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Diet influence on the gut microbiota and dysbiosis related to nutritional disorders

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ABSTRACT

Studies concerning the gut microbiota have exponentially increased since the 1970s. A healthy gut microbiota is essential for growth and weight gain in infants as well as for a thorough harvest of energy from diet through a role in digestion. Study techniques include culture-independent and culture-dependent methods aiming at describing the gut microbiota taxonomically and functionally. Healthy gut microbiota plays a role in digestion by metabolizing indigestible macronutrients resulting in short chain fatty acids and other bioactive compounds. Diet was proven to influence the composition of the gut microbiota with specific changes to the major macronutrient contained in the diet. Since diet has an influence on gut microbiota's composition, nutritional disorders such as obesity, severe acute malnutrition and anorexia nervosa are linked to an alteration of the gut microbiota mirroring the physiopathology of the nutritional disorder. These alterations should be the target of future therapeutic interventions in nutritional disorders.

Contents

Abbreviations: BMI, Body Mass Index; FISH, Fluorescent *in situ* Hybridization; FOS, fructo-oligosaccharides; GCPR, G Coupled Protein Receptors; HAZ, height-for-age z-score; HGC, high gene count; HMOs, Human Milk Oligosaccharides; LAB, Lactic Acid Bacteria; LGC, low gene count; SAM, severe acute malnutrition; SCFA, short chain fatty acids; SD, standard deviation; WAZ, weight-for-age z-score; WHZ, weight-for-height z-score; WHO, World Health Organization.

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Introduction

Over the last decades, interest for the human microbiota and more specifically the gut microbiota has strikingly increased. This diverse ecosystem consists mostly in bacteria alongside archaea, fungi and parasites [1] and is described as the biggest endocrine organ of the human body as it is responsible for the synthesis of several hormones. In fact, it contains ten times more cells than the human body and 150 times more genes than the human genome [2]. The gut microbiota appears to be essential for health and largely implicated in the homeostasis of the human body. A major role of the gut microbiota resides in its support of the digestion all through the gastro-intestinal tract. As such, the gut microbiota is important for energy balance. Many factors such as host genetics, environment, age and diet play a role when it comes to shaping the gut microbiota [3,4]. In this review of the literature, we focus on the diet impact on the healthy gut microbiota and how this microbiota can be affected by nutritional disorders.

Healthy gut microbiota

Exploration techniques

Over the years, the methods of choice to study the gut microbiota have evolved alongside technology. In the early years of gut microbiota studies, culture-based methods were used [5–7]. Because of the anaerobic nature of most of the bacteria in the human gut, culture-based techniques uncovered only 10–25% of the diversity in the gut microbiota [7,8] as proven in the recent years by molecular methods. Nowadays, a majority of studies exploring the gut microbiota diversity are based on 16S rRNA based sequencing and whole genome sequencing of metagenomes [9]. Nevertheless, as a shift of the interest in the gut microbiota is occurring from description to functional capacities, more functional metagenomics and metabolomics studies are being performed on the gut microbiota [9,10]. It should be noted that functional studies of the gut microbiota did not begin with metagenomics studies but with studies of the biochemical activities of the gut microbiota [6]. Other molecular methods to study the gut microbiota include quantitative PCR, reverse transcription quantitative PCR and Fluorescent *in situ* Hybridization (FISH) which in addition to identification, also allow quantification of bacterial cell numbers [2,11,12]. Reproducibility rate between molecular studies is very low, most probably because of sampling, conservation of the samples and DNA extraction methods [2]. Molecular techniques also present a depth bias, detecting species at a minimal concentration of 10^5 bacteria/g. Conversely, the "microbial culturomics" concept allows the detection of species present in low concentrations in addition to the tremendous advantage of having physical strains; the return to culture methods such as culturomics, highly complementary to metagenomics appears to be essential for a thorough exploration of the gut microbiota diversity [7,13,14]. Feces are the most used samples when studying the gut microbiota because of their easy availability. Nevertheless, they do not represent accurately the entire gut microbiota diversity since it varies taxonomically and functionally in each anatomical part of the gastro-intestinal tract [15–17]. This is a factor to be considered when designing studies and interpreting data.

