

Understanding Brain-Body Interactions to Advance Brain Health

The Brain Gut Microbiome System

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Disclosures

Member of Scientific Advisory Boards

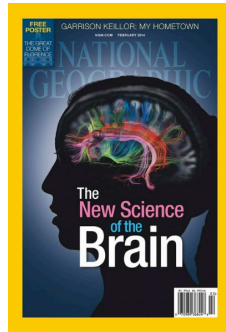
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- Tiny Health
- Danone
- Ginger
- Salvo
- Seed
- EatWell

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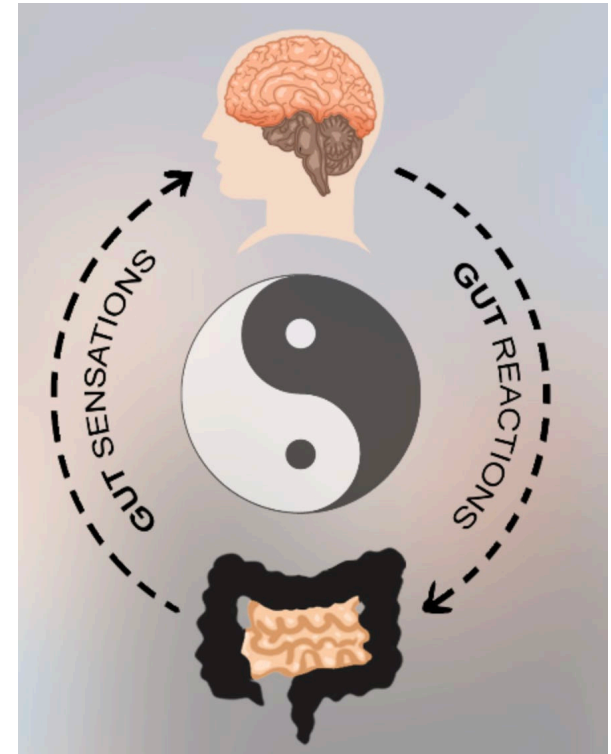
100 Years of Evolution of Our Understanding of Brain Gut Interactions



Fritz Kahn, 1926



The Brain Gut Supercomputer



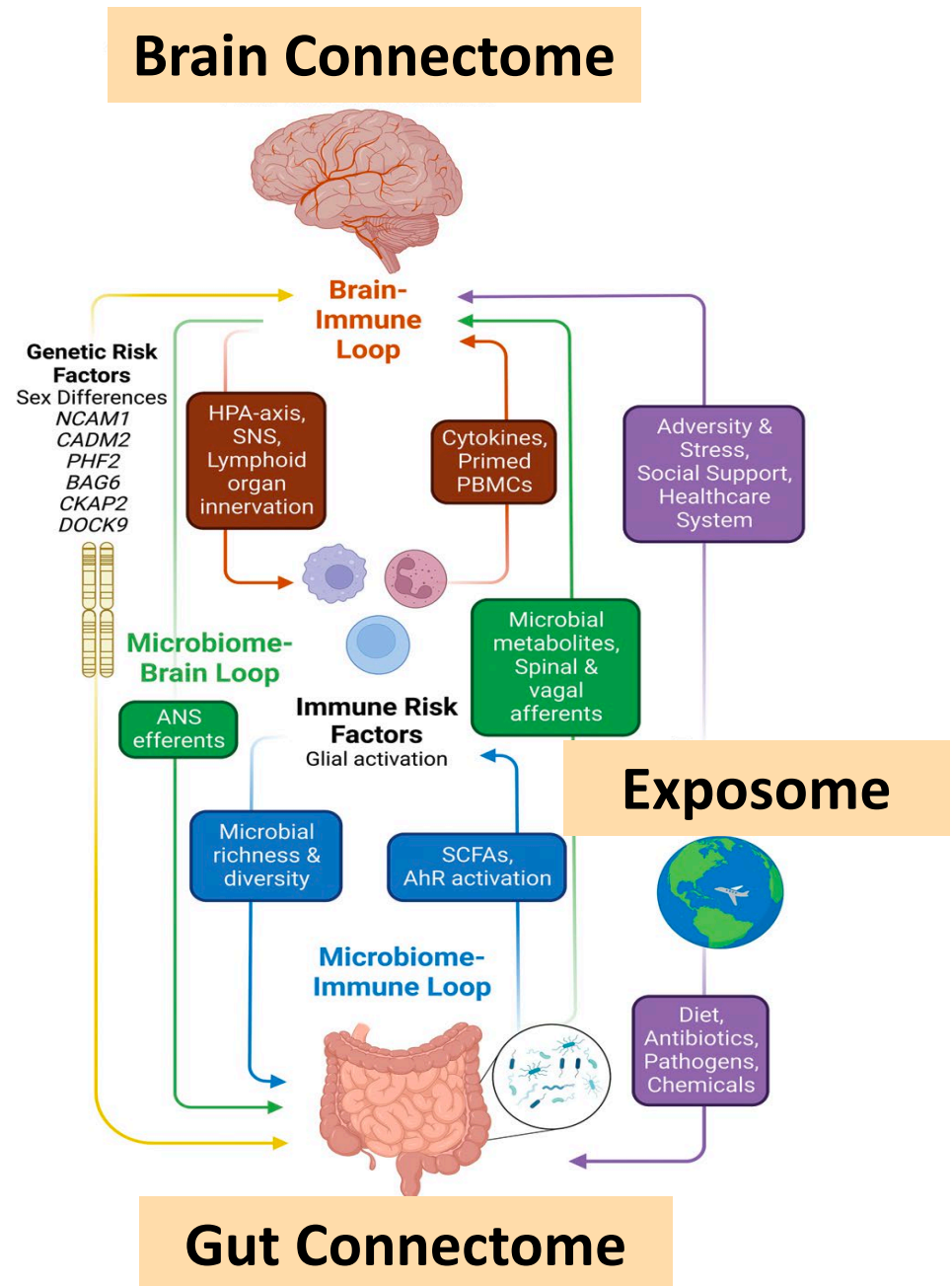
Gut feelings: the emerging biology of gut-brain communication

[Emeran A. Mayer](#)

[Nature Reviews Neuroscience](#) 12, 453–466 (2011) | [Cite this article](#)

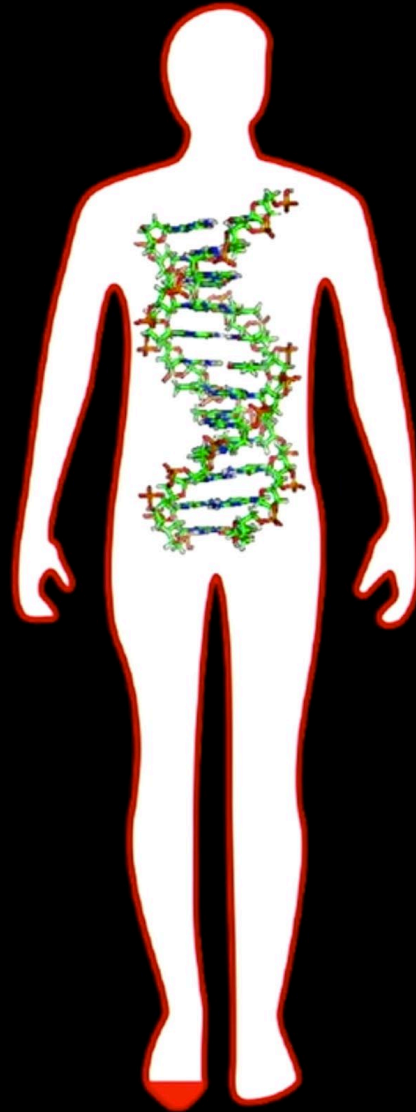
The Brain Gut Microbiome Immune System

The brain, gut, microbiome and immune system are interconnected via multiple bidirectional communication loops. This BGM systems receives input from interoceptive bodily signals and from the exposome.



