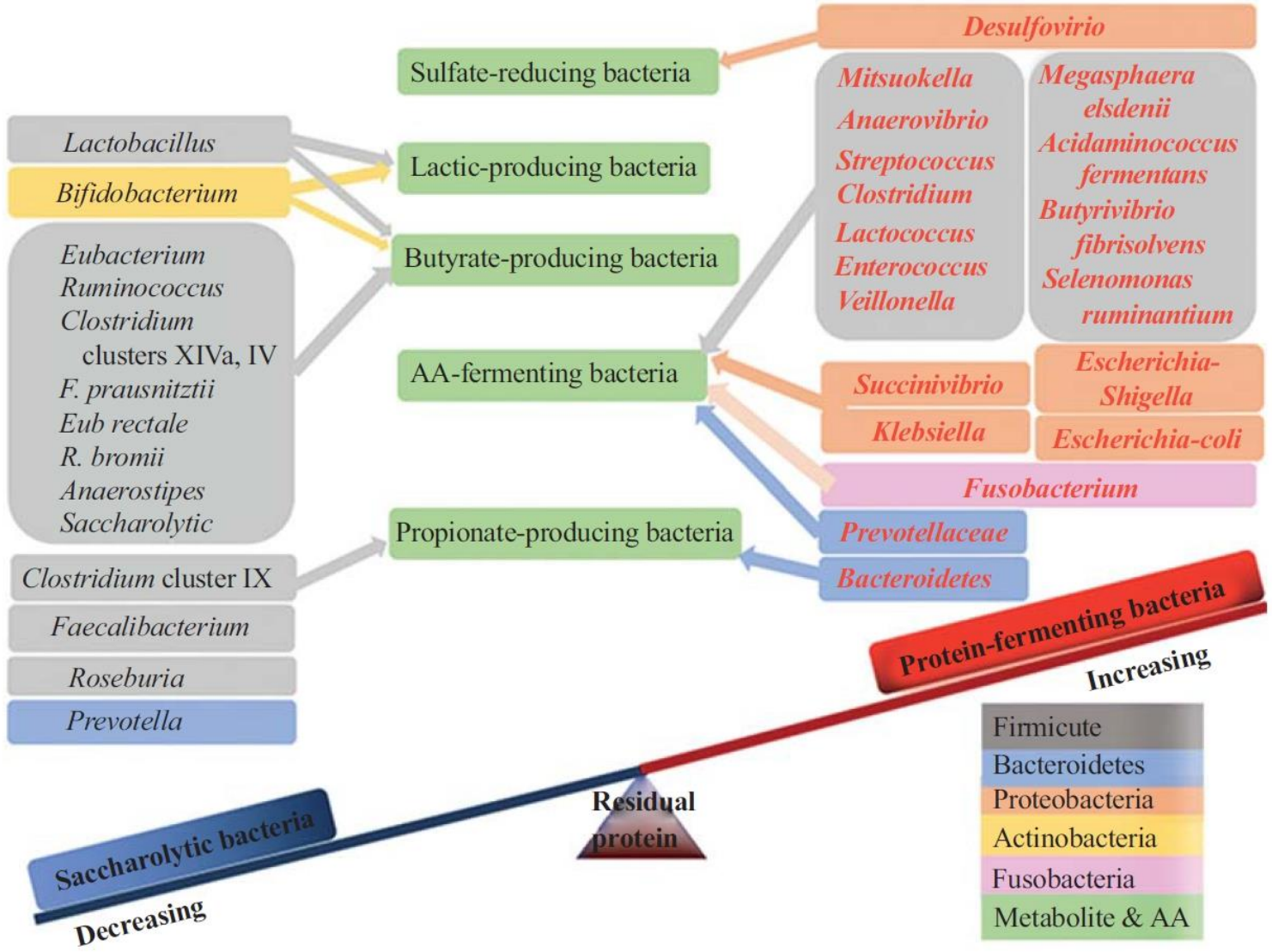
Cardiovascular Disease

Leaky Gut
Diarrhea
Infl. Bowel Disease
Constipation

Immune Disorders
Low Body Protection
From Diseases

Rheumatoid Arthritis
Fibromyalgija
Fatigue

Suplementação irregular



Reação de Maillard

D-aminoácidos

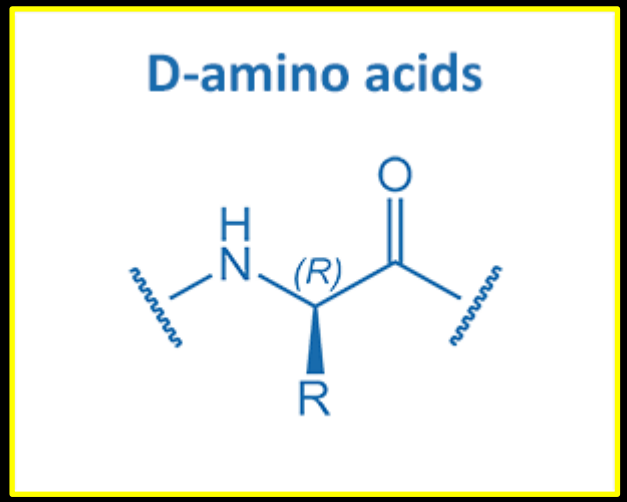
Phip

Amônia

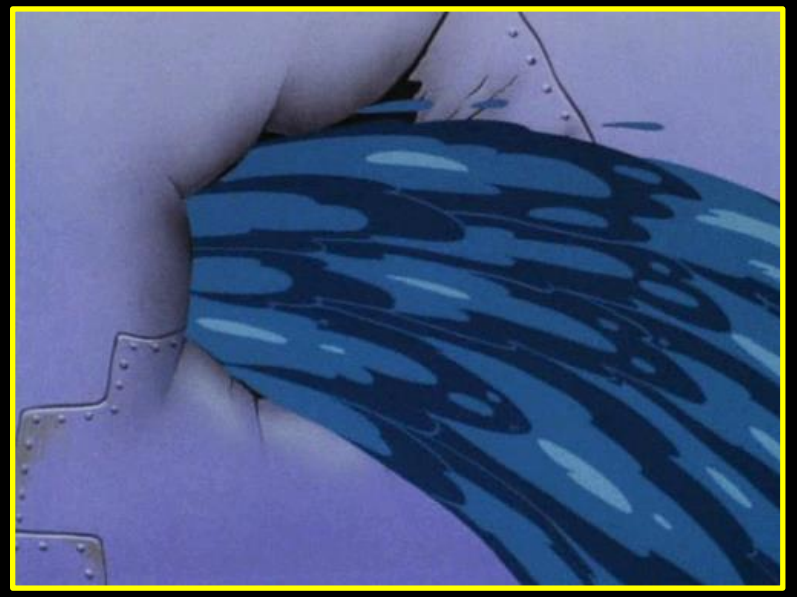
- GABA

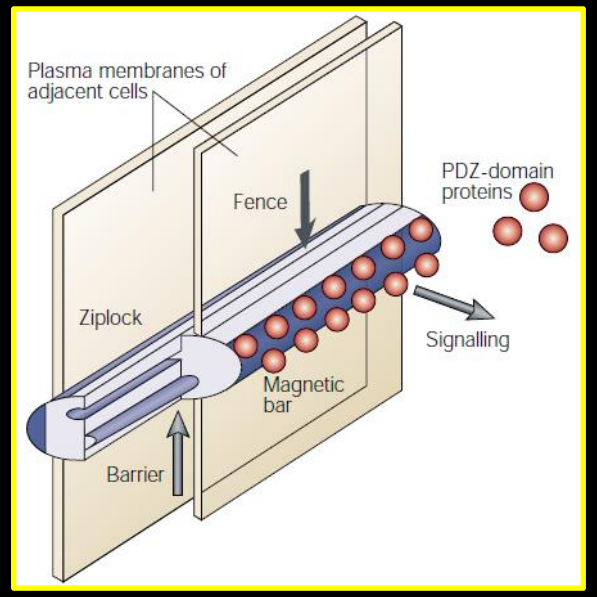
- Butirato

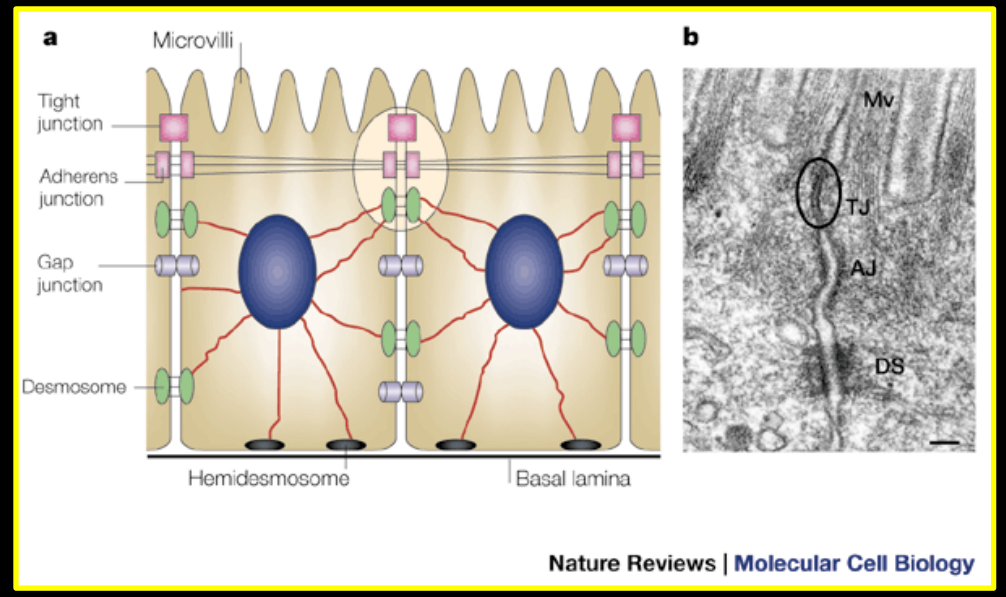
Encefalopatia hepática não alcoólica



Estabelecimento do Leaky gut (ocludina, claudina, caderinas e zonulinas)