Composition of the healthy gut microbiota

Healthy gut microbiota composition is subject to variation due to age, genetics, environment, diet and gut wall structure [2,12]. Gut colonization starts at birth with a composition depending on the type of delivery and subsequently on the type of diet [18,19].

Infant gut microbiota

Colonization is commonly believed to start at birth with the mother's vaginal microbiota for vaginally delivered newborns. When delivered using C-section, the newborn's gut microbiota is first colonized by the mother's skin microbiota and the environment (Fig. 1) [19,20]. The composition of the gut microbiota of infants evolves rapidly during the first year of life at which point the majority of species belong to the *Clostridium coccoides* group, the *Clostridium botulinum* group, the *Bacteroides* and *Veillonella* genera, the *Verrucomicrobia* phylum represented by *Akkermansia muciniphila* (Fig. 2) [19]. Great inter-individual and even greater intra-individual variations are observed in the diversity of children gut microbiota [21].

Adult gut microbiota

Human gut microbiota presents a low diversity at the phylum level with only one archaeal phylum, *Euryarchaeota* and seven bacterial phyla represented: *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, *Fusobacteria*, *Verrucomicrobia* and *Cyanobacteria*-like (Fig. 2) [2,8]. Healthy adult gut microbiota are dominated by three bacterial phyla, *Firmicutes* namely *Lachnospiraceae* and *Ruminococcaceae* families, *Bacteroidetes* namely *Bacteroidaceae*, *Prevotellaceae* and *Rikenellaceae* families and *Actinobacteria* namely *Bifidobacteriaceae* and *Coriobacteriaceae* families (Fig. 2), and one major methanogenic archaeon, *Methanobrevibacter smithii* [2,8,22]. The MetaHIT Consortium suggests a classification of the gut flora into three distinct enterotypes: Enterotype 1 presents a high abundance of *Bacteroides* and a wide saccharolytic potential, Enterotype 2 presents a high abundance of *Prevotella* and a high potential for mucin glycoprotein degradation and Enterotype 3 which presents a high abundance of *Ruminococcus* and potential for mucin degradation and membrane transport of sugars [8]. A more recent classification system based on metagenomics analysis divided the population into carriers of two types of diversity within the gut microbiota: high gene count (HGC) carriers and low gene count (LGC) carriers [12,23]. These classifications systems have been criticized because of the large interpersonal variability in the composition of the gut microbiota at the species level. However, a core group of species seems to be present or absent in each individual alongside a variable microbiome which composition depends on diet and environment [3].

Role of the human gut microbiota in digestion

Composition of the gut microbiota varies through each anatomic site depending on temperature, pH, redox potential, oxygen

