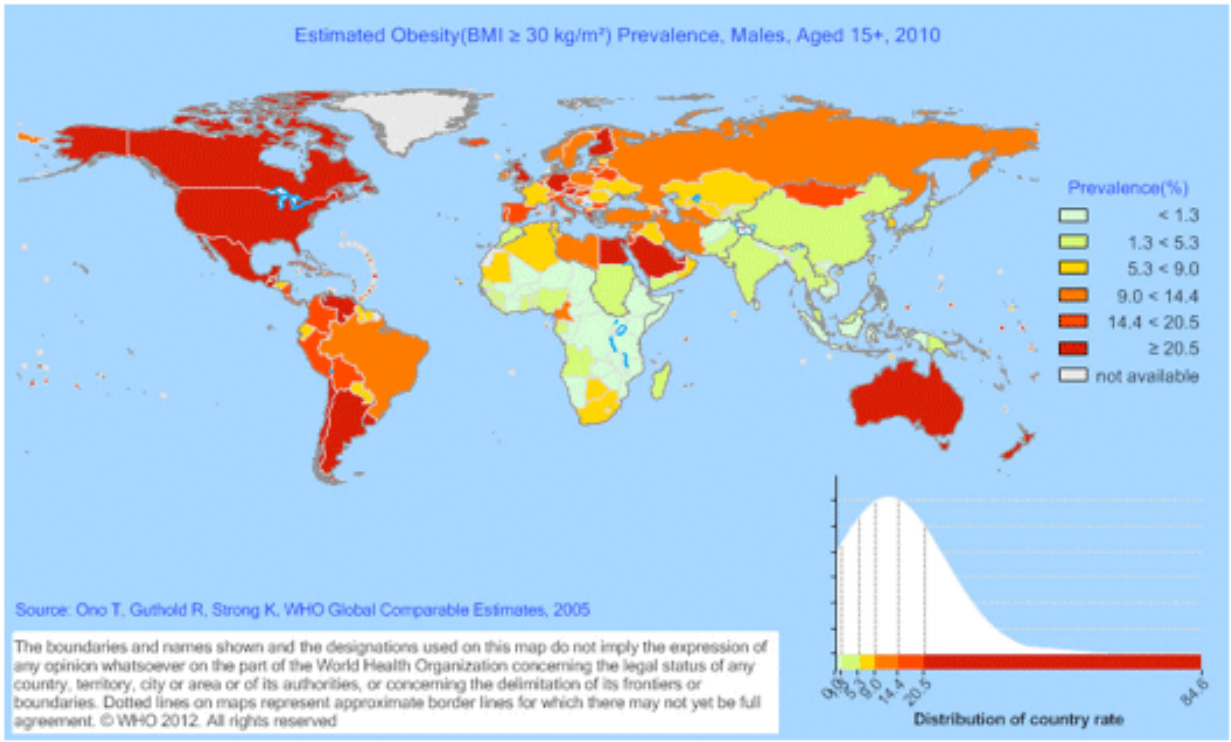
CIBO E CERVELLO

Neurogastronomia tra piaceri alimentari e disordini dietetici

Globesity, un problema… di testa

Ferruccio Cavanna

image: Paul Lachine / newsart



Ferruccio Cavanna

Source: WHO

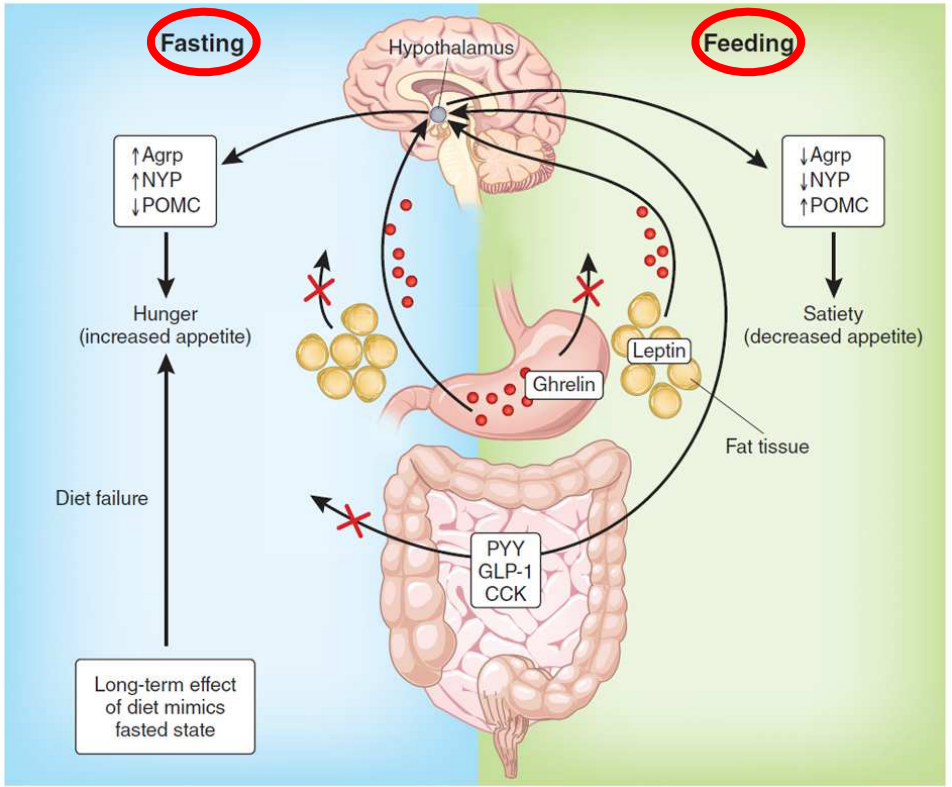
La stragrande maggioranza delle nostre conoscenze relative al controllo dell'appetito sono basate sulle cascate di segnali molecolari, da cui emerge che il cervello è il sito chiave di regolazione del bilancio fame/sazietà.