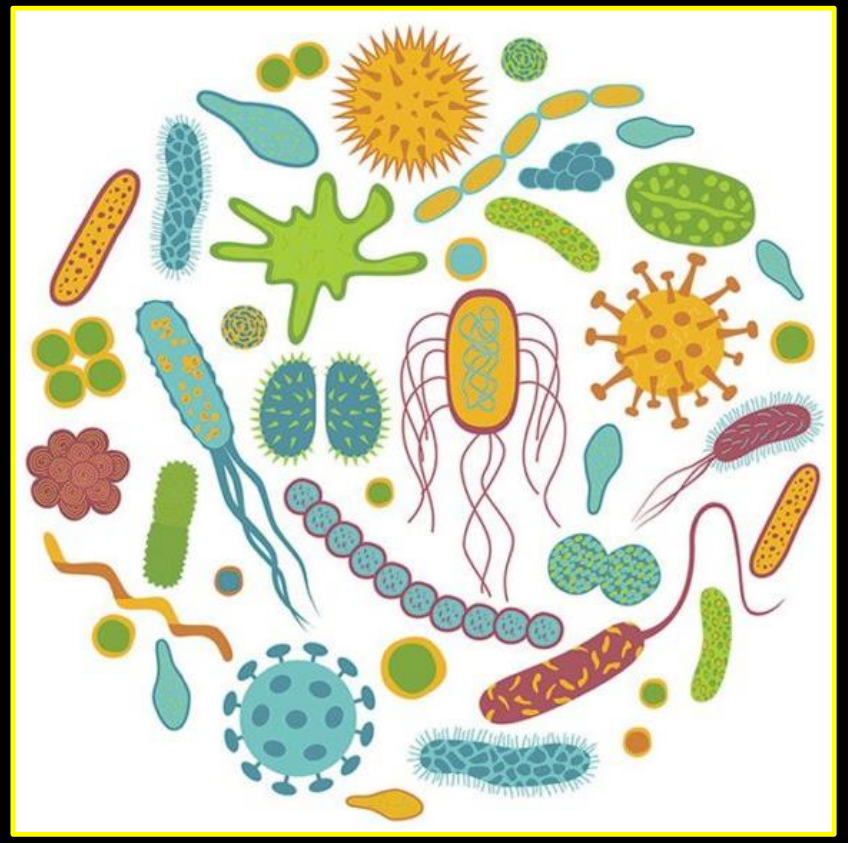




As ferramentas microbiológicas

Os probióticos e seus “postbiotics”

“Microrganismo vivo que administrado na dose correta cause benefício ao hospedeiro” (Roy Fuller 1989) – Vida limitada



Espécie

VS

Linhagem

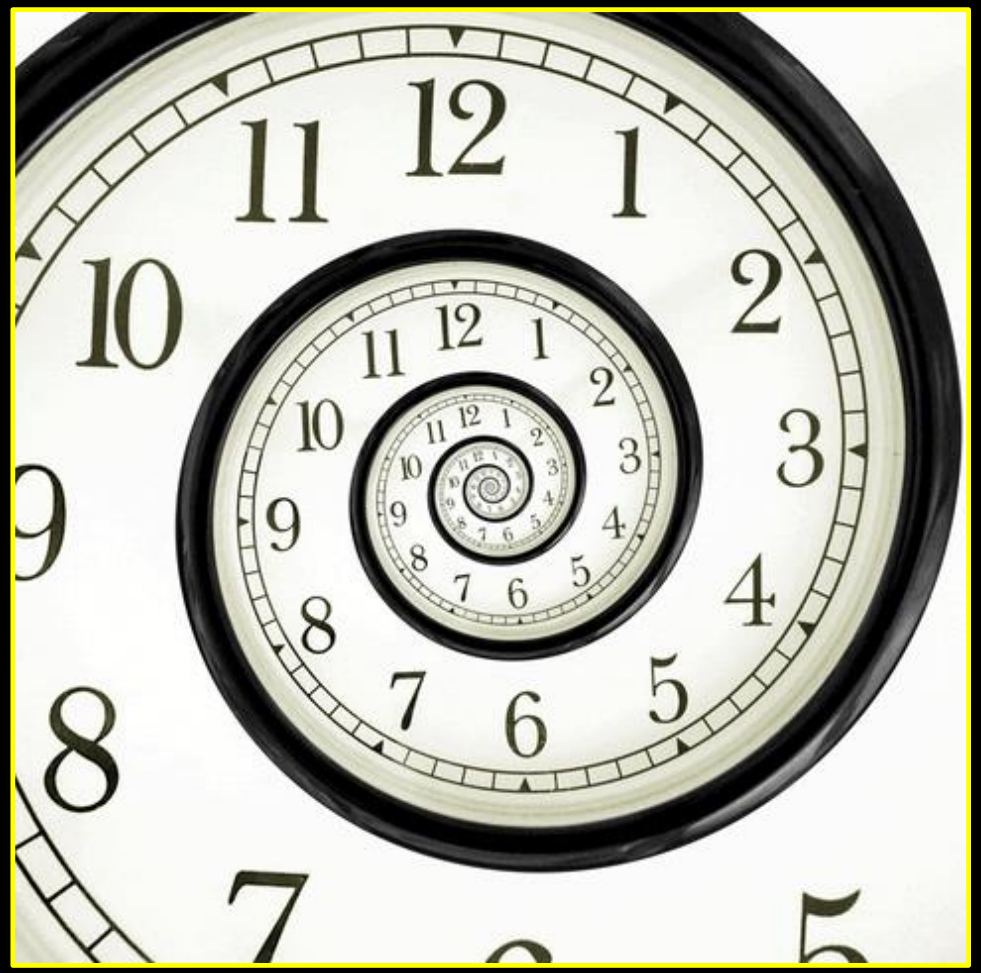
Aerobios Anaerobios Microaerofilos

Probióticos tradicionais

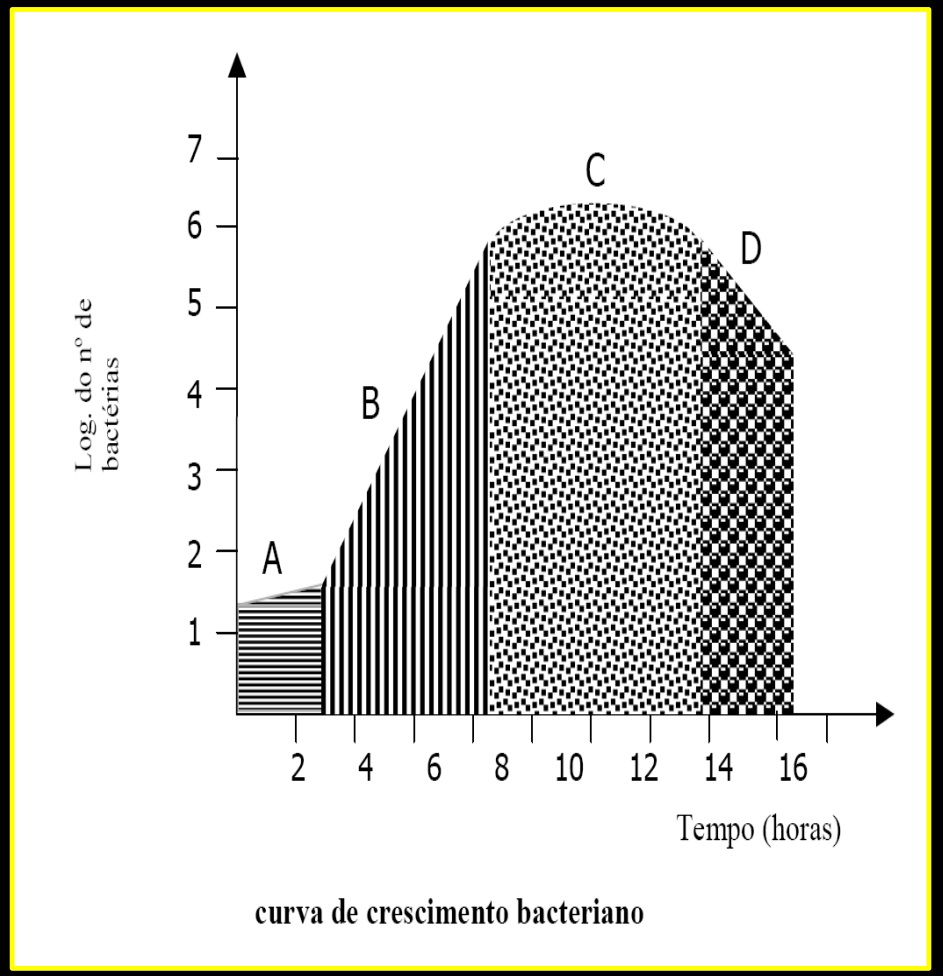
Next generation probiotic (NGP)