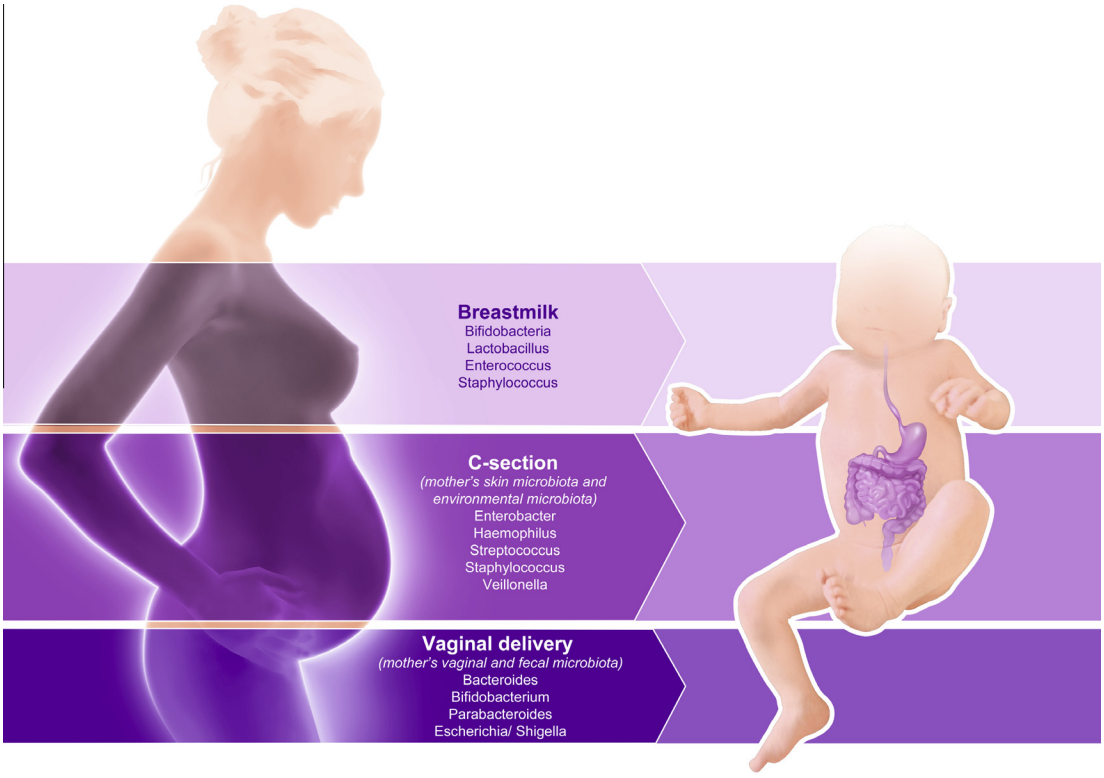

Fig. 1. Early colonization of the gastro-intestinal tract in newborns. Early colonizers of the gastrointestinal tract are specific to the type of delivery. In the case of a vaginal delivery, early colonizers originate from the mother's vaginal and fecal microbiota whereas for C-sections, early colonizers belong to the environment of birth and the mother's skin microbiota. Breast milk microbiota also colonizes the gastrointestinal of newborns.

tension, water activity, salinity and light [2]. The composition of the gut microbiota is also depending on the functional role of each region of the gut microbiota in digestion. The gut microbiota intervenes mainly in the colon where no digestive enzymes are secreted to metabolize macronutrients not digested in the ileum [2,8]. These indigestible macronutrients consist mainly of oligo- and polysaccharides which fermentation by commensal bacteria of the colon results in the synthesis of short chain fatty acids (SCFA), and phenolic compounds which metabolism produces bioactive compounds [8]. Saccharolytic species include species belonging to the *Bacteroides*, *Bifidobacterium*, *Clostridium*, *Eubacterium*, *Lactobacillus* and *Ruminococcus* genera [2]. Fermentation of proteins by the gut microbiota takes also place in the colon via bacterial proteinase and peptidase thanks to species such as *Clostridia*, *Propionibacterium* spp., *Prevotella* spp., *Bifidobacterium* spp. and *Bacteroides* spp. [2,8].

Influence of diet in the gut microbiota composition

Macronutrients related effect

Several studies have explored the link between diet and the gut microbiota because of the potential of dietary interventions to shape the composition of the gut microbiota. Each type of macronutrients (proteins, dietary fibers, fat) influences the gut microbiota specifically (Fig. 3). Changes are observed more at a metabolic level than at a taxonomic level with a quick change in gene expression depending on the macronutrients [12,23,24]. Nevertheless, transient changes can be observed in the diversity of the gut microbiota associated with each macronutrient. These changes affect only specific species which metabolic activity can be affected by the investigated macronutrient [25]. For example, dietary fiber consumption leads to an increase in butyrate-producing species which ferment these fibers in the distal colon (*Roseburia*, *Blautia*, *Eubacterium rectale*, *Faecalibacterium prausnitzii*), in the *Actinobacteria* phylum (*Bifidobacteria*, *Lactobacilli*) and variations in *Bacteroidetes* proportion depending on the type of dietary fiber [2,12,26,27]. A high protein diet is usually a low carbohydrate diet; as such this type of diet stimulates a decrease in butyrate producing species and an increase of species with proteolytic activities such as *Bacteroides* spp [2,12]. Dietary fat has an indirect impact on the gut microbiota diversity: a high fat diet stimulates the production of bile acids which in turn select the growth species with the ability to metabolize biles acids and/or induce the loss of some species due to the antimicrobial activity of bile acids [2,12].