Infatti il cervello riceve una gran varietà si segnali omeostatici che riguardano lo stato energetico che vengono integrati con segnali sociali (ambiente) ed edonicistici (personali)

Producendo come risposta:

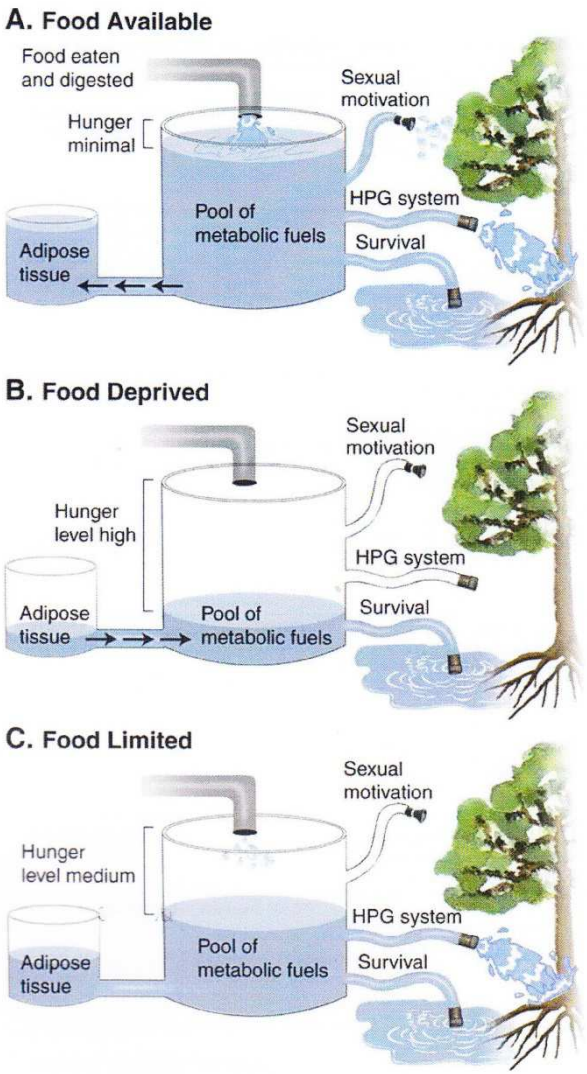
1. **Un segnale di fame: promuovendo l'assunzione di cibo**

2. **Un segnale di sazietà: inducendo una limitazione all'assunzione di alimenti**



Tuttavia dobbiamo rilevare un fenomeno paradossale ossia il fatto che un aumento di peso (presumibilmente relativo ad un superimmagazzinamento di energia) non induce una diminuzione dell'assunzione di energia.

In altre parole il sistema di controllo sembra molto più sensibile ad una diminuzione di energia ed al contrario molto tollerante in caso di surplus energetico.



..possiedo questo gene bastardo

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REVIEW ARTICLE

Microbes and the gut-brain axis

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Abstract

Background *The 'gut-brain' or 'brain-gut axis', depending on whether we emphasize bottom-up or top-bottom pathways, is a bi-directional communication system, comprised of neural pathways, such as the enteric nervous system (ENS), vagus, sympathetic and spinal nerves, and humoral pathways, which include cytokines, hormones, and neuropeptides as signaling molecules. Recent evidence, mainly arising from animal models, supports a role of microbes as signaling components in the gut-brain axis.* ***Aims*** *The purpose of this review is to summarize our current knowledge regarding the role of microbes, including commensals, probiotics and gastrointestinal pathogens, in bottom-up pathways of communication in the gut-brain axis. Although this has clear implications for psychiatric co-morbidity in functional and inflammatory conditions of the gut, the focus of this review will be to discuss the current evidence for a role of bacteria (commensals, probiotics, and pathogens) as key modulators of gut-brain communication.* ***Results & Conclusions*** *The strongest evidence for a role of microbes as signaling components in the gut-brain axis currently arises from animal studies and indicate that mechanisms of communication are likely to be multiple. There is need for the concepts generated in animal models to be translated to the human in the future.*

INTRODUCTION

Clinicians and researchers have long recognized the link between gastrointestinal function and the central nervous system (CNS). Although the original description of a gut-brain axis related to the modulation of cholecystokinin secretion by bombesin,[1] the concept has since then been extended to describe any interaction between the gastrointestinal tract and the CNS. Recently, results in animal models have generated great interest into the role of intestinal microbes as key players in gut-brain communication (Fig. 1). The neural aspects and the role of centrally-driven pathways in gut-brain axis communication have recently been reviewed in detail by Mayer *et al.*[2] and O'Mahony *et al.*[3]

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Intestinal microbiota and gut homeostasis

The intestinal microbiota involves a wide diversity of microbial species[4] and can be considered a postnatal acquired organ that performs different functions for the host. Intestinal microbes have developed a mutualistic relationship with its host and play a crucial role in the development of innate and adaptive immune responses,[5,6] influence physiological systems throughout life by modulating gut motility, intestinal barrier homeostasis,[7,8] absorption of nutrients and the distribution of somatic and visceral fat.[9,10]

The intestinal microbiota consists of a community of bacteria that colonize the gastrointestinal tract after birth and persist throughout adult life, and 'transient' bacteria, such as probiotic bacteria, which are temporarily acquired during ingestion of certain foods. The composition of the intestinal microbiota is established during the first few years of life and is likely shaped by multiple factors including maternal vertical transmission, genetic make up of the individual, diet, medications such as antibiotics, gastrointestinal infections and stress[11–15] (Fig. 2). Until recently composition of this microbial community was considered unique for each individual and relatively stable over time.[16,17] However, using deep sequencing of stool samples from

PROGRESS

The interplay between the intestinal microbiota and the brain

Stephen M. Collins, Michael Surette and Premysl Bercik

Abstract | The intestinal microbiota consists of a vast bacterial community that resides primarily in the lower gut and lives in a symbiotic relationship with the host. A bidirectional neurohumoral communication system, known as the gut–brain axis, integrates the host gut and brain activities. Here, we describe the recent advances in our understanding of how the intestinal microbiota communicates with the brain via this axis to influence brain development and behaviour. We also review how this extended communication system might influence a broad spectrum of diseases, including irritable bowel syndrome, psychiatric disorders and demyelinating conditions such as multiple sclerosis.