The Human Microbiome – We Are Only Scratching On the Surface

20,000
human genes



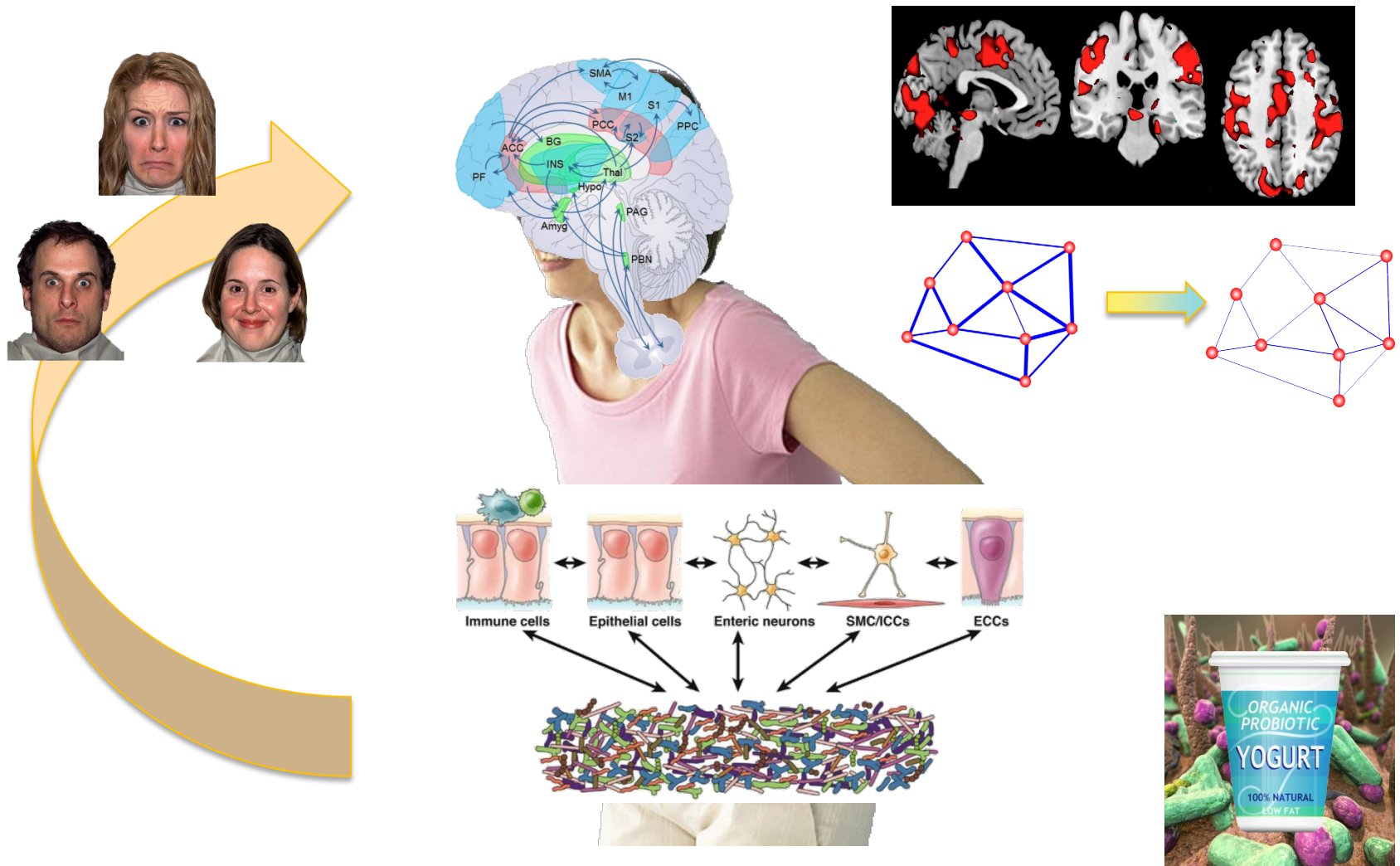
2-20 million
microbial genes

1%

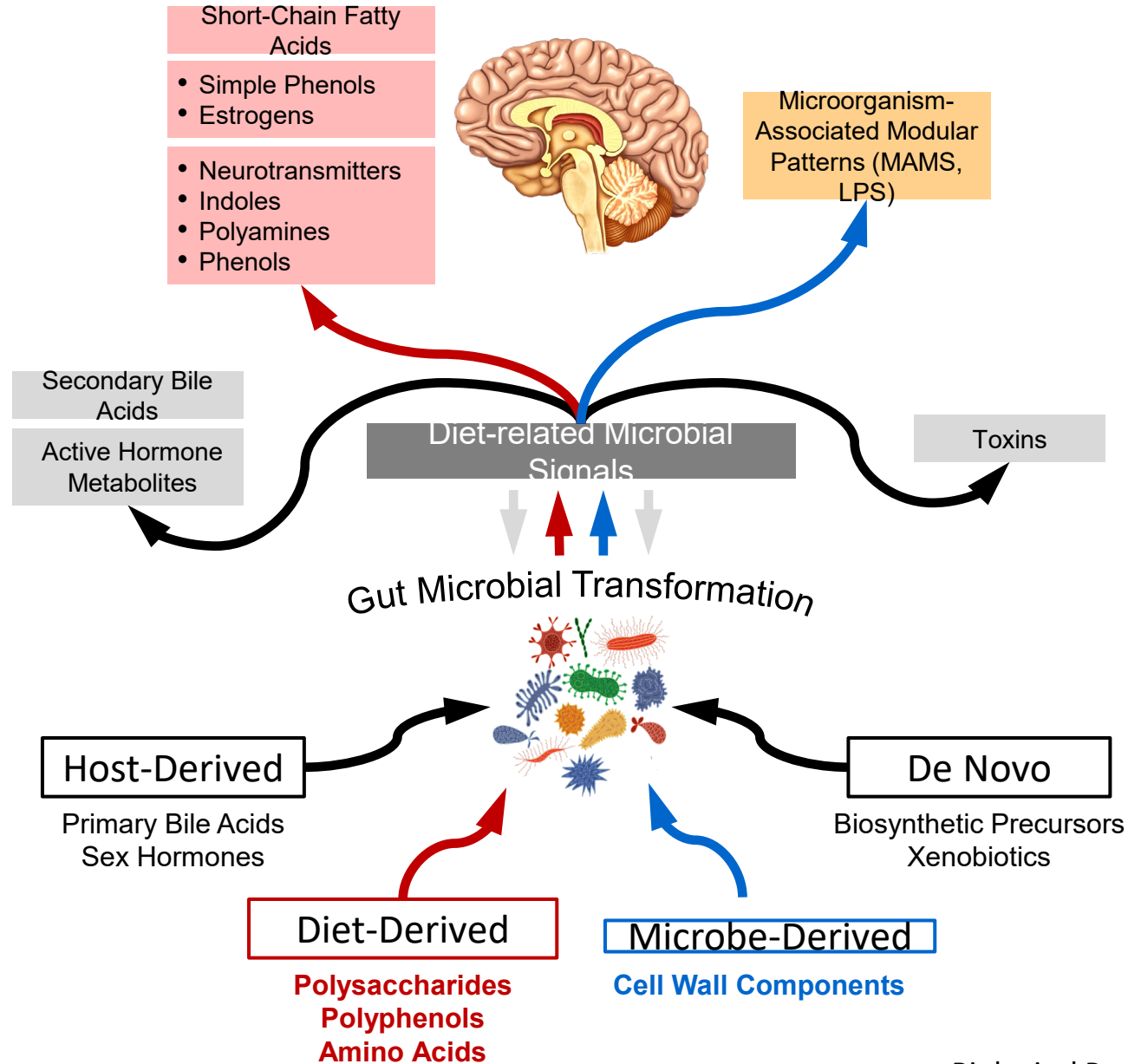
We neglect 99%
of the system!