Live Biotherapeutic Product (LBP) that is “a biological product that contains live organisms; is applicable to the prevention, treatment or cure of a disease or condition of human beings; and is not a vaccine (including genetically modified bacteria - FDA)

Melhores horários para administração

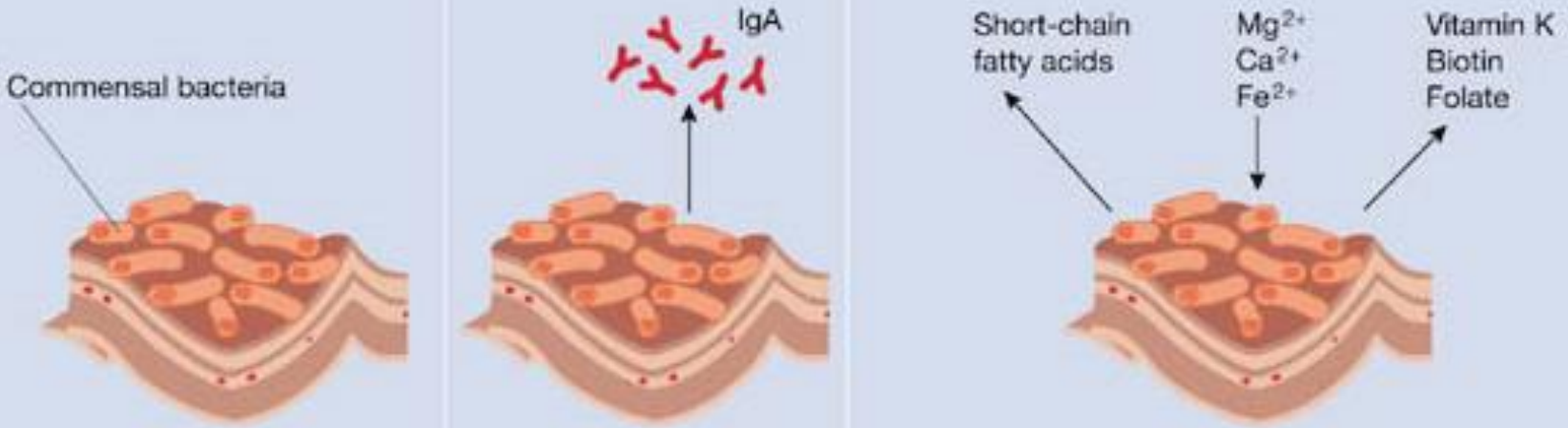


Curava de crescimento bacteriano

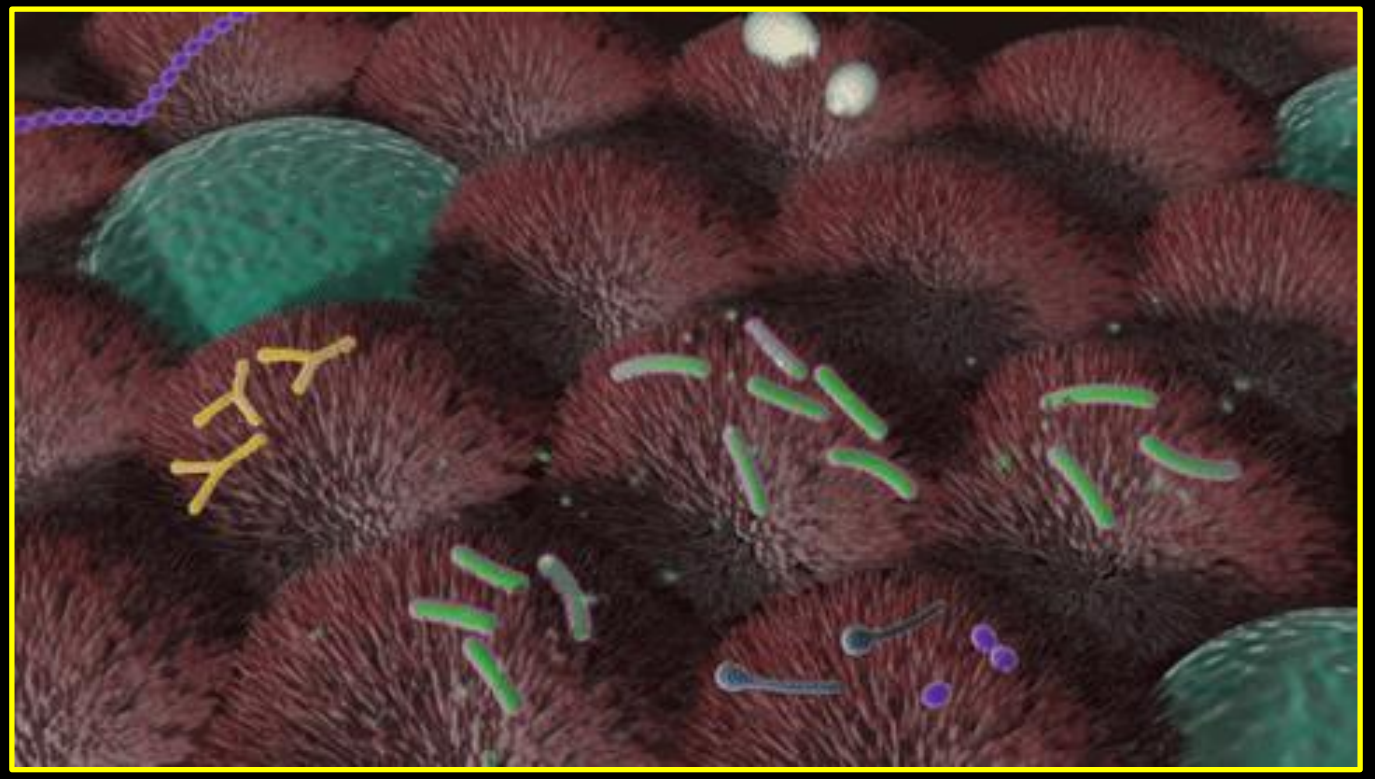


curva de crescimento bacteriano

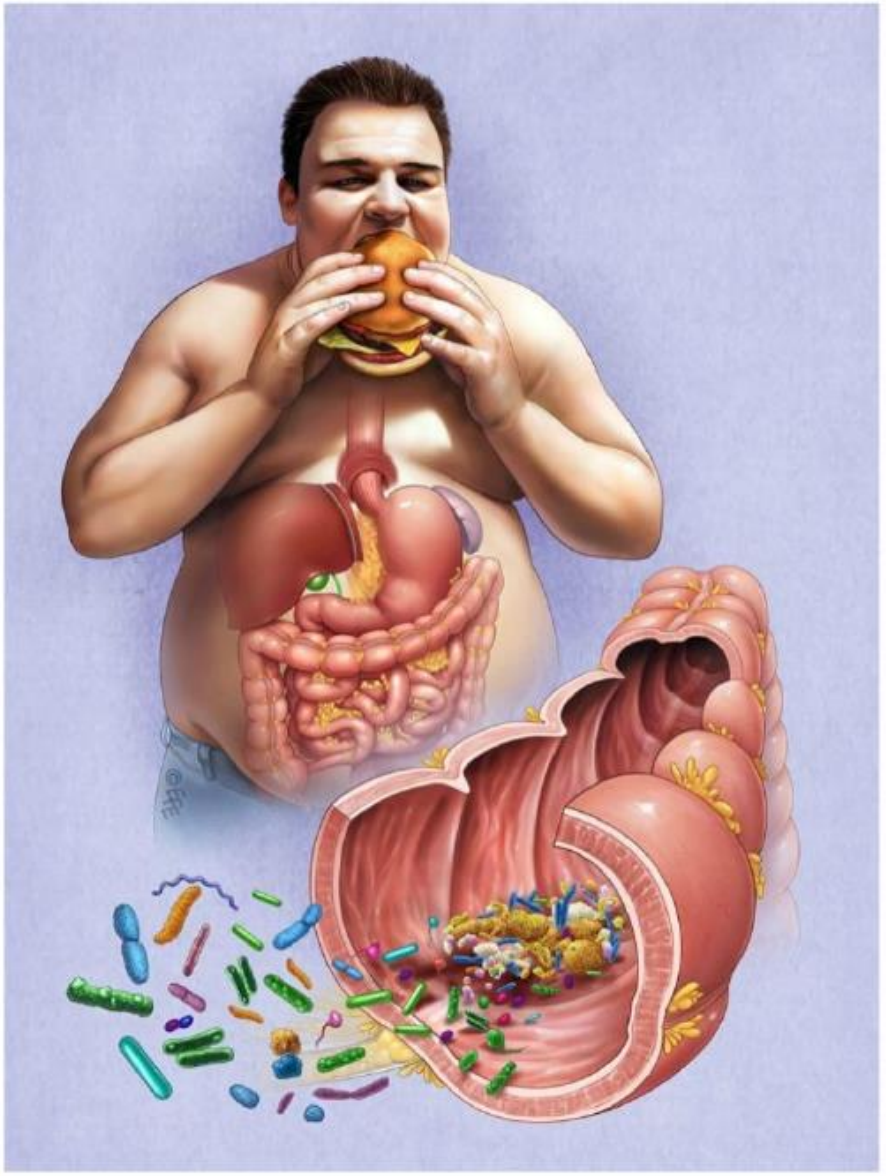
Protective functions	Structural functions	Metabolic functions	
Pathogen displacement	Barrier fortification	Control IEC differentiation and proliferation	Ferment non-digestible dietary residue and endogenous epithelial-derived mucus
Nutrient competition	Induction of IgA	Metabolize dietary carcinogens	Ion absorption
Receptor competition	Apical tightening of tight junctions	Synthesize vitamins e.g., biotin, folate	Salvage of energy
Production of anti-microbial factors e.g., bacteriocins, lactic acids	Immune system development		