Humans coexist in a mutualistic relationship with the intestinal microbiota, a complex microbial ecosystem that resides largely in the distal bowel. The lower gastrointestinal tract contains almost 100 trillion microorganisms, most of which are bacteria. More than 1,000 bacterial species have been identified in this microbiota, primarily using molecular-based approaches because the majority of bacteria are strict anaerobes and have not yet been cultivated. Two bacterial divisions, the genus *Bacteroides* and the phylum Firmicutes, account for over 90% of the known phylogenetic categories in the intestinal microbiota. Although there is considerable intersubject variation in the intestinal microbiome, a core microbiome exists that is shared between individuals[1]. The microbiota collectively encodes more than 3.3 million non-redundant genes[1] — exceeding the number encoded by the human host genome by 150-fold — and many microbial gene products have important effects on metabolism and the health of the host. The advent of massively parallel DNA sequencing has enabled metagenomic and metatranscriptomic analyses that, coupled with proteomic and metabolomic studies, have brought about a resurgence of interest in the intestinal microbiome and its impact on a wide range of host processes in health and disease. In particular, recent studies have hinted that the microbiota can have dramatic effects on the development and function of the host brain.

The notion that the commensal intestinal microbiota can influence brain function has at least one clear clinical origin: the observation that orally administered antibiotics can reverse encephalopathy in patients with decompensated liver disease[2]. Furthermore, psychiatric disorders frequently coexist with common gastrointestinal conditions, such as irritable bowel syndrome (IBS), that are also associated with disturbances of the intestinal microbiota[3]. Emerging animal-based research has extended the idea of microbiota–brain interactions to other psychiatric disorders, as well as to immunologically mediated neurological conditions such as multiple sclerosis (MS) and to the exciting area of early brain development. Thus, this rapidly emerging field has the potential not only to increase our understanding of a broad spectrum of human disease, but also to generate novel therapies for these conditions based on the identification of mechanisms underlying microorganism–host interactions.

Here, we review recent progress in understanding the bidirectional interactions between the intestinal microbiota and the brain, and propose a novel conceptual model of a 'microbiota–gut–brain axis', as illustrated in FIG. 1. We go on to assess the evidence for the microbiota–gut–brain axis in a range of neurological diseases.

The gut–brain axis

The gut–brain axis is a communication system that integrates neural, hormonal and immunological signalling between the gut and the brain[4] (BOX 1), and provides the intestinal microbiota and its metabolites with a potential route through which to access the brain. This communication system is bidirectional, enabling the brain to influence gastrointestinal functions (such as motility, secretion and mucin production) as well as immune functions[4] (including the modulation of cytokine production by cells of the mucosal immune system[5]). Emotional factors such as stress or depression influence the natural history of chronic gastrointestinal illnesses such as inflammatory bowel diseases[6] (the two most common of which are Crohn's disease and ulcerative colitis) and IBS[4] via the gut–brain axis. These conditions are also associated with dysbiosis[7]. Stress has been shown to influence the integrity of the gut epithelium and to alter gut motility, secretions and mucin production, thereby altering the habitat of resident bacteria and promoting changes in microbial composition or activity[8]. In addition, stress-induced release of catecholamines into the gut might influence the microbial community by interfering with interbacterial signalling as well as with the expression of bacterial virulence genes[9,10].

Brain development

Studies using well-established behavioural tests[11] (BOX 2) of young germ-free animals have demonstrated the ability of the intestinal microbiota to influence brain development. The response of the hypothalamic pituitary to mild stress is exaggerated in germ-free mice and is normalized following monocolonization of mice with *Bifidobacterium longum* subsp. *infantis* (strain not identified) at 6 weeks of age but not at 14 weeks[12]. Interestingly, in specific-pathogen-free mice (SPF mice), the response is only partially attenuated, indicating that the microbiota contains bacteria that can either enhance or suppress the hypothalamic pituitary axis[12]. Recent studies[13,14] have shown that germ-free mice exhibit more exploratory and risk-taking behaviours as well as more locomotion than SPF mice, and