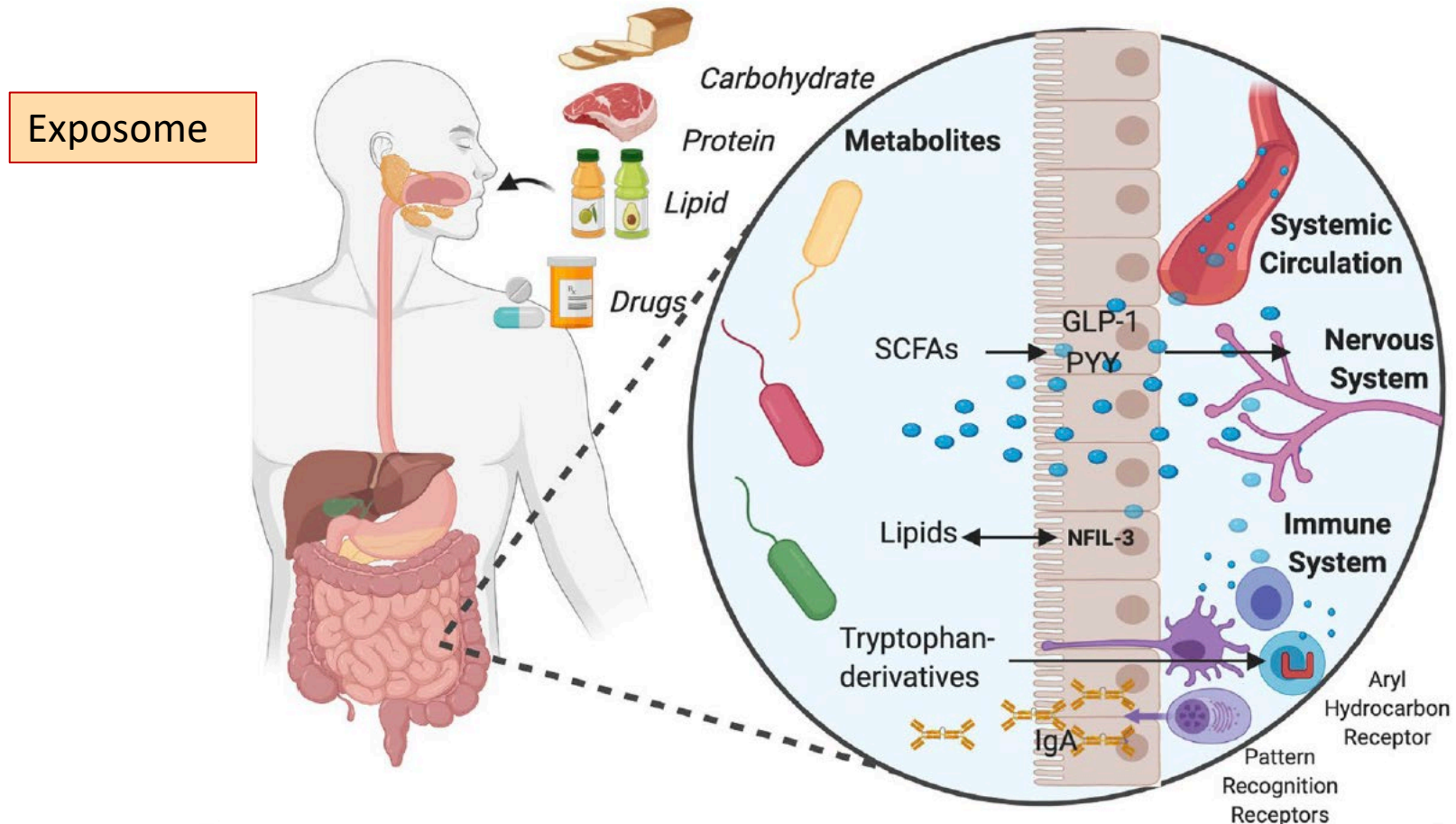
Microbes in the Gut Can Talk to the Brain



The Gut Talks to the Brain



The Microbiome Translates Food Components into Thousands of Biologically Active Metabolites Circulating throughout the Body, Including the Brain



The Gut and its Microbiome Are a Mirror Image of our Emotions

Psychosocial
Stress

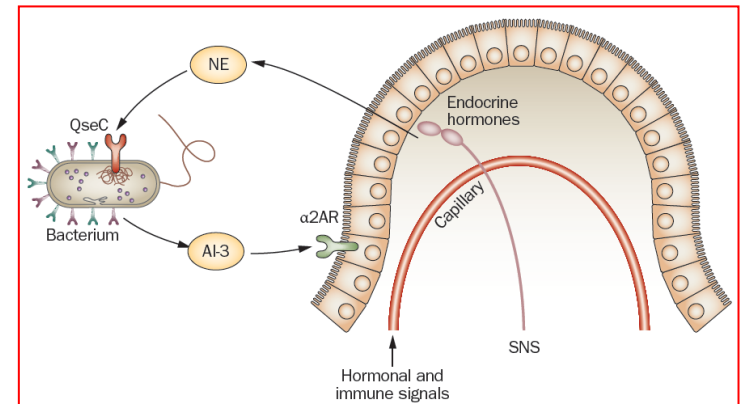
Anxiety, fear
Anger
Sadness



Changes of the microbial habitat:

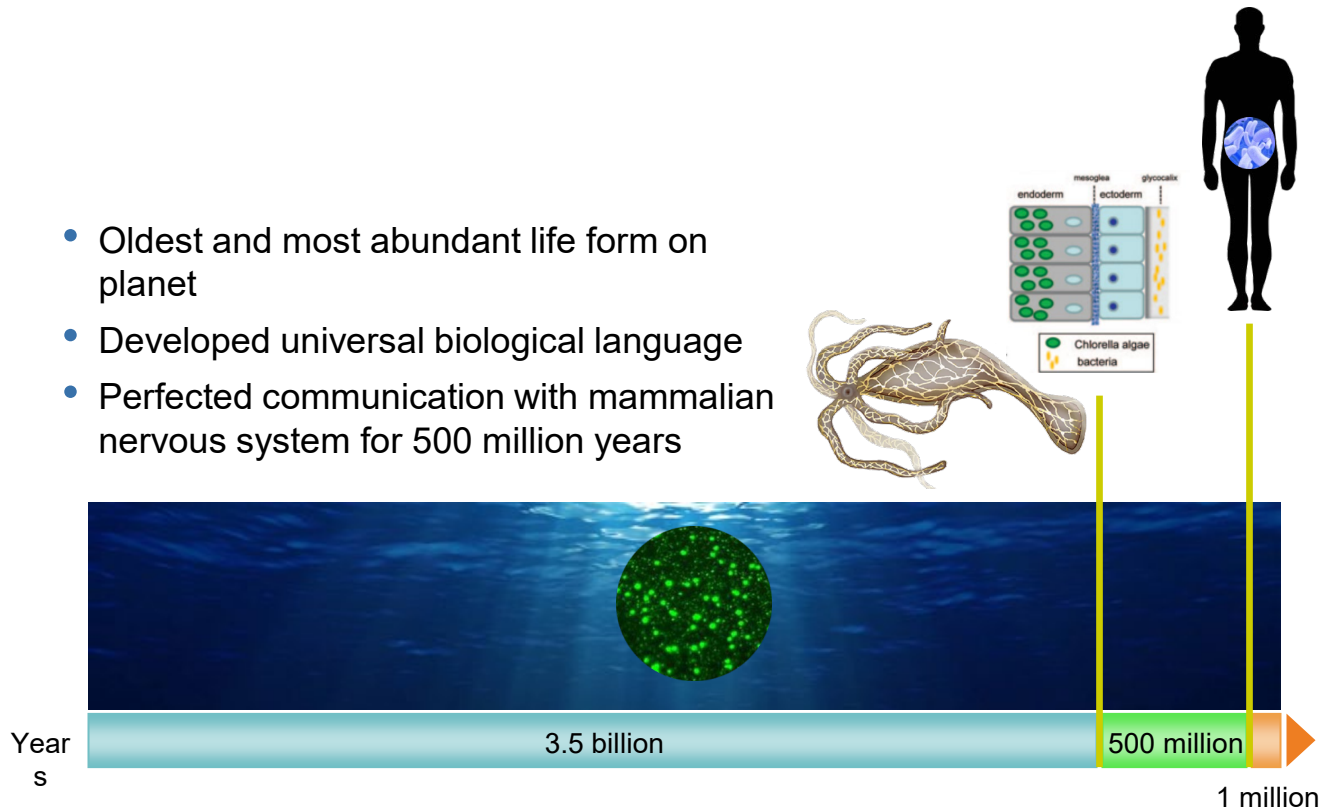
- Regional GI motility and transit
- Intestinal fluid and mucus secretion (biofilm?)
- Gastric/bile acid secretion
- Paneth cell secretion (antimicrobials)
- **Enteroendocrine cell function**
- Intraintestinal pH
- **Immune modulation**
- Epithelial & blood brain barrier permeability