Influence of the type of diet on the gut microbiota composition

Depending on the major macronutrient in a type of diet, it has been highlighted that specific categories of species are stimulated in the gut microbiota (Fig. 3). Vegetarian and vegan diets tend to have a high carbohydrate content associated to a lower protein and fat content. Omnivorous and animal based diets conversely show a high protein and fat content and low carbohydrate content [10]. The latter diets are associated with an increase of bile tolerant bacteria such as *Bacteroides*, *Alistipes* and *Bilophila* [2,23], butyrate producing bacteria, specifically the *Clostridium* cluster XVIa [12]. Since vegetarian and vegan diets have a high carbohydrate content, their gut microbiota are dominated with bacteria with high carbohydrate fermenting bacteria such as the *Prevotella* [23], *Clostridium clostridioforme* and *Faecalibacterium prausnitzii* [12]. Vegetarians

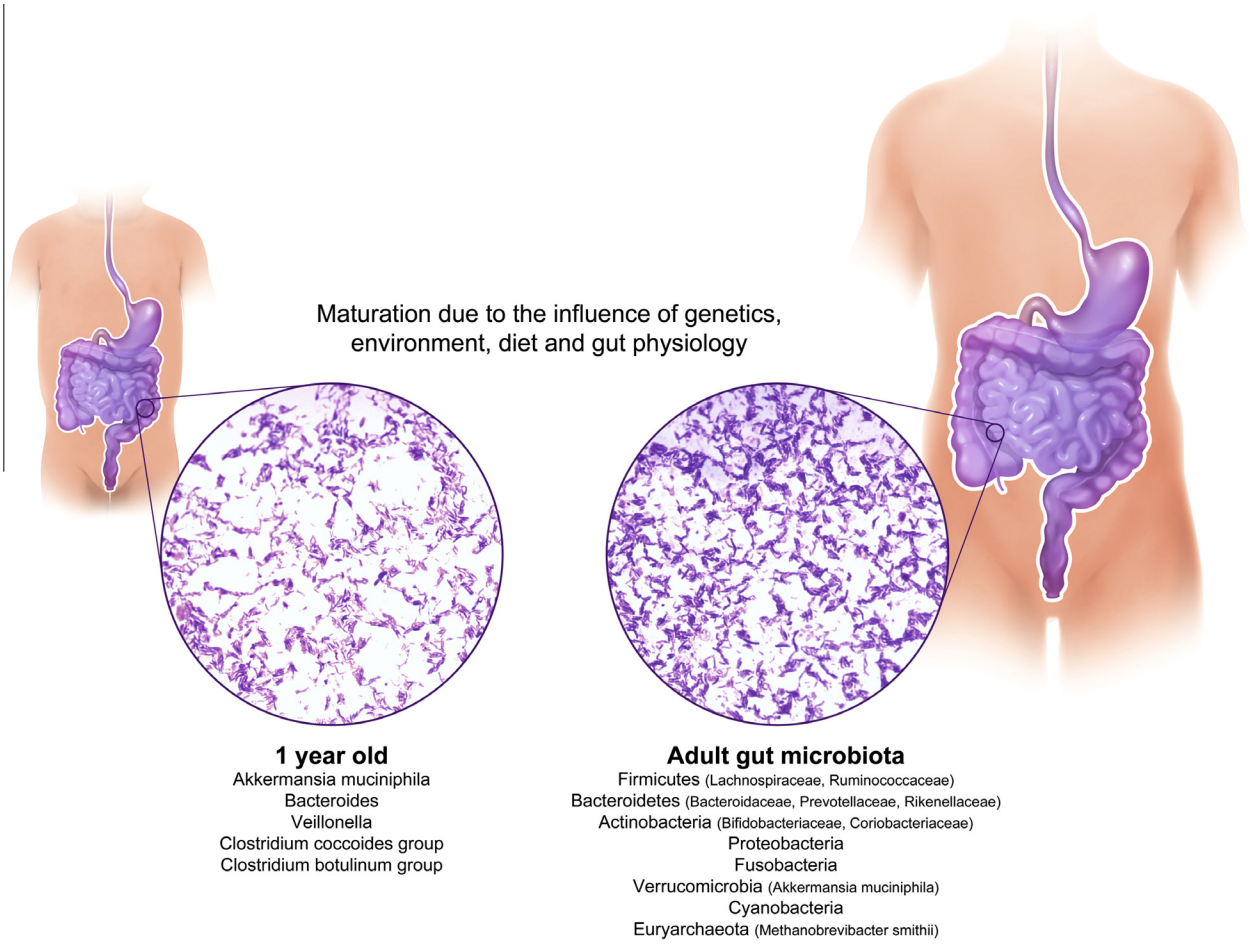

Fig. 2. Maturation of the gut microbiota. The composition of the gut microbiota in children varies greatly during the first year of life before reaching a more stable and mature composition. Maturation into an adult state is due to several factors such as genetics, environment, gut physiology and diet.

show specifically compared to omnivores an increase in the *Clostridium* cluster XVIII (*Lachnospiraceae* and *Clostridium ramosum* group). On the other hand, vegan show a decrease in *Bacteroides*, *Bifidobacteria*, *Enterobacteriaceae* species [8].

Geographic locations such as country, continent or metropolitan areas as opposed to rural areas seem to have an influence on the gut microbiota diversity but this influence to the variation in diet associated with geographic location [21]. Western diets usually present high amounts of fat, processed carbohydrates and low amounts of fibers; as such, they are associated with lower global diversity in the gut microbiota, an increase of *Bacteroides* and a decrease *Prevotella* compared to non-western diets [2]. These diets, especially in rural areas, are characterized by high fiber and complex carbohydrates content and are therefore associated with an abundance of high polysaccharides fermenting bacteria