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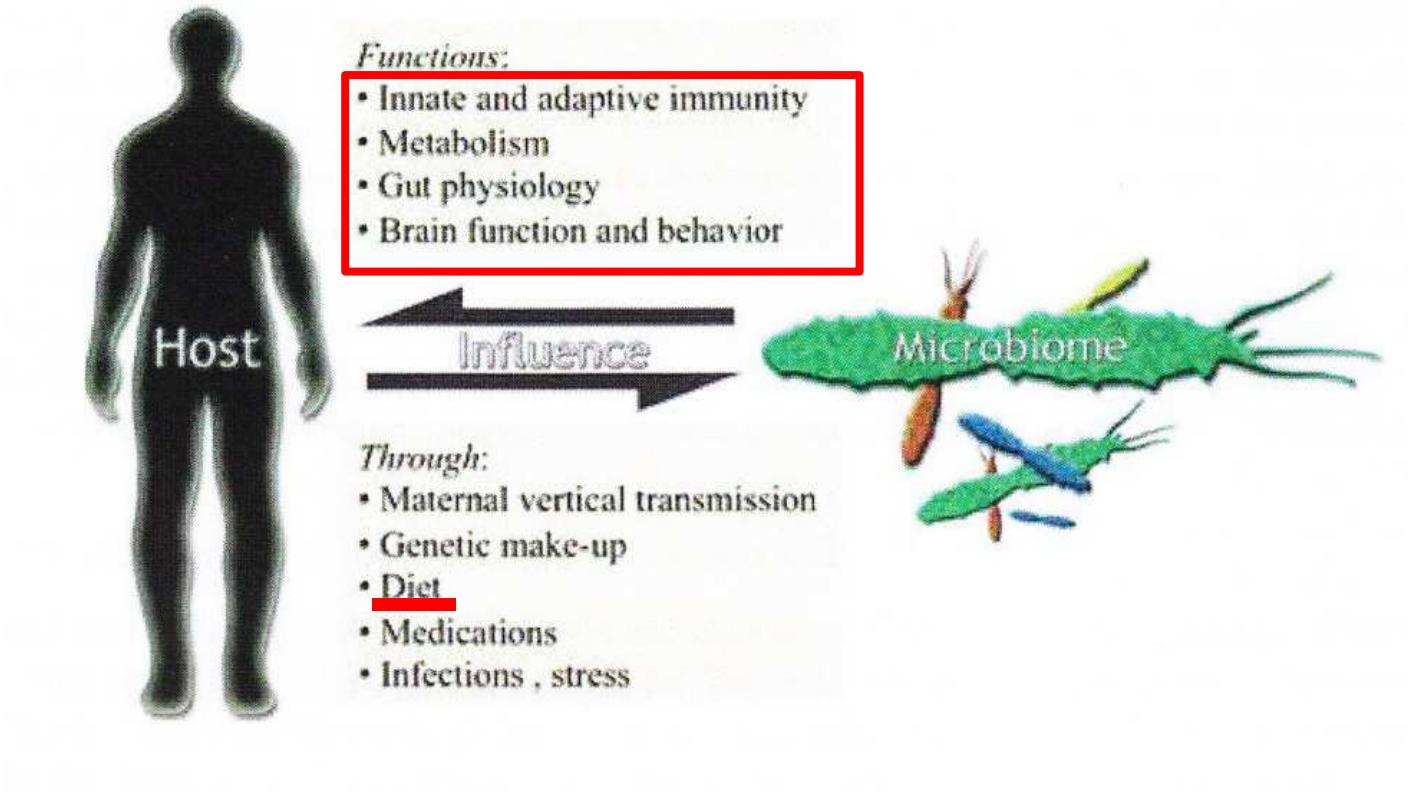
Il ruolo della microflora intestinale è stato largamente sottovalutato fino agli anni ‘80.
Questo disinteresse derivava fondamentalmente da due valide ragioni:

1. Ragione **colturale**, nel senso che la stragrande maggioranza dei batteri fecali non potevano essere coltivati e di conseguenza microbiologicamente era difficile la loro classificazione

1. Ragione **culturale**: la microflora è sempre stata considerata dai clinici come potenzialmente nemica, per cui si è focalizzato l’interesse sulle tossine pericolose frutto delle fermentazioni batteriche.

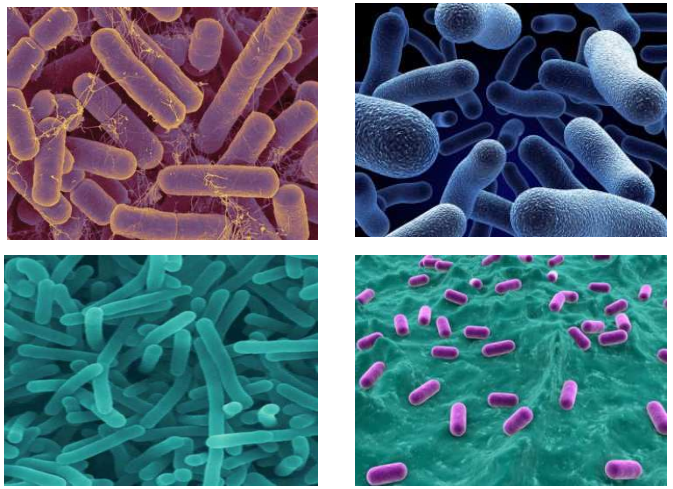
Poi negli anni ‘90 la grande scoperta che i microbi della microflora intestinale non solo **NON** sono patogeni (pericolosi) ma addirittura fondamentali per la fisiologia umana.



Immediatamente dopo la nascita tutti i mammiferi iniziano un lungo processo di colonizzazione da parte di microrganismi esterni, che diventano “indigeni”, delle superfici più facilmente esposte all’ambiente esterno (pelle, bocca, vagina, ma soprattutto intestino)
Modulati da millenni di evoluzione alcune associazioni ospite-batterio si sono sviluppate in relazioni di mutuo beneficio.
L’esempio chiave ci è fornito dal vasto numero e dalla diversità di batteri che si trovano nel tratto gastrointestinale:

50 generi di organismi
500 specie diverse
10 volte il numero di cellule che costituiscono l‘organismo umano
100 volte il numero di geni del genoma umano

MICROBIOTA



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Gli adulti del genere umano convivono con uno dei più complessi ecosistemi del pianeta che conta:
SIMBIONTI: batteri che vivono con beneficio dell'organismo ospite
COMMENSALI: batteri che convivono beneficiando di un organismo ospite
PATOBIONTI: organismi che convivono con un organismo ospite senza recar danno o beneficio in condizioni normali

PATOGENI: batteri esterni che infettando un organismo ospite scatenano un´infezione

I batteri **SIMBIONTI** sono apprezzati per i numerosi benefici che apportano all'organismo ospite:

- forniscono nutrienti essenziali
- metabolizzano composti che altrimenti sarebbero indigeribili
- difendono contro la colonizzazione di patogeni indesiderati
- addirittura contribuiscono all'architettura e funzionalità intestinale