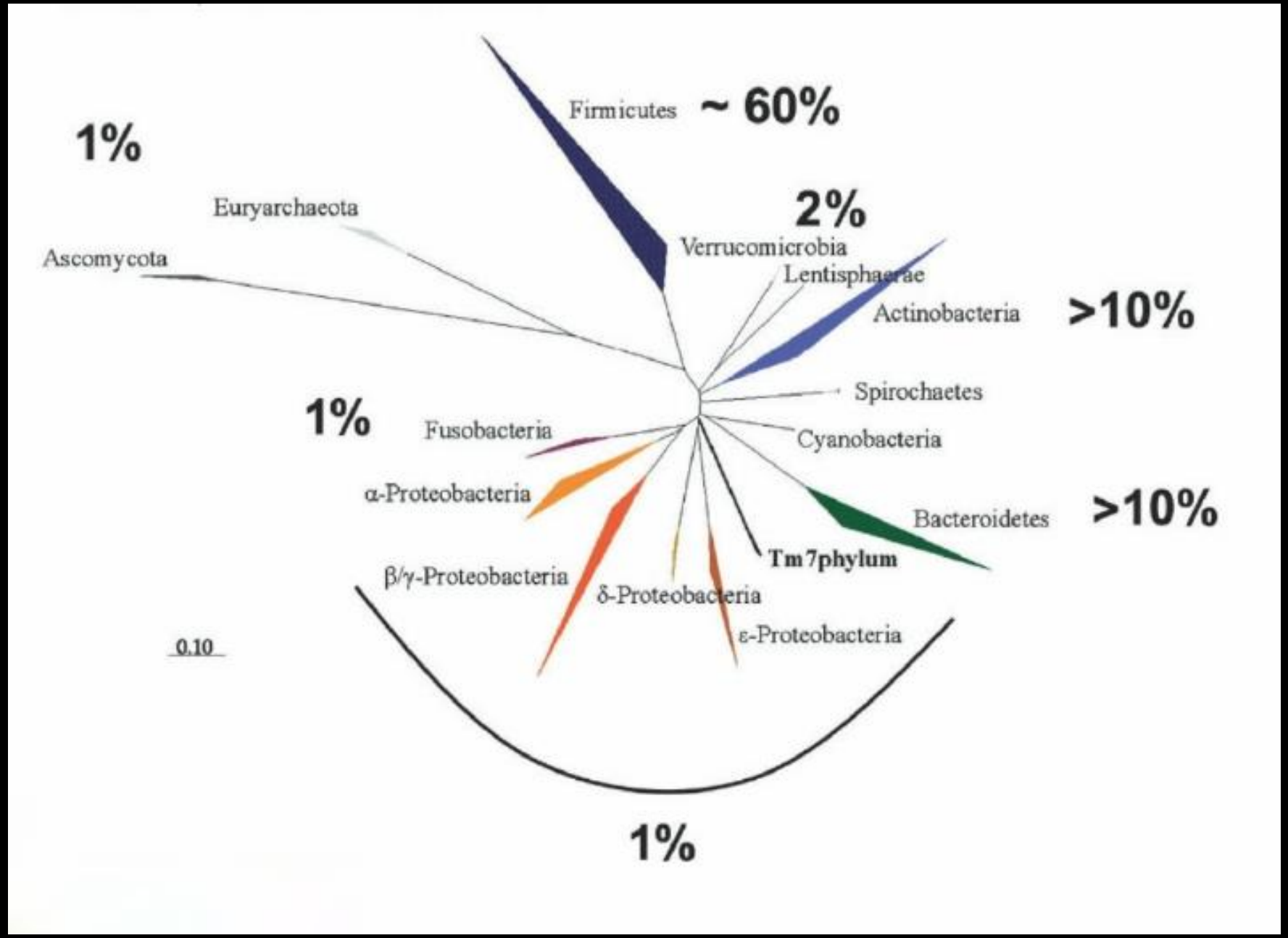


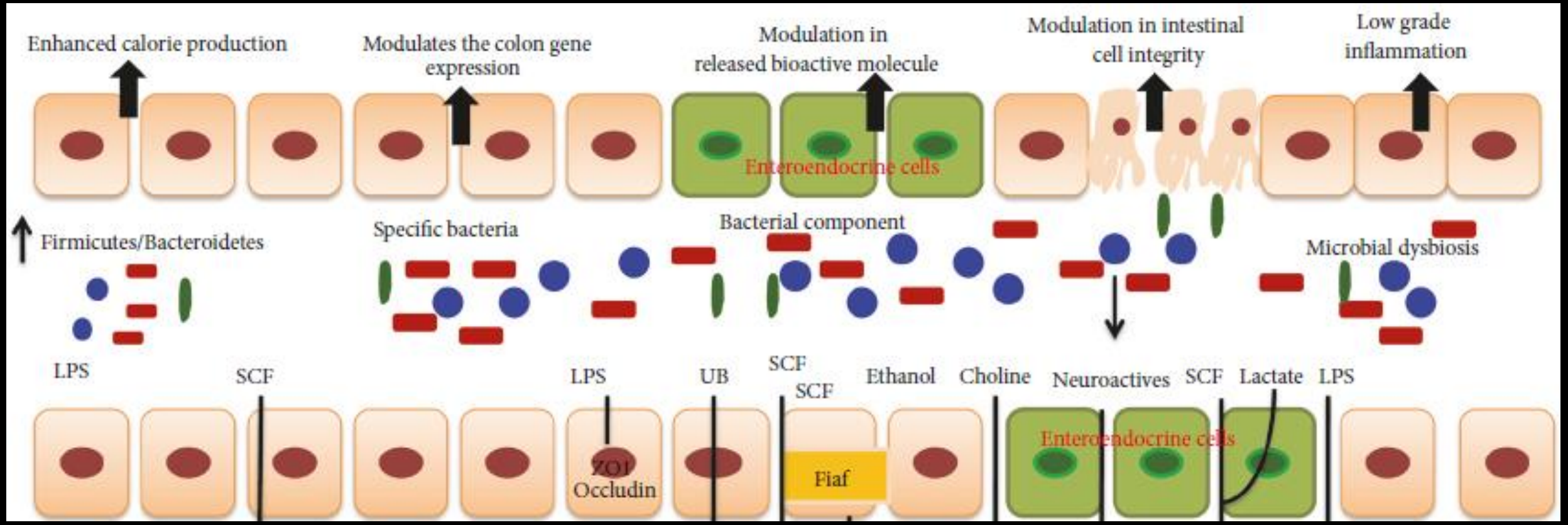
Aumento da imunidade

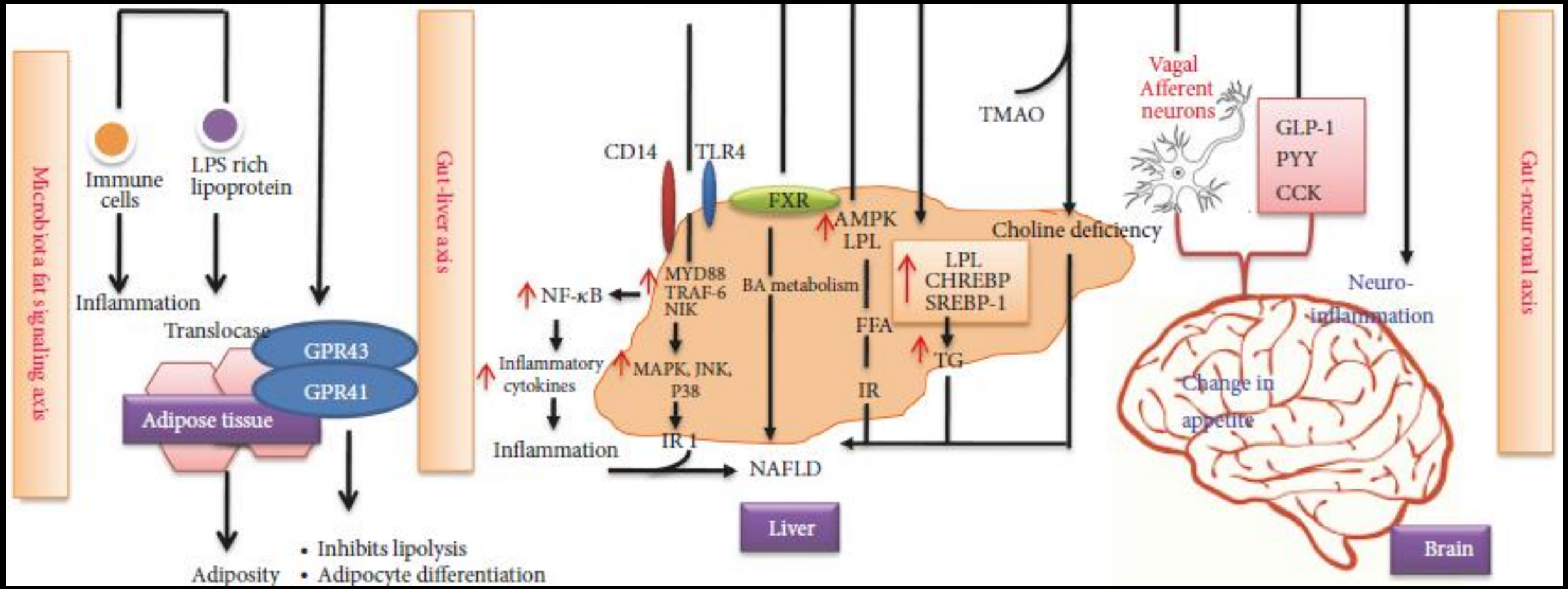


Microbiota e Obesidade




Firmicutes
~ 60%
1%
Euryarchaeota
2%
Verrucomicrobia
Ascomycota
Lentisphaerae
Actinobacteria
>10%
Spirochaetes
1%
Fusobacteria
Cyanobacteria
α-Proteobacteria
Bacteroidetes
>10%
Tm7phylum
β/γ-Proteobacteria
δ-Proteobacteria
ε-Proteobacteria
0.10
1%


Enhanced calorie production
Modulates the colon gene expression
Modulation in released bioactive molecule
Modulation in intestinal cell integrity
Low grade inflammation
Enteroendocrine cells
Firmicutes/Bacteroidetes
Specific bacteria
Bacterial component
Microbial dysbiosis
LPS
SCF
LPS
UB
SCF
SCF
Ethanol
Choline
Neuroactives
SCF
Lactate
LPS
ZO1
Occludin
Fiaf
Enteroendocrine cells


Microbiota fat signaling axis
Immune cells
LPS rich lipoprotein
Inflammation
Translocase
GPR43
GPR41
Adipose tissue
Adiposity
• Inhibits lipolysis
• Adipocyte differentiation
Gut-liver axis
CD14
TLR4
FXR
AMPK
LPL