Changes in microbial behavior:

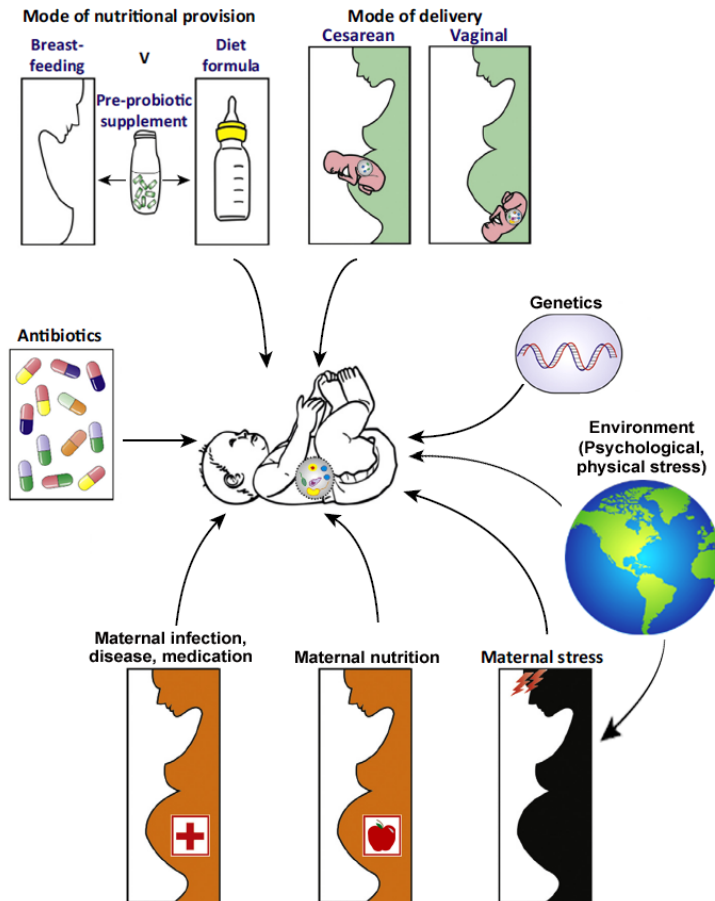


The Origin Story of the Human Gut Microbiome with the Brain

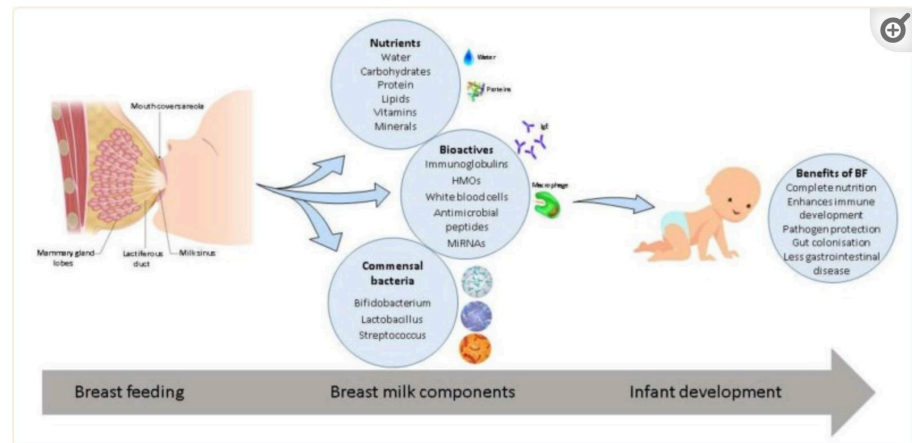
- Oldest and most abundant life form on planet
- Developed universal biological language
- Perfected communication with mammalian nervous system for 500 million years



The Origin Story of the Human Gut Microbiome



Prenatal Programming



Postnatal Programming

Lyons et al, Nutrients 2020

Jasarevic & Bale, 2019

Systems View of the Effects of Chronic Stress on Brain Gut Microbiome Interactions