Stomach

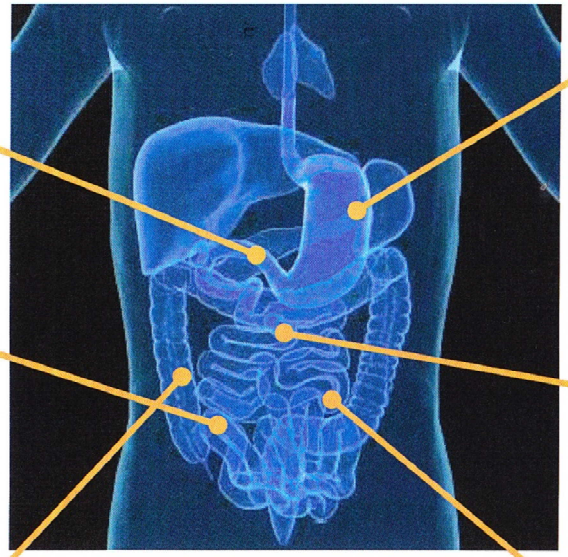
10^1-10^3 cfu/ml

- Lactobacillus
- Candida
- Streptococcus
- Helicobacter pylori
- Peptostreptococcus

Duodenum

10^1-10^3 cfu/ml

- Lactobacillus
- Streptococcus



Distal Ileum

10^7-10^8 cfu/ml

- Clostridium
- Bacteroides sp
- Coliforms

Jejunum

10^2 cfu/ml

- Lactobacillus
- Streptococcus

Proximal Ileum

10^3 cfu/ml

- Lactobacillus
- Streptococcus
- Actinobacteria

Colon

10^{11}-10^{12} cfu/ml

- Clostridium coccoides
- Clostridium leptum
- Fusobacterium
- Bacteroides
- Bifidobacterium

Review series

Gut microbiome, obesity, and metabolic dysfunction

Herbert Tilg[1] and Arthur Kaser[2]

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[2]Division of Gastroenterology and Hepatology, Department of Medicine, University of Cambridge, Cambridge, United Kingdom.

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REVIEWS IN ADVANCE

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Interaction Between Obesity and the Gut Microbiota: Relevance in Nutrition

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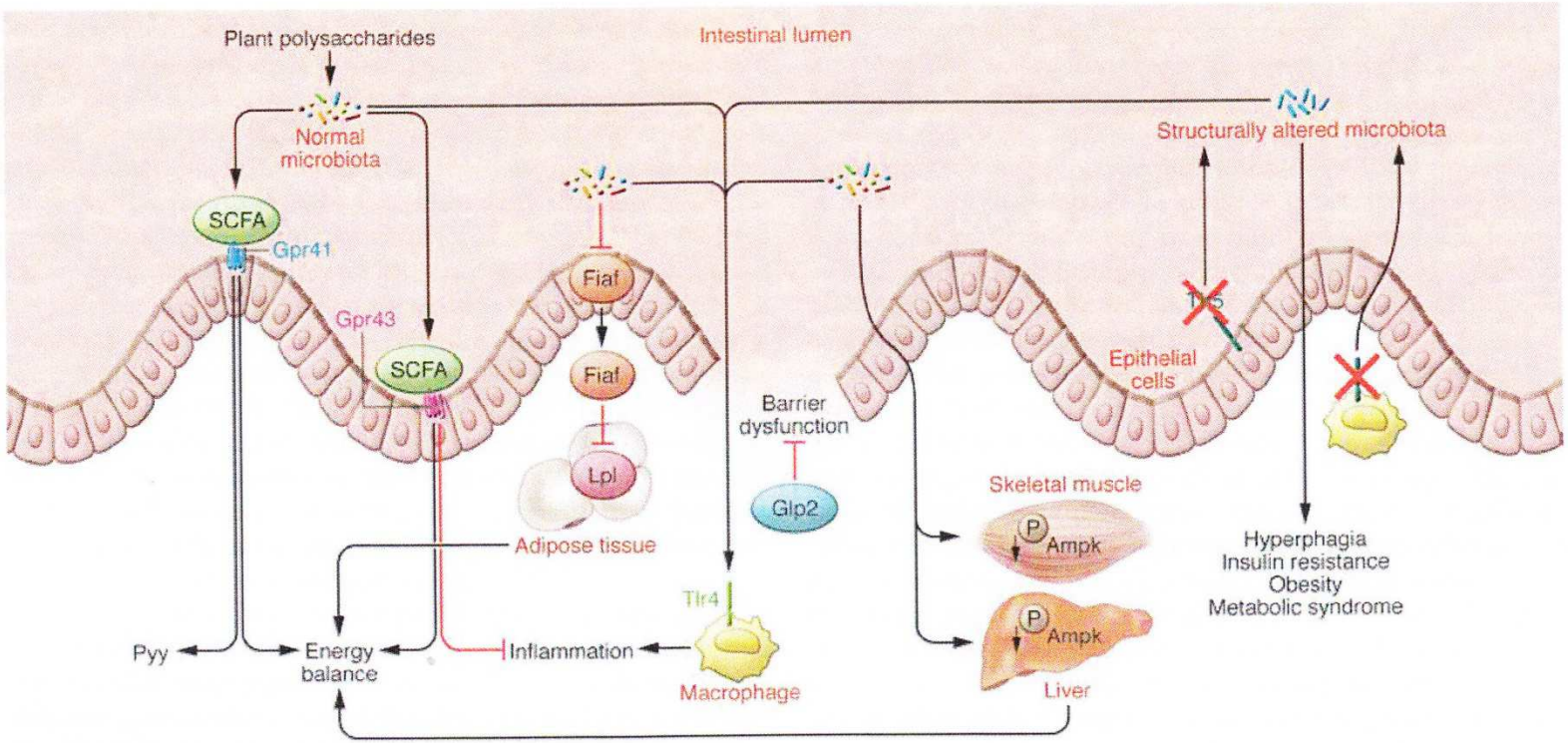