TMAO
Choline deficiency
NF-κB
MYD88
TRAF-6
NIK
BA metabolism
LPL
CHREBP
SREBP-1
FFA
TG
IR
Inflammatory cytokines
MAPK, JNK, P38
IR 1
Inflammation
NAFLD
Liver
Vagal Afferent neurons
GLP-1
PYY
CCK
Neuro-inflammation
Change in appetite
Brain
Gut-neuronal axis

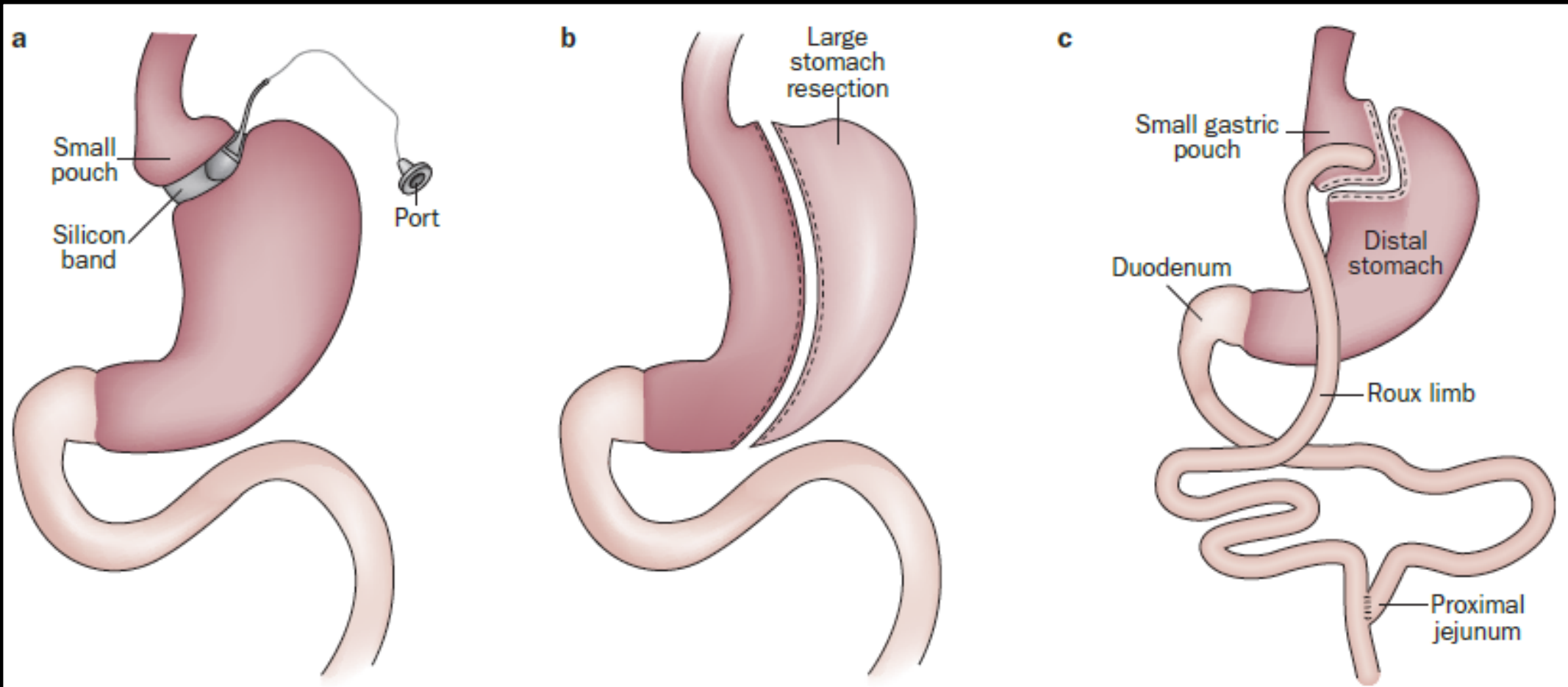


Figure 2 | The three main bariatric surgical interventions. **a** | Laparoscopic adjustable gastric banding. A small pouch is created in the upper part of the stomach. A silicon band is connected to a port placed in a subcutaneous position to enable adjustment of the band. **b** | Sleeve gastrectomy. A large stomach resection is carried out to create a tube of about 60 ml, leaving the pyloric sphincter intact. This surgery is irreversible. **c** | Roux-en-Y gastric bypass. This surgery creates a small gastric pouch (~30 ml) directly linked to the distal jejunum by the Roux limb. The distal stomach, duodenum and proximal part of the jejunum is subsequently anastomosed 1.5 m below the gastrojejunal anastomosis.