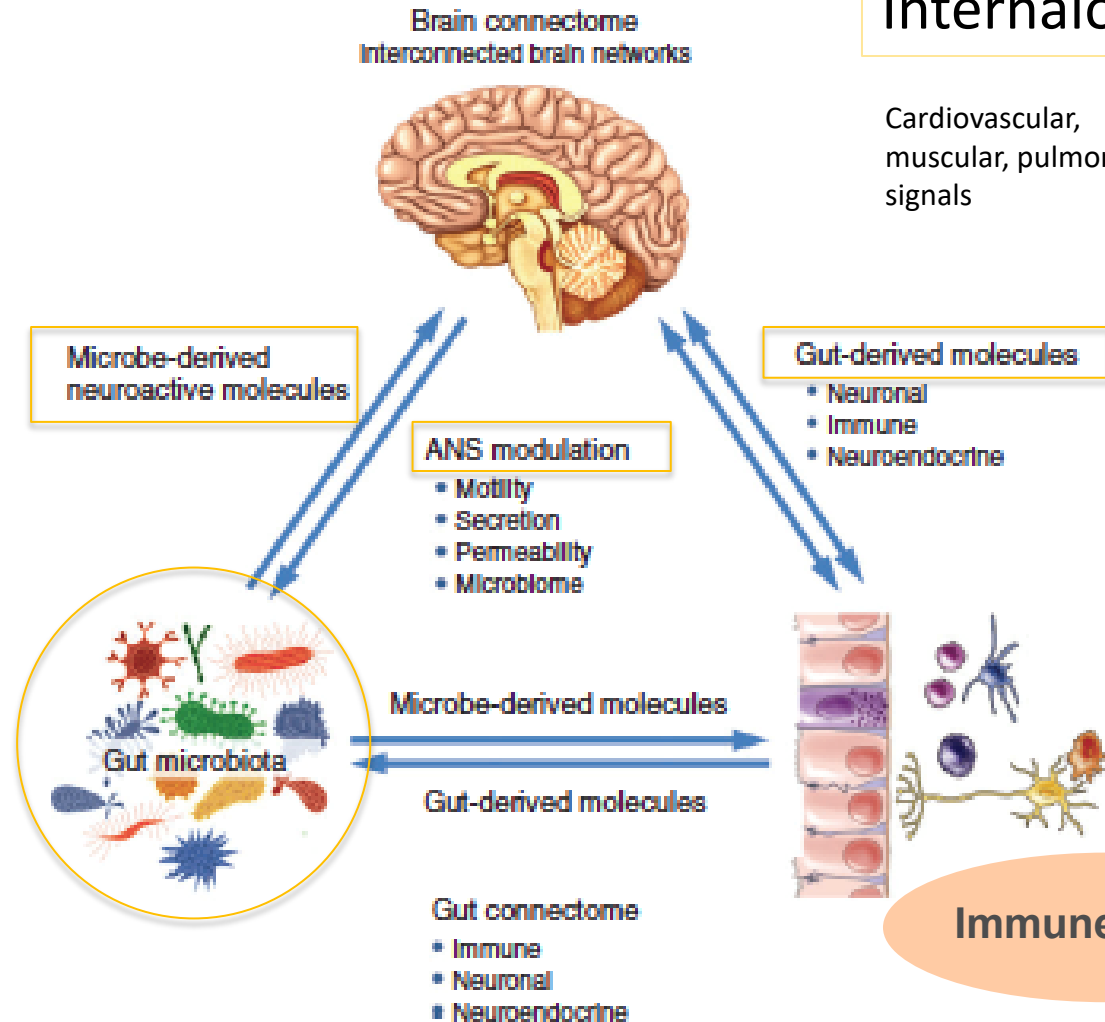
Exposome

Brain-targeted Stress

Allostatic load
Loneliness, isolation
Discrimination

Dietary Stress

Low fiber, high sugar
Chemicals
Ultra processed



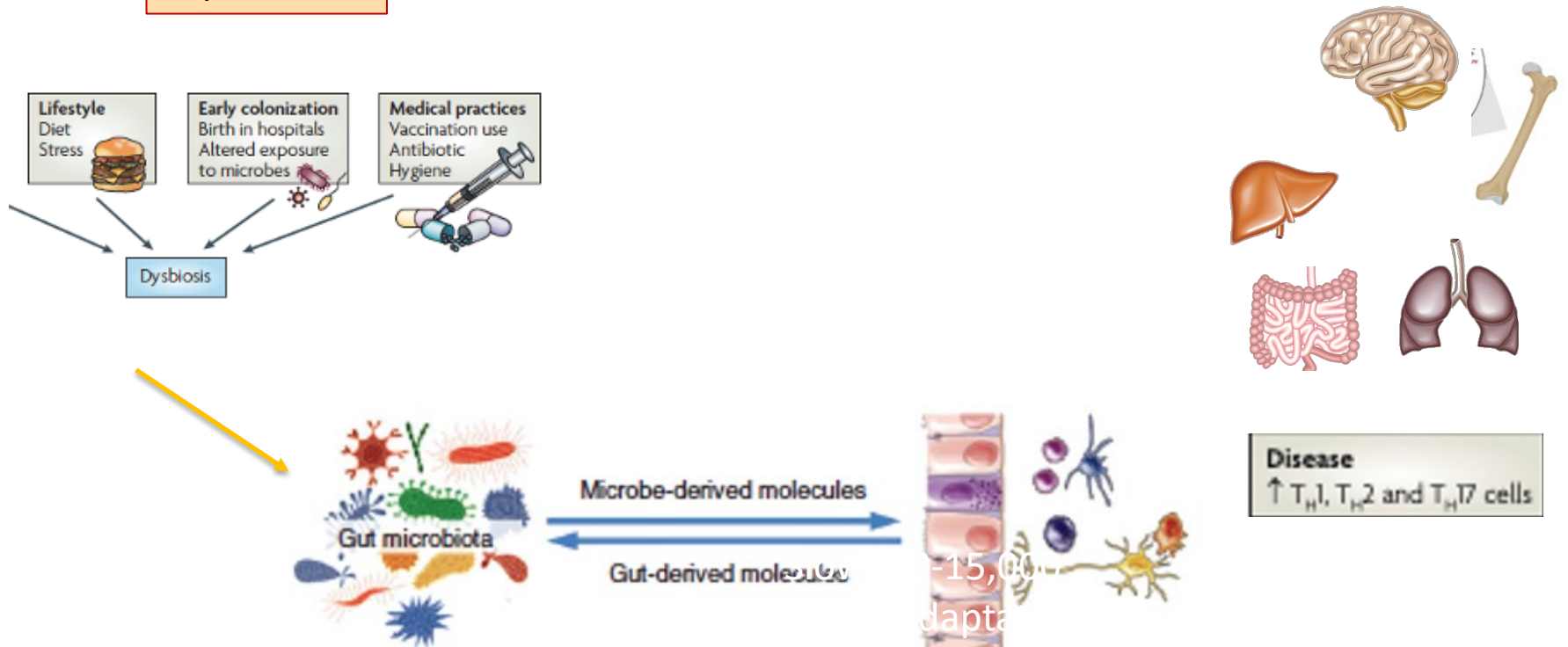
Internalome

Cardiovascular,
muscular, pulmonary
signals

Immune Stress

How Rapid Changes in the Exposome have Lead to Widespread Effects on the Body

Exposome



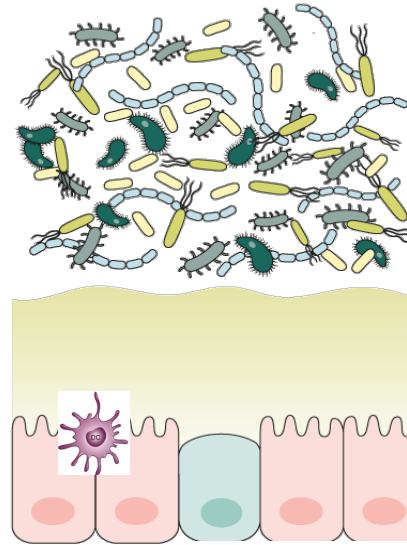
Healthy Diet

- Complex carbohydrates
- High fiber
- ↑ Fiber degradation
- ↑ Gut microbiome diversity
- ↑ Abundance of mucus-stimulating microorganisms
- ↑ Prevotella abundance

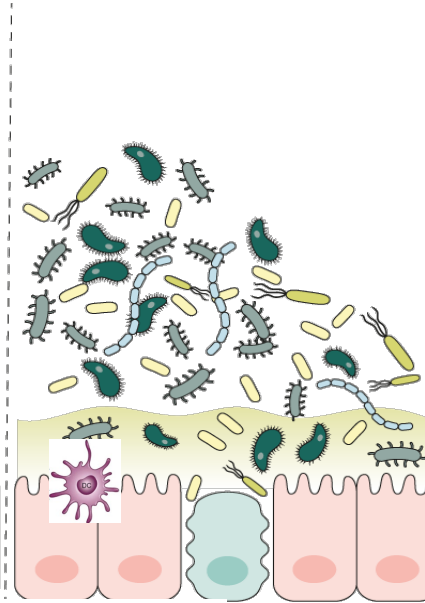
↑ Mucus thickness

Intact gut barrier

Healthy Gut



"Leaky" Gut



Chronic Stress

Western diet

- Refined carbohydrates, sugar
- High fat
- Low fiber
- ↓ Fiber degradation
- ↓ Gut microbiome diversity
- ↓ Abundance of mucus-stimulating microorganisms
- ↓ Prevotella abundance