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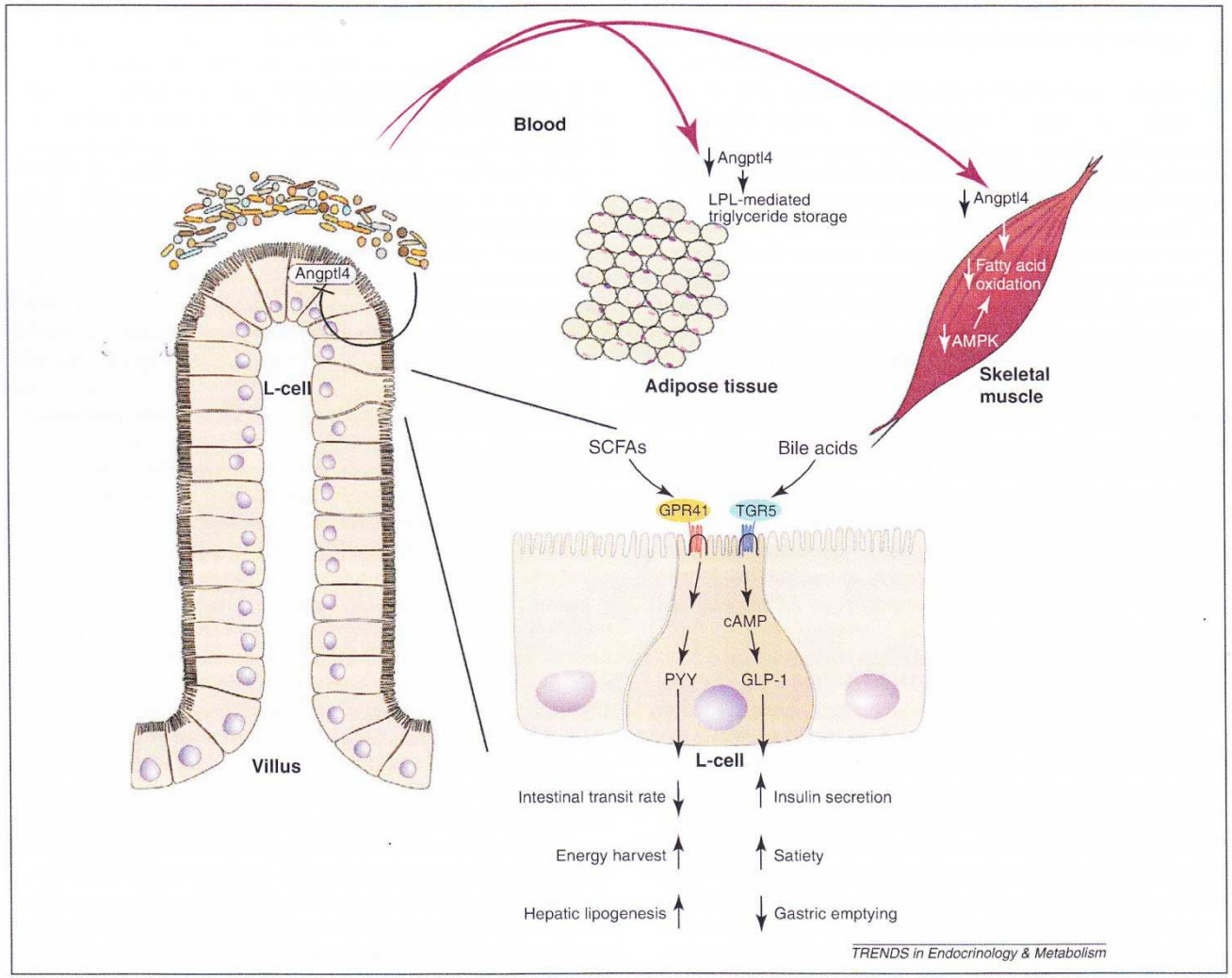

Figure 1. Gut microbiota regulation of host metabolism. The gut microbiota suppresses enterocyte expression of Angptl4; this alleviates LPL inhibition and promotes LPL-mediated triglyceride storage in adipose tissue. In addition, reduced Angptl4 levels together with diminished activation of AMPK reduce fatty acid oxidation in skeletal muscle. The gut microbiota has also direct effects on enteroendocrine L-cells: microbially generated short-chain fatty acids (SCFAs) bind to the G-protein-coupled receptor (GPCR) Gpr41 which stimulates secretion of the gut hormone PYY. Secretion of PYY leads to reduced intestinal transit, increased energy harvest, and stimulates hepatic lipogenesis. The gut microbiota generates secondary bile acids that are the major ligands for the GPCR TGR5. Stimulation of TGR5 enhances GLP-1 secretion, and this promotes increased insulin secretion, satiety, and reduced gastric emptying.

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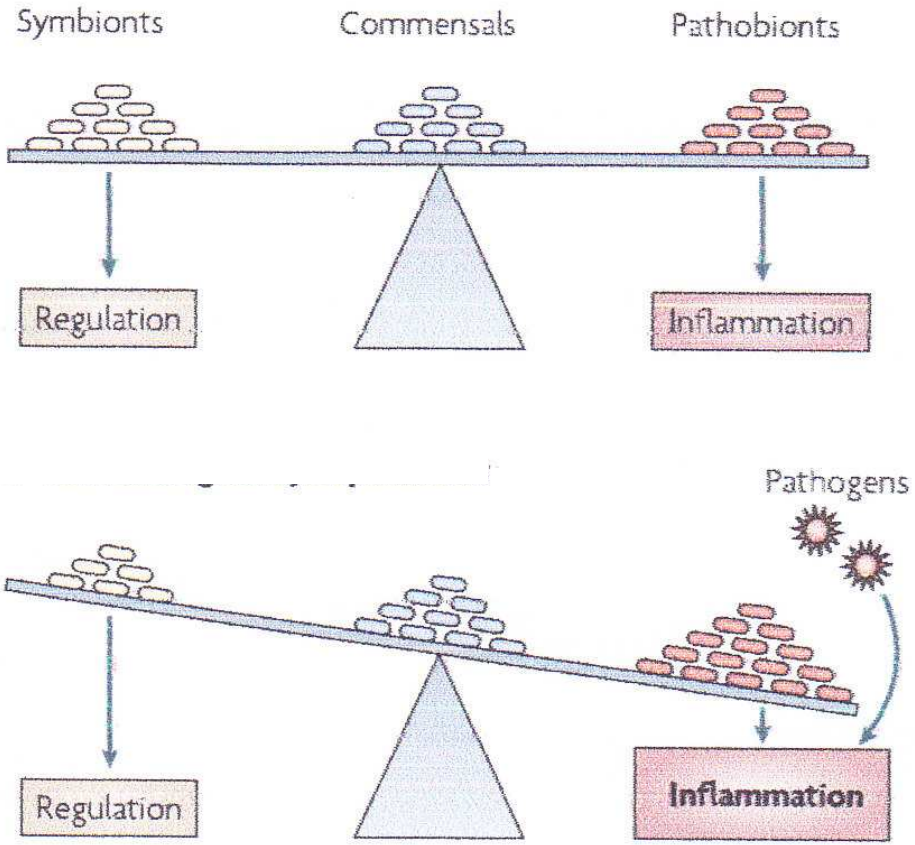
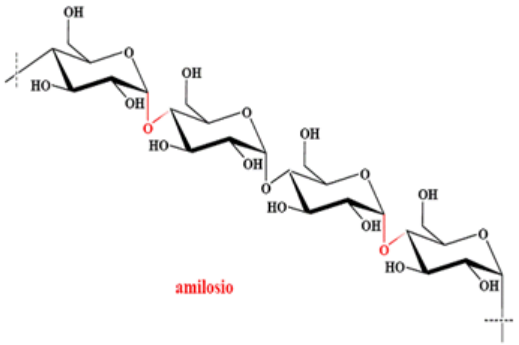
E’ facile ipotizzare che alterazioni nello sviluppo e/o nella composizione della flora perturbino la partnership ospite-batteri con significative ripercussioni sulla fisiologia generale, questa situazione è denominata **DISBIOSI**.