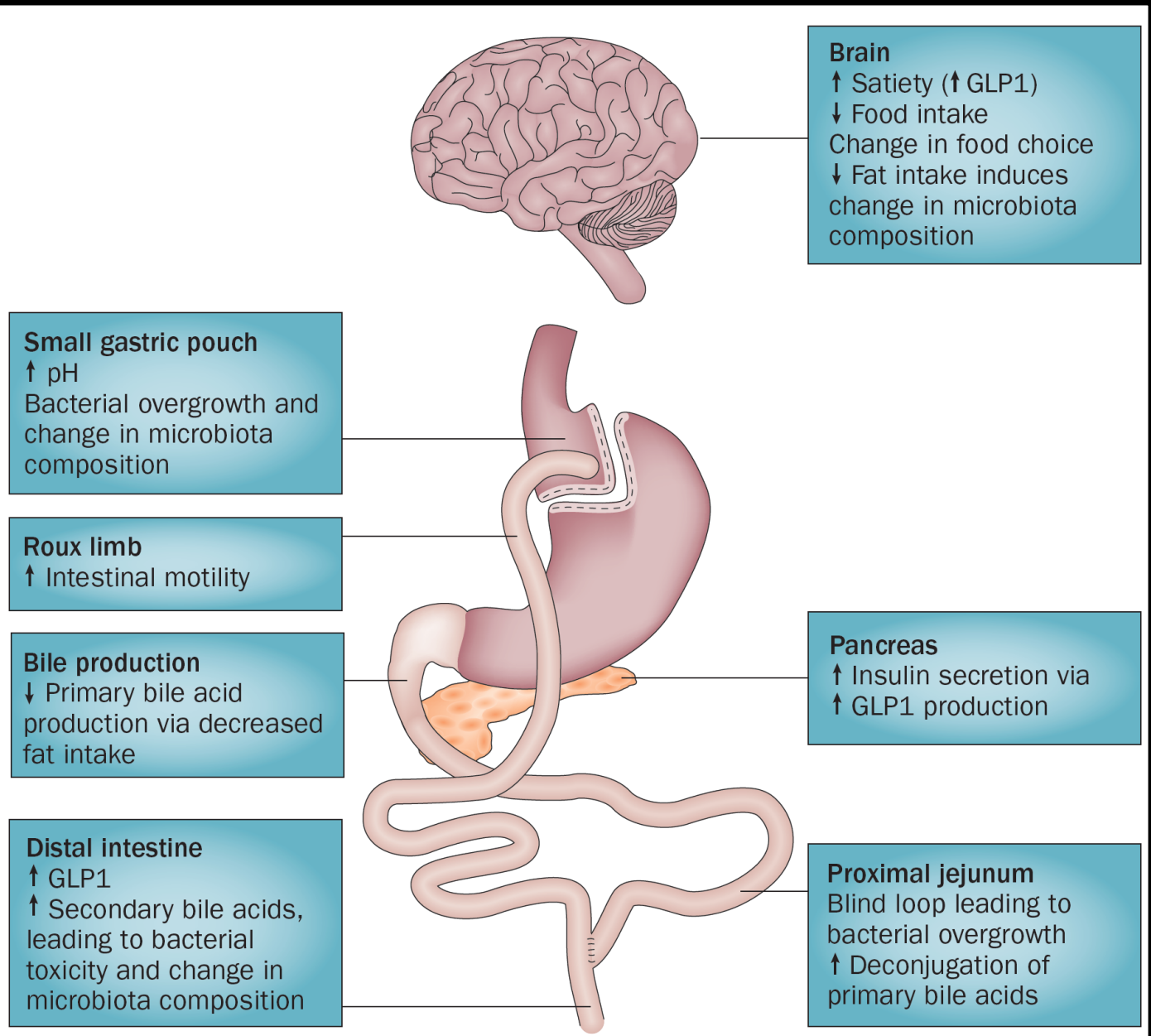


Figure 3 | Roux-en-Y gastric bypass induces various environmental, systemic and anatomical changes that might directly or indirectly affect the composition of the gut microbiota. Abbreviation: GLP1, glucagon-like peptide-1.

Table 1: Influence of probiotic supplementation on obese people.

Intervention	Dose	Duration of the study	Clinical outcomes	Conclusions
Hypocaloric diet (1500 kcal/d), and cheese containing *Lactobacillus plantarum* TENSIA	Calorie restricted diet and 50 g of cheese per day	3 weeks	↓BMI BMI associated with lactobacilli load in the intestine. ↓ Morning systolic BP.	Calorie restriction and probiotic supplementation significantly reduced the BMI, and systolic BP in people with obesity and hypertension.
L. gasseri BNR17	6 capsules per day (10^{10} CFU per capsule)	12 weeks	↓ Weight, waist and hip circumferences.	Reduced the body weight, waist and hip circumferences compared to baseline.
L. gasseri BNR17	10^{10} CFU per day	12 weeks	↓ Visceral adipose tissue, waist circumferences.	The probiotic supplementation reduced the visceral fat accumulation and waist circumference.
L. gasseri SBT2055 mediated fermented milk (FM)	200 g of FM per day (10^{6} / 10^{7} / 10^{8}CFU per g of FM)	12 weeks	↓ Abdominal visceral fat ↓ Body weight, waist and hip circumferences ↓BMI	Low concentration of SBT2055 supplementation reduced the obesity associated health problems, but continuous consumption is needed to maintain the effect.
VSL#3 and /or omega 3 fatty acid (OFA)	1 capsule per day (112.5 × 10^{9} CFU per capsule); 1 OFA capsule per day (180 mg EPA, and 120 mg DHA)	6 weeks	VSL#3 alone or in combination of OFA supplementation: ↓ Total cholesterol, triglyceride, LDL, VLDL, and hsCRP ↑ HDL level, insulin sensitivity. Altered the gut microbiota positively. OFA supplementation did not affect the microbiota.	The combination of VSL#3 and OFA showed more pronounced effects.

Intervention	Dose	Duration of the study	Clinical outcomes	Conclusions
L. salivarius UCC118	1 capsule per day (10^9 CFU per capsule)	4 weeks	↓BMI No changes in glycemia, and pregnancy outcomes	UCC118 supplementation had not significantly affected the metabolic profile, fasting glucose level, and pregnancy outcomes.
Vivomixx®	A mixture of probiotic strains (4.5×10^{10} CFU per day)	Depends∗	↓ weight gain and pregnancy consequences	Altered the microbiota in a positive way and reduced the complications of pregnancy and weight gain.
L. paracasei F19 or flaxseed mucilage (FM)	9.4×10^{10} CFU per day or 10 g of FM	6 weeks	FM intervention altered the microbiota and improves insulin sensitivity. But F19 supplementation had no effect on the metabolic profile in the subjects	FM improved the health status of obese postmenopausal women
Ecologic® (*Bifidobacterium bifidum* W23, *L. salivarius* W24, *L. acidophilus* W37, *B. lactis* W51, *B. lactis* W52, *L. casei* W56, *L. brevis* W63, *Lactococcus lactis* W19, and *L. lactis* W58)	High dose (1×10^{10} CFU per day); Low dose (2.5×10^9 CFU per day)	12 weeks	Level of LPS, fat mass, glucose, HOMA-IR index, LDL, subcutaneous fat, total cholesterol, TG, insulin, uric acid, waist circumference	Both high and low dose of Ecologic® supplementation improved the cardiometabolic parameters and intestinal permeability in obese postmenopausal women.

Intervention	Dose	Duration of the study	Clinical outcomes	Conclusions
Probiotic preparation (*B. bifidum, B. longum, B. infantis, L. acidophilus, L. casei, L. lactis*)	3×10^{10} CFU per day	4 weeks	No changes in waist circumference, body weight, glucose level. ↓ Energy intake	Probiotic supplementation reduced the energy intake compared to baseline. It can be used as an adjuvant for the weight loss program.
Synbiotic formula (*L. rhamnosus* CGMCC1.3724, inulin, oligofructose)	3.24×10^{8} CFU per day; 90 g inulin, 210 g oligofructose per day	12 weeks	↑ Weight loss in women. ↑ Satiety efficiency↓ Disinhibition and hunger scores, food craving.	The intervention of synbiotic preparation influenced the appetite control and associated behavior in obese people during weight loss program
Psychobiotics (*B. bifidum* SGB02, *B. animalis* subsp. *lactis* SGB06, *Streptococcus thermophilus* SGSt01, *S. thermophiles, L. plantarum* SGL07, *L. delbrueckii* spp. *bulgaricus* DSM 20081, *L. reuteri* SGL01, *L. acidophilus* SGL11, *Lactococcus lactis* subsp. *lactis* SGLc01)	Each 1.5×10^{10} CFU per day	3 weeks	↓ BMI, Fat mass ↓ Psychopathological scores ↓ Bacterial overgrowth syndrome ↓ BUT_GSI scale ↑ Free fat mass Improved the meteorism and defecation frequency	Psychobiotics supplementation improved the body composition, reduced the dysbiosis, and reduced the psychopathological scores in preobese-obese and normal weight obese people.

Intervention	Dose	Duration of the study	Clinical outcomes	Conclusions
B. breve B-3	2×10^{10} CFU per day	12 weeks	↓ Body fat mass, TG ↑ HDL	B-3 supplementation reduced the body fat effectively in pre-obese subjects.
Calorie restricted diet and fortified yogurt (*S. thermophiles, L. bulgaricus* and *B. lactis Bb-12*, inulin, whey protein, vitamin D_3, calcium)	500 g of fortified yogurt per day	10 weeks	↓ Body fat mass ↓ Waist circumference, body fat percentage, TG level, HOMA-IR value. ↑ HDL, 25-hydroxyvitamin D level, QUICKI.	Improved the body composition, and metabolic profile in obese people
B. animalis subsp. *lactis* CECT 8145	10^{10} CFU per day	12 weeks	↓ BMI, visceral fat ↓ Conicity index ↓ Waist circumference ↓ Waist circumference/ height ratio ↑ *Akkermansia* spp. in the gut microbiota	CECT 8145 supplementation effectively reduced the obesity associated consequences in abdominally obese people
B. pseudocatenulatum CECT 7765	$10^{9\text{-}10}$ CFU per day	13 weeks	↓ BMI, hsCRP, monocyte chemoattractant protein-1 ↑ Omentin-1, and HDL. ↑ *Alistipes* spp.	CECT 7765 supplementation improved the lipid profile and inflammatory markers in obese children

- Lactobacillus plantarum 299v (Lp299v®)
- Lactobacillus bulgaricus Lb-87
- Lactobacillus paracasei DSM 13434
- Lactobacillus plantarum DSM 15312
- Lactobacillus salivarius Ls-33
- Lactobacillus brevis Lbr-35
- Lactobacillus acidophilus La-14
- Bifidobacterium lactis Bl-04
- Lactobacillus paracasei Lpc-37
- Lactobacillus casei Lc-11