↓ Mucus thickness

↓ Gut barrier

- Metabolic endotoxemia

Increased genetic risk

Metabolic syndrome

Osteoporosis

NAFLD

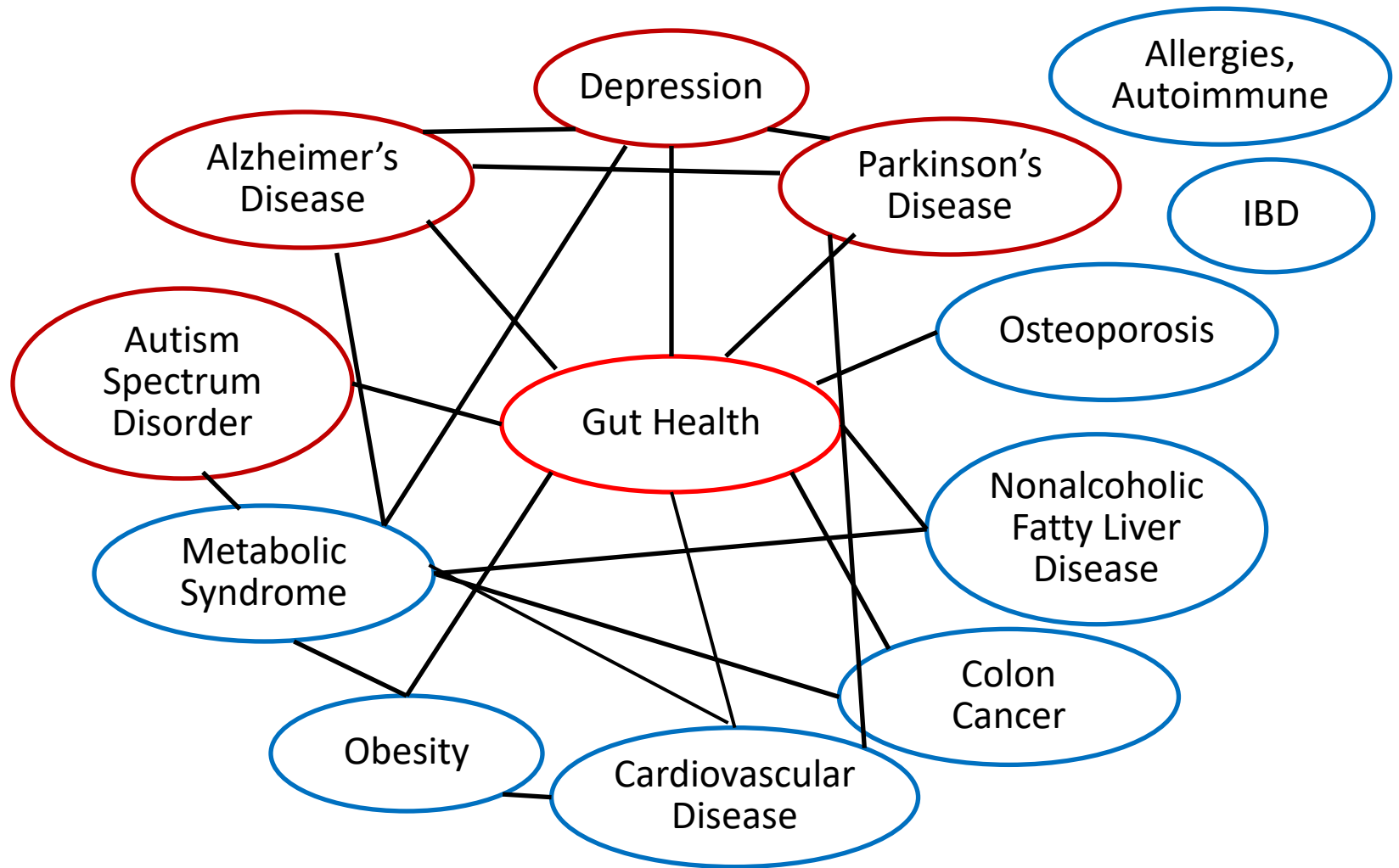
Colon cancer

Depression

Cognitive decline (AD)

Parkinson's Disease

Gut Health is at the Center of the Chronic Non-Communicable Disease Network



Parkinson's Disease

“a disordered state of the stomach and bowels may induce a morbid action in a part of the medulla spinalis”



“there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped.”

Gastrointestinal manifestations of Parkinson's Disease

- Dysphagia
- Gastroparesis
- Slow transit constipation
- Dyschezia
- Visceral hypersensitivity

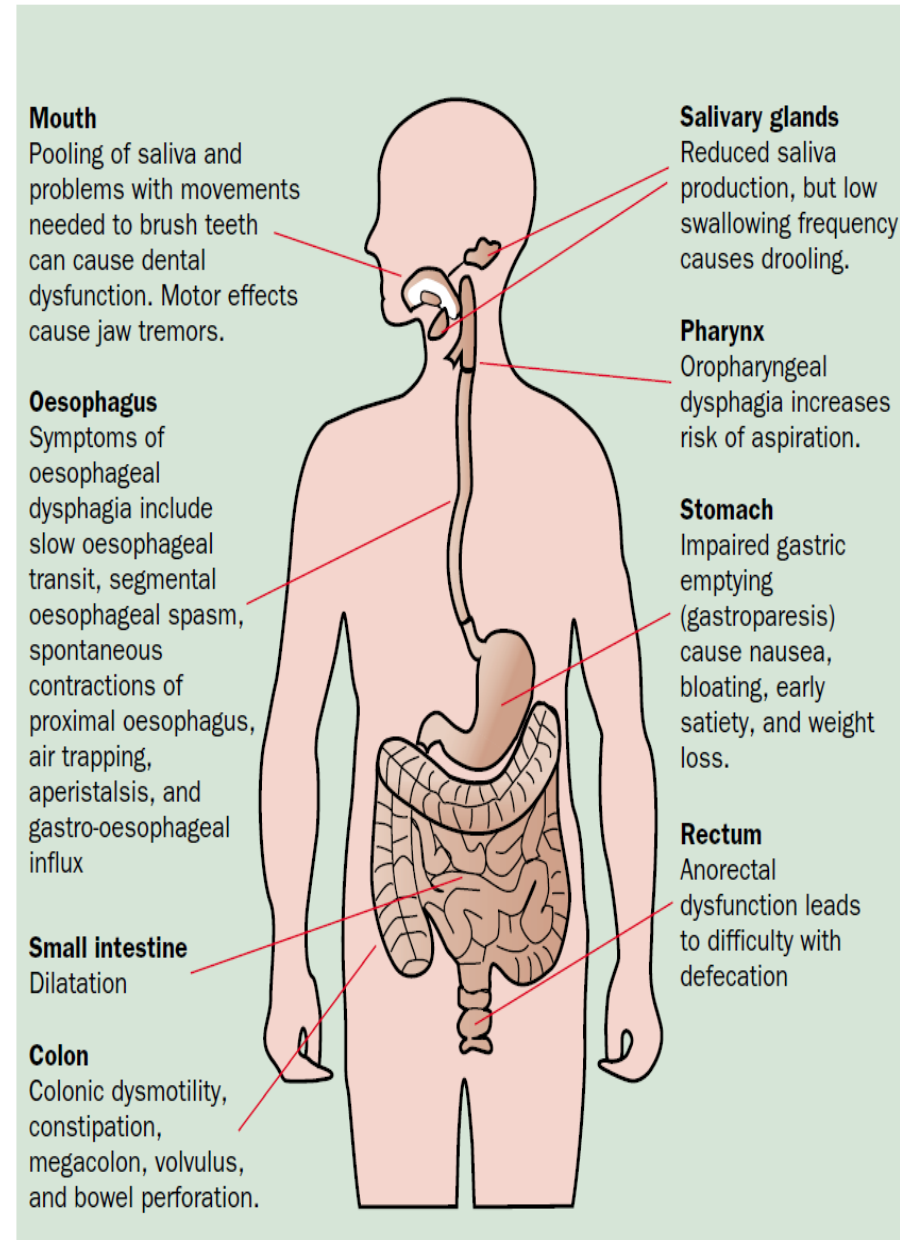


Figure 1. Overview of gastrointestinal dysfunction in PD.