such as *Prevotella*, *Succinivibrio*, *and Treponema*. The *Prevotella* genus seems to be a discriminatory taxon between high and low carbohydrate diets and moreover, rural and metropolitan diets, in the gut microbiota of children and adults [8,11,12,21]. The difference between western and non-western diets is mainly due to the presence of processed food in western diet [8].

Bifidobacteria are very abundant in breastfed infants' gut microbiota due to the presence of human milk oligosaccharides (HMOs) which stimulates their growth [2,28] whereas in adults, they seem to be associated with the consumption of agro-pastoral derived products [12].

Influence of prebiotics, probiotics on the gut microbiota

Probiotics are bacterial species with a recognized beneficial effect for health when ingested viable in adequate amounts by individuals. These probiotics are often associated with prebiotics which are non-digestible carbohydrates which metabolization stimulates specific species among which probiotics. The combination of probiotic and prebiotic is called a synbiotic [8,29]. Prebiotics can be used to improve the growth of specific species with probiotics characteristics, modifying the gut microbiota composition in the process and restoring health as a consequence. In fact, the fermentation products of prebiotics are usually SCFA [8] which main beneficial effects for the health include anti-inflammatory and anti-apoptotic activities and prevention of colorectal cancer and colitis [23].

In breastfed infants, prebiotics are represented by HMOs from the maternal milk which promote colonization by *Bifidobacterium* species. This effect is also obtained with galacto-oligosaccharides and fructo-oligosaccharides (FOS) supplementation in infant formula. In turn, *Bifidobacterium* species produce SCFA by fermenting prebiotics and participate in the stimulation of the immune system [2]. As for the adults, classical prebiotics include FOS, inulin, galacto-oligosaccharides and lactulose, all naturally present in vegetables such as artichokes, onions, chicory, garlic and leeks [2]. An increase of abundance in *Latobacilli*, *Bacteroides*, *Lachnospiraceae* and *F. prausnitzii* has been observed as a result of supplementation