J Gastrointest Surg (2009) 13:1198–1204

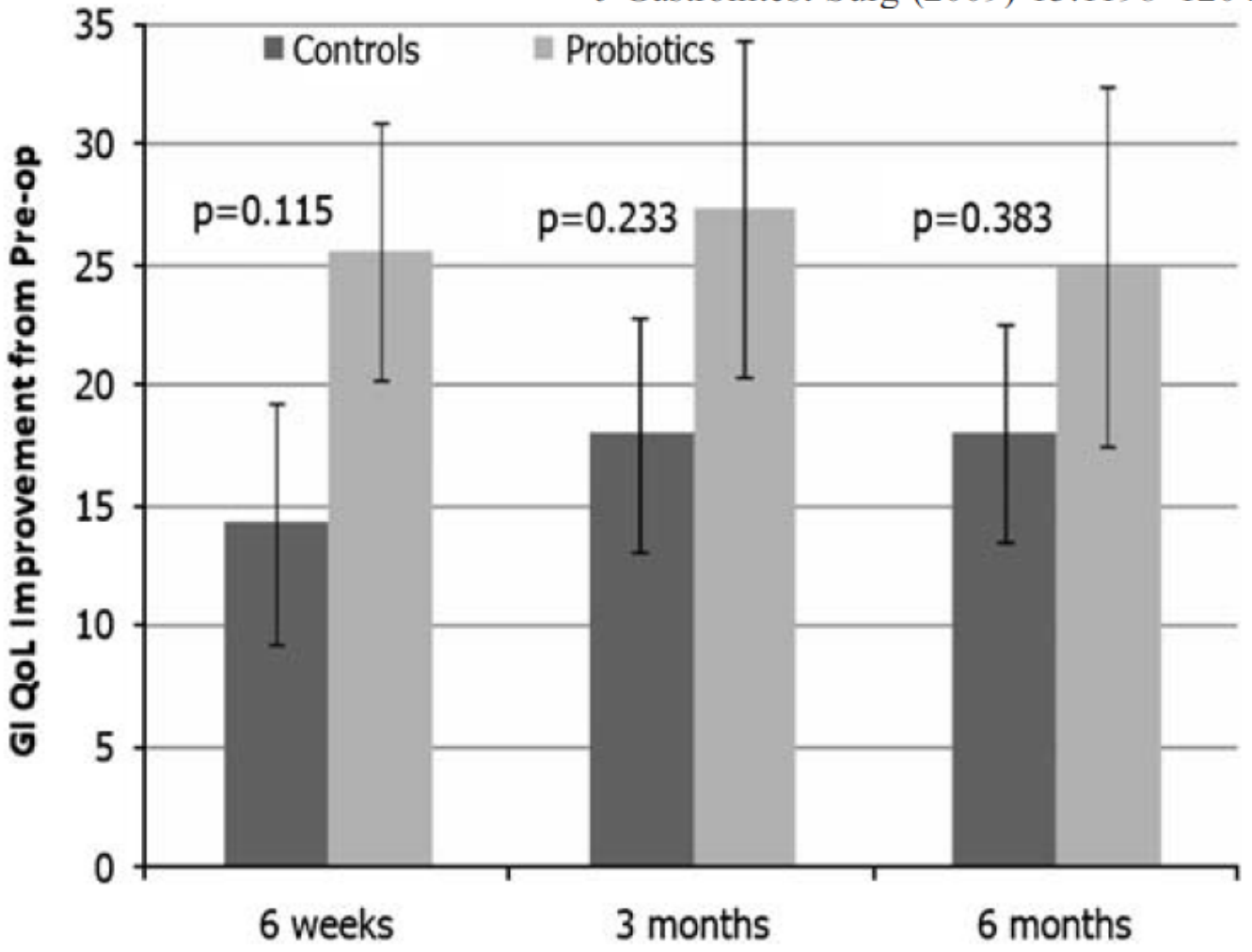


Figure 4 Percent improvement in GI quality of life postoperatively. GI QoL scores were significantly improved from preoperative in both groups. The probiotic group underwent a greater relative increase in GI QoL scores but these results were not statistically significant by two-sample *t* test with equal variances.

J Gastrointest Surg (2009) 13:1198–1204

		Controls (95% CI)	Probiotics (95% CI)	*p* value
6 weeks	*N*	20	18	
	% EWL	25.50 (22.01, 28.98)	29.90 (26.79, 33.03)	0.0577
3 months	*N*	22	17	
	% EWL	38.55 (33.24, 43.87)	47.68 (41.70, 53.65)	0.0222
6 months	*N*	20	15	
	% EWL	60.78 (53.08, 68.45)	67.15 (57.67, 76.64)	0.2730

Table 4 Effects of Probiotic Use on Weight Loss

Effect of probiotics on postoperative quality of gastric bypass surgeries: a prospective randomized trial

Jung-Chien Chen, M.D., Wei-Jei Lee, M.D., Ph.D., Jun-Juin Tsou, R.N., Tsang-Pai Liu, M.D., Pei-Ling Tsai, R.N.

DOI: https://doi.org/10.1016/j.soard.2015.07.010 | CrossMark

Methods

This double-blind, randomized trial was conducted between March 2010 and September 2010 with 60 patients who underwent gastric bypass for severe obesity and experienced postoperative symptomatic GI episodes. Patients were randomly assigned to the probiotics group A (n = 20; 1 g *Clostridium butyricum* MIYAIRI twice daily); probiotics group B (n = 20; *Bifidobacterium longum* BB536 twice daily); or digestive enzymes group (n = 20; Aczym, containing 100 mg takadiastase N, 20 mg cellulase AP, 50 mg lipase MY, and 100 mg pancreatin, twice daily). Quality of life was measured using the modified Gastrointestinal Quality of Life Index (mGIQLI) before and after the 2-week intervention.

Results

Preintervention patient characteristics and mGIQLI scores were similar among the 3 groups. After the 2-week intervention, the mean mGIQLI score improved from 57.4 to 63.9 points in the entire sample and also within each group for 7 items specifically for 7: excessive passage of gas, foul smell of flatulence, belching, heartburn, abdominal noises, abdominal bloating, and abdominal pain.

Conclusions

Administration of probiotics or digestive enzymes may improve symptomatic GI episodes after gastric bypass surgeries and improve quality of life, at least initially.

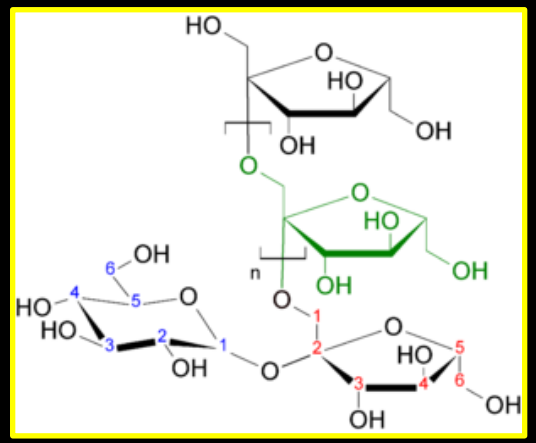
Prebióticos:

"non-digestible food ingredients or substances that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon, and thus attempt to improve host health"

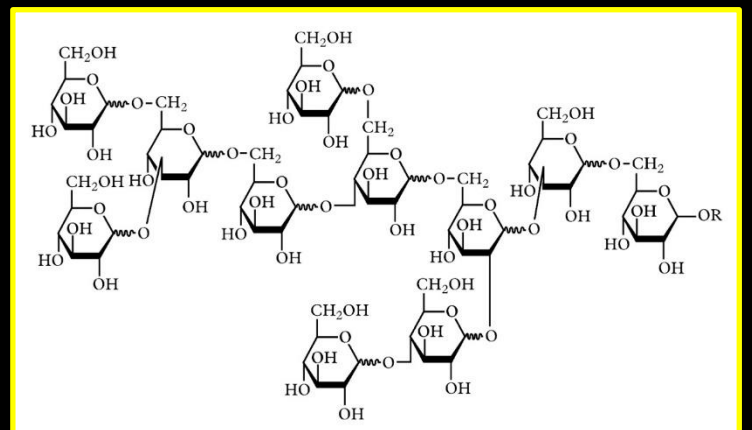
Fibra solúvel:

"Qualquer carboidrato não digerível e fermentável."