Parkinson's Disease

Putative Role of Gut Microbial Brain Communication

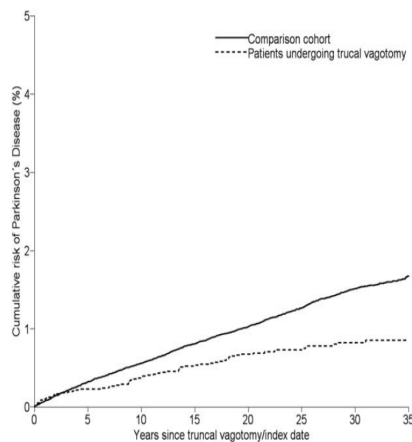
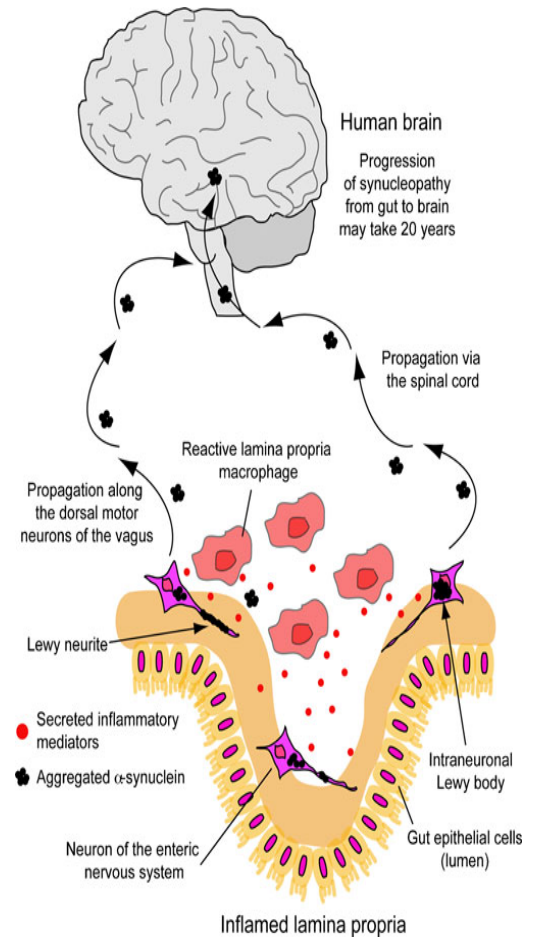
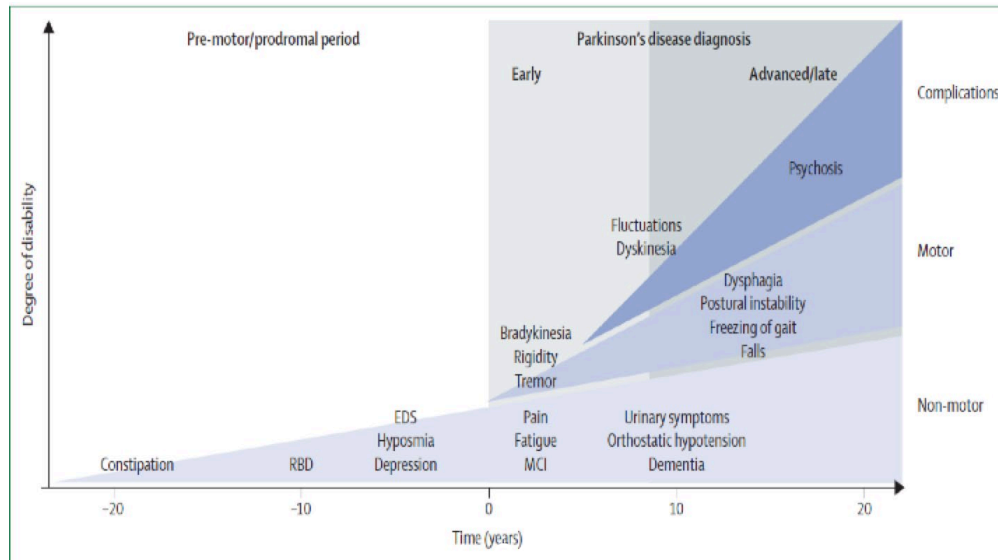


FIGURE 1: Cumulative incidence curves of Parkinson's disease for patients who underwent truncal vagotomy compared to a matched general population cohort.

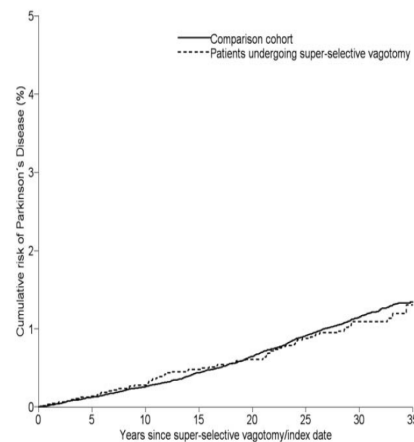


FIGURE 2: Cumulative incidence curves of Parkinson's disease for patients undergoing superselective vagotomy compared to a matched general population cohort.

Gut Microbiome Alterations in Depression

nature communications



Article

<https://doi.org/10.1038/s41467-022-34502-3>

Gut microbiome-wide association study of depressive symptoms

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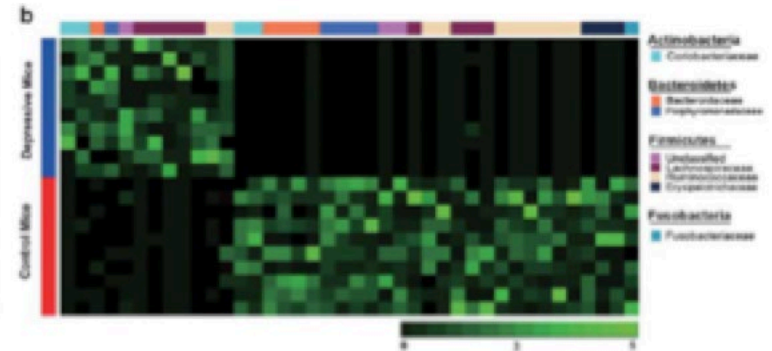
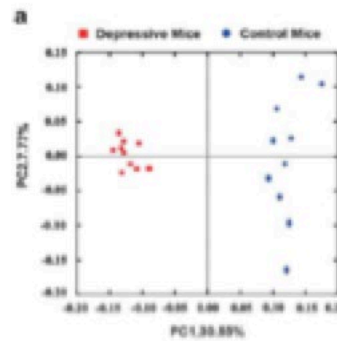
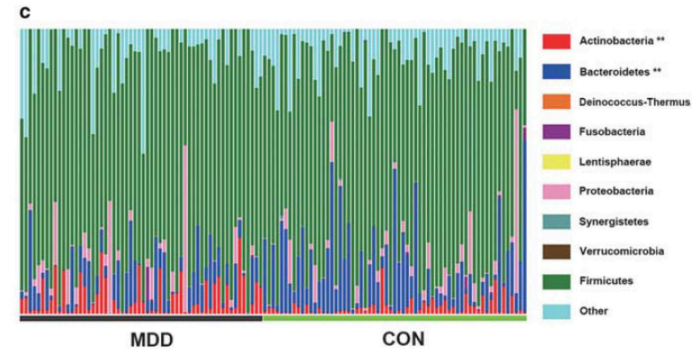
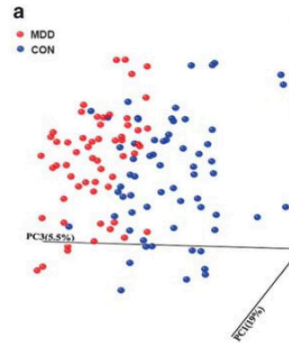
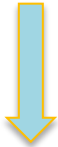
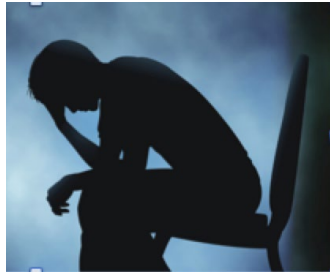
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Annemarie I. Luik ⁴, Max Nieuwdorp ⁶, Anja Lok ⁷, Cornelia M. van Duijn ^{4,8},
Robert Kraaij ¹ ✉ & Najaf Amin ^{4,8} ✉

Thirteen microbial taxa, including genera Eggerthella, Subdoligranulum, Coprococcus, Sellimonas, Lachnoclostridium, Hungatella, Ruminococcaceae, Lachnospiraceae, Eubacterium and family Ruminococcaceae were associated with depressive symptoms.