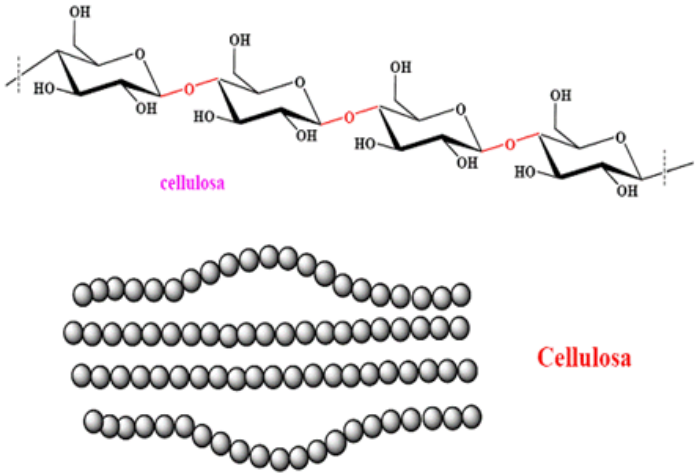


LE FIBRE

la fibra alimentare è la componente dietetica resistente alla degradazione da parte degli enzimi del corredo enzimatico.

Dal punto di vista chimico si tratta per lo più di polisaccaridi, ossia di molecole di zucchero legate tra di loro