Inulina



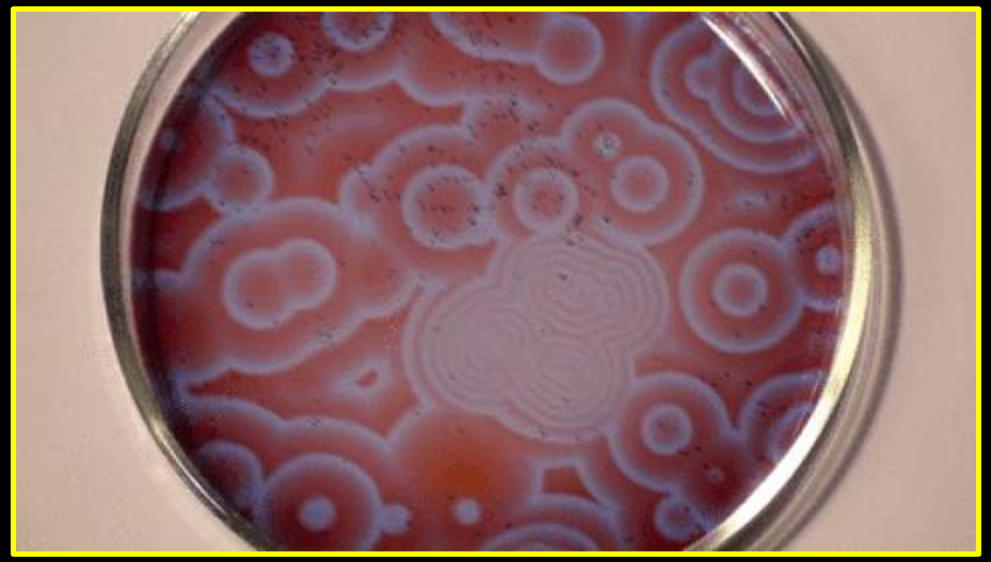
Polidextrose



Alimentação

Fermentação

Meio de cultura para nossas bactérias

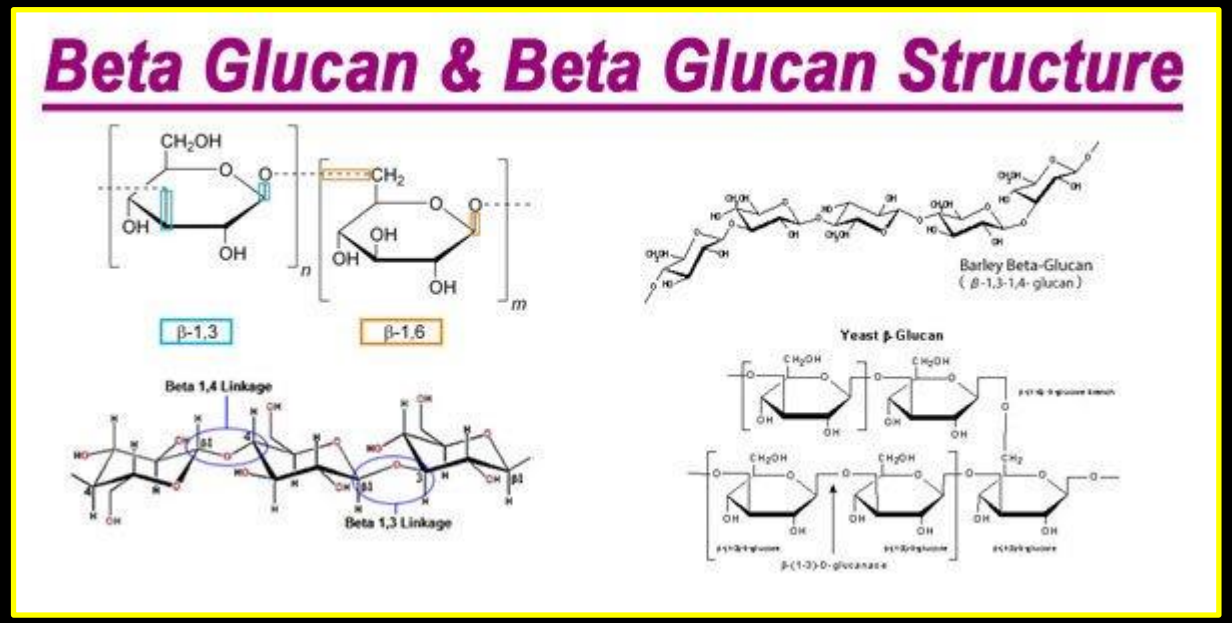


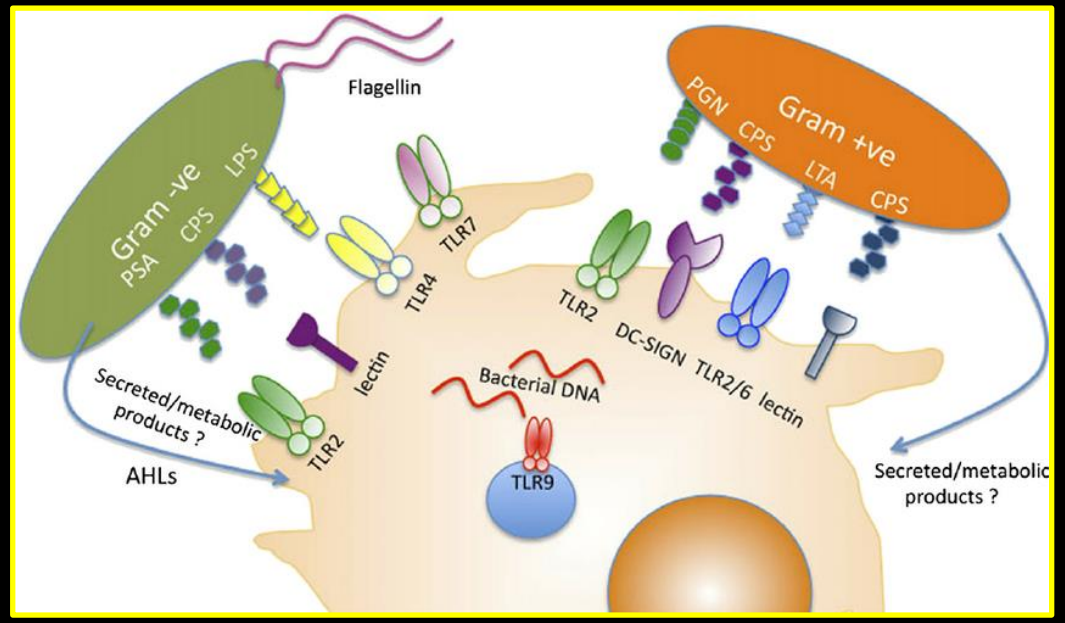
Paraprobióticos e as “Partículas microbianas”

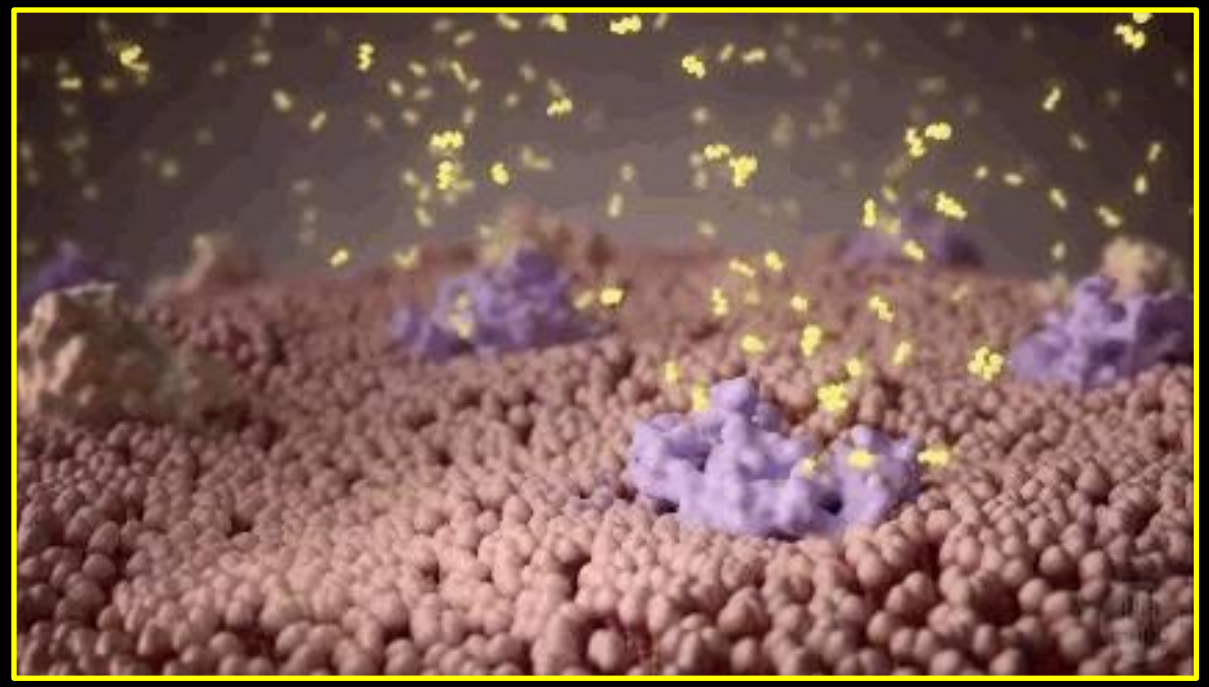
MAMPs, (microbe associated molecular patterns)

PAMPs, (Pathogen associated molecular patterns)

Probiotical Cell Fragments (PCFs)





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Anamnese:

- **Nascimento: Cessária ou parto norma?**

- **Infância: Muitos acometimentos alérgicos?**
- **Rinites, Otites, Sinusites, dermatites.**
-
- **Antibióticoterapia? Quais?**

- **Corticóides?**

- **Consistência Fecal**

Flutua?

Difícil higiene?

Cheiro?

Gases?

Dores? Alivia com a evacuação?

Intestino solto ou preso? Quantas vezes Evacua ao dia?

Meteorismo?

Cor

ho'oponopono

ho'oponopono colônico

Microbiota sinto muito

Microbiota me perdoe

Microbiota sou grato

Microbiota EU TE AMO!

OBRIGADO PELA ATENÇÃO