“These bacteria are known to be involved in the synthesis of glutamate, butyrate, serotonin and gamma amino butyric acid (GABA), which are key neurotransmitters for depression”

Depression:

Fecal Microbial Transfer of Altered Gut Microbiota from Patients with Major Depressive Disorder to GF Mice



SCIENTIFIC REPORTS



OPEN

Long-term benefit of Microbiota Transfer Therapy on autism symptoms and gut microbiota

Received: 3 December 2018

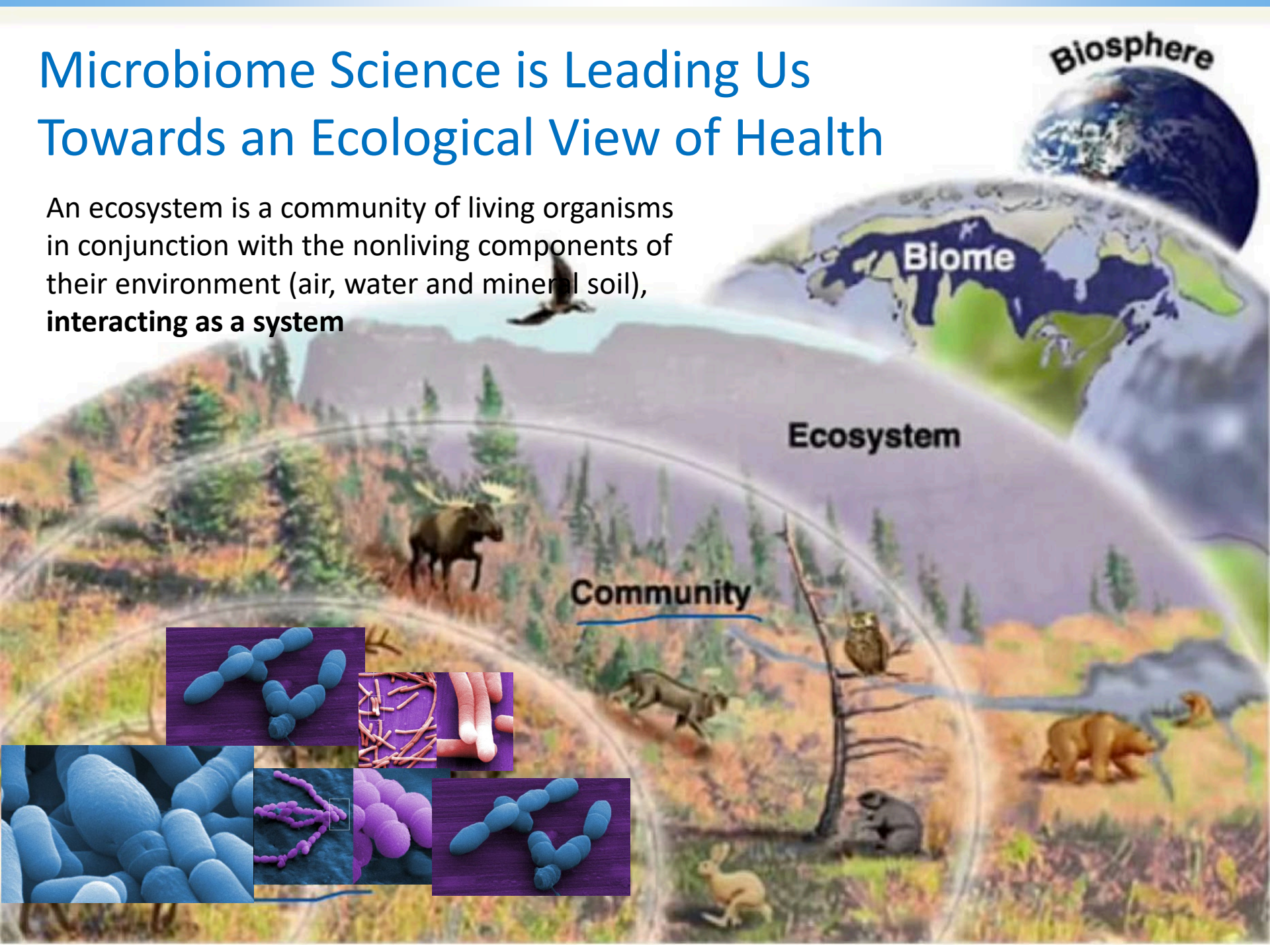
Accepted: 5 March 2019

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Microbiome Science is Leading Us Towards an Ecological View of Health

An ecosystem is a community of living organisms in conjunction with the nonliving components of their environment (air, water and mineral soil), **interacting as a system**



Conclusions

- The microbiome with its billions of years of evolution stored in millions of genes is the thread weaving human, animal, plant, and planetary health
- The human gut microbiome has the highest density of microorganisms on the planet and it translates dietary factors and environmental toxins into signals modulating the immune, metabolic and nervous system.
- Major disturbances of the health of our natural ecosystems by how we grow our food, how we interact socially, our exposure to chronic stress and how we have treated our gut microbiome during the past 100 years are being translated into different aspects of human health and chronic diseases.

Conclusions

- Ecosystem deterioration and extinction of key players decreasing diversity, and richness is impacting key determinants of human and animal health:
 - Widespread low grade immune system activation
 - Reduced resilience to perturbations by the exposome to natural and pathogenic perturbations leading to reduced resilience
- **The understanding and treatment of our most common chronic diseases require a systems biological understanding based on the interconnectedness of brain and body and of multiple ecosystems on planet Earth**

Is Microbiome Science Causing a Fundamental Transformation of Our View of Health?

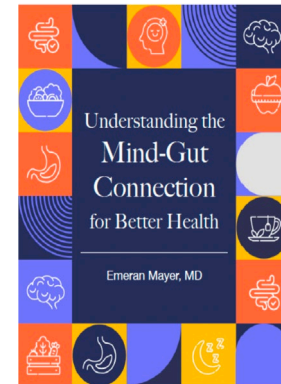
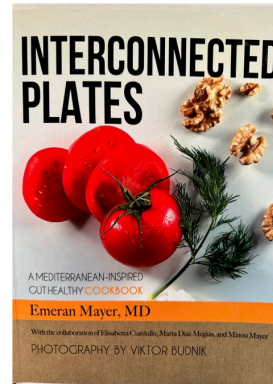
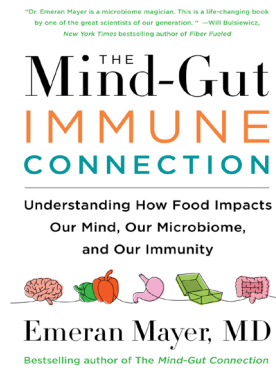
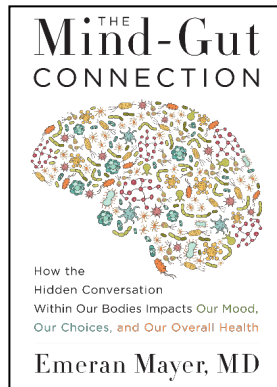
Science is a series of peaceful interludes punctuated by intellectually violent revolutions ... in each of which one conceptual world view is replaced by another..

The Structure of Scientific Revolutions,
Thomas S. Kuhn, 1962



Courtesy of E.
Schadt

Thank You!



Scan