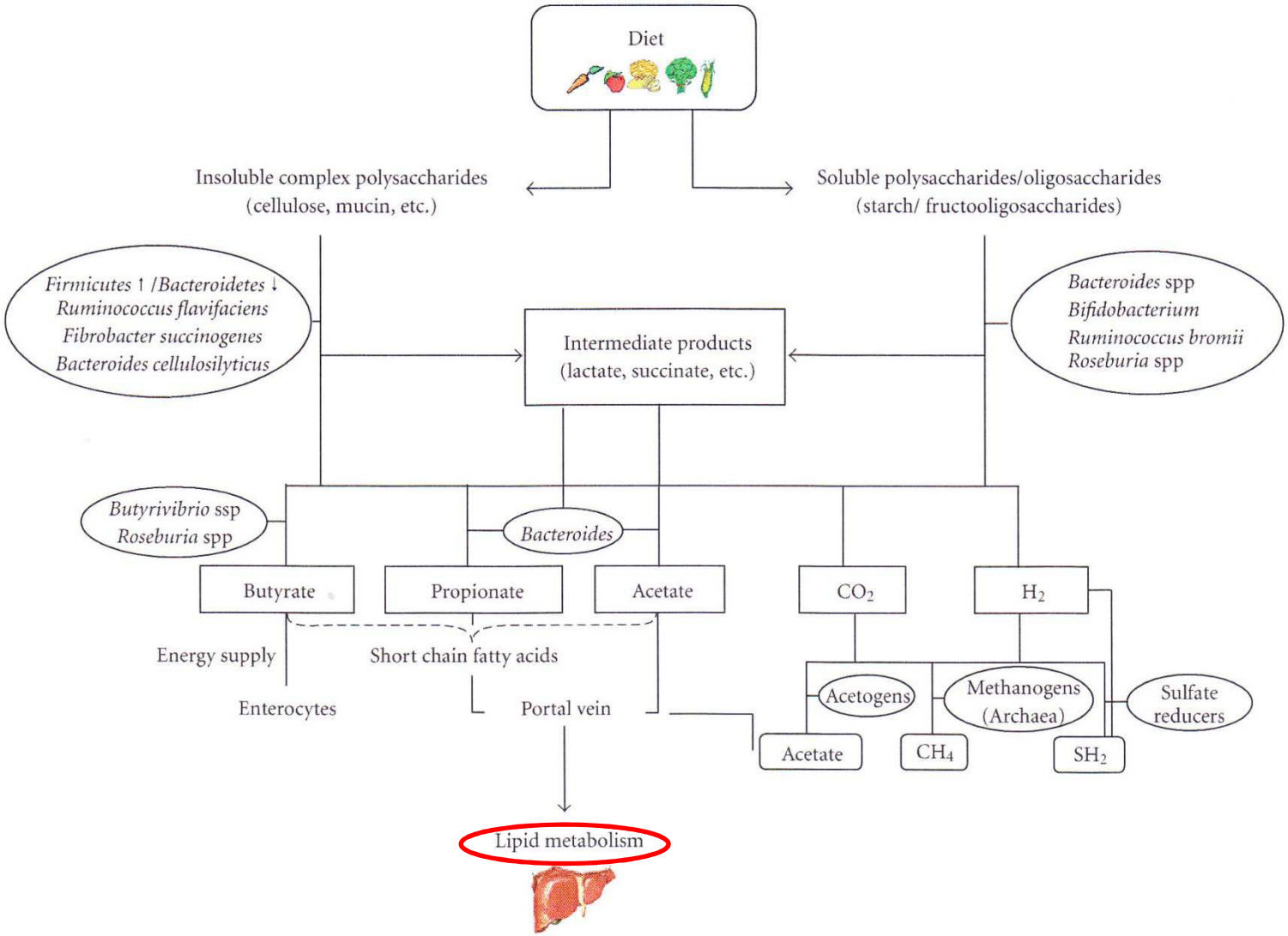


FIBRE SOLUBILI presenti:

- Crusca d‘avena
- Orzo perlato
- Legumi
- Frutta secca
- Riso integrale
- Mela, Albicocca
- Cicoria, Topinambur, Carciofi

FIBRE INSOLUBILI presenti:

- Cereali integrali
- Crusca di grano
- Verdure in genere
- Legumi (fave, fagioli, ceci, piselli)
- Melanzane
- Carote
- Radicchio
- Pera



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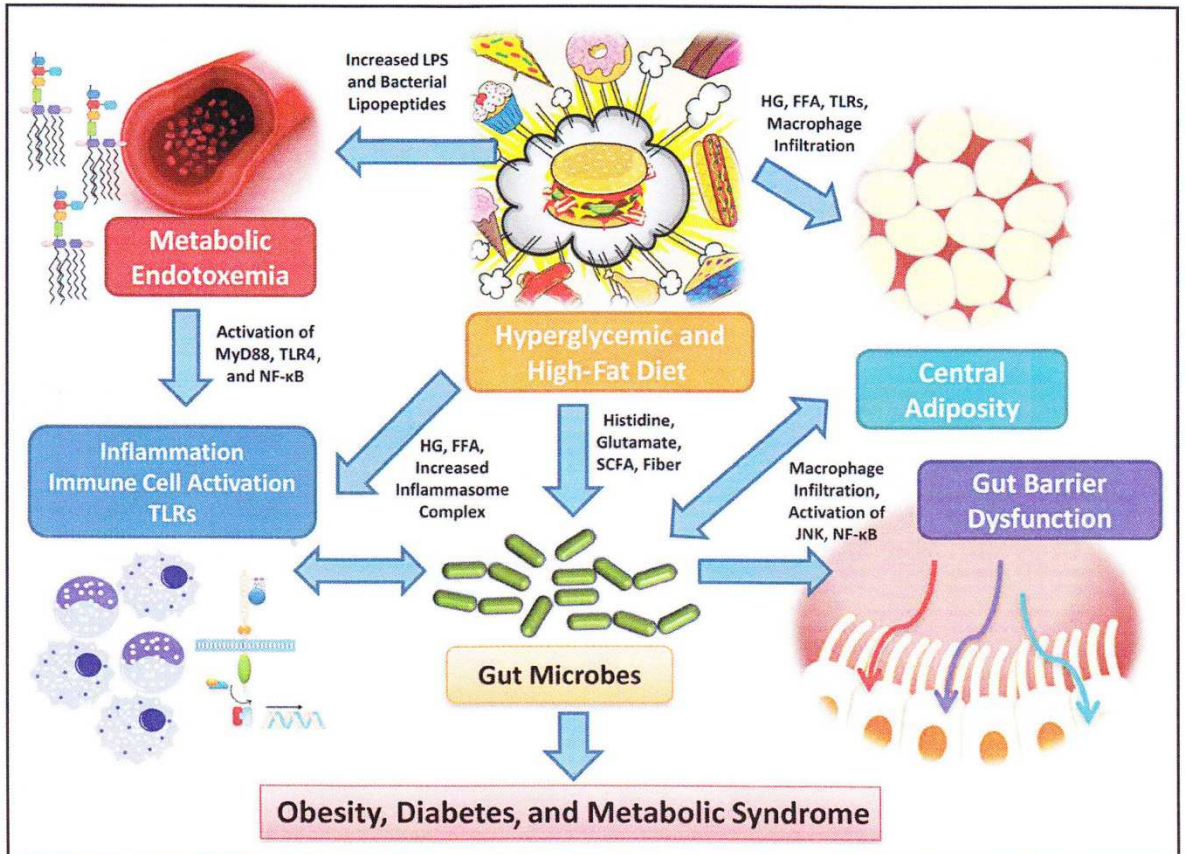

Fig. 1. Hyperglycemia (HG) and increased free fatty acids (FFA), which are hallmarks of obesity, metabolic syndrome, and diabetes, combined with a high-fat, high–glycemic load diet, could result in increased activation of the inflammasome complex as well as increase the activation of macrophages via increased TLR activation and nuclear factor κB (NF-κB) activation.

Increased metabolic endotoxemia may occur and activate the TLR4 pathway via the adapter protein, MyD88, leading to immune cell activation and inflammation. Also, macrophages could infiltrate the adipose tissue and activate mitogen-activated protein kinases, such as c-Jun aminoterminal kinase (JNK) and NF-κB, resulting in increased cross-talk and adipose-tissue–derived adipokines. A hyperglycemic and high fat diet could also result in changes to the gut microbiome by altering the content of histidine, glutamate, SCFAs, and other factors and promote gut-barrier dysfunction and conditions prevalent in obesity, metabolic syndrome, and diabetes by altering the host response. All of these metabolic alterations that result in increased systemic inflammation, macrophage activity, and TLR activation contribute to the increased cardiometabolic burden in obesity, diabetes, and metabolic syndrome.

CIBO E CERVELLO

Neurogastronomia tra piaceri alimentari e disordini dietetici

Globesity, un problema… di testa e di pancia?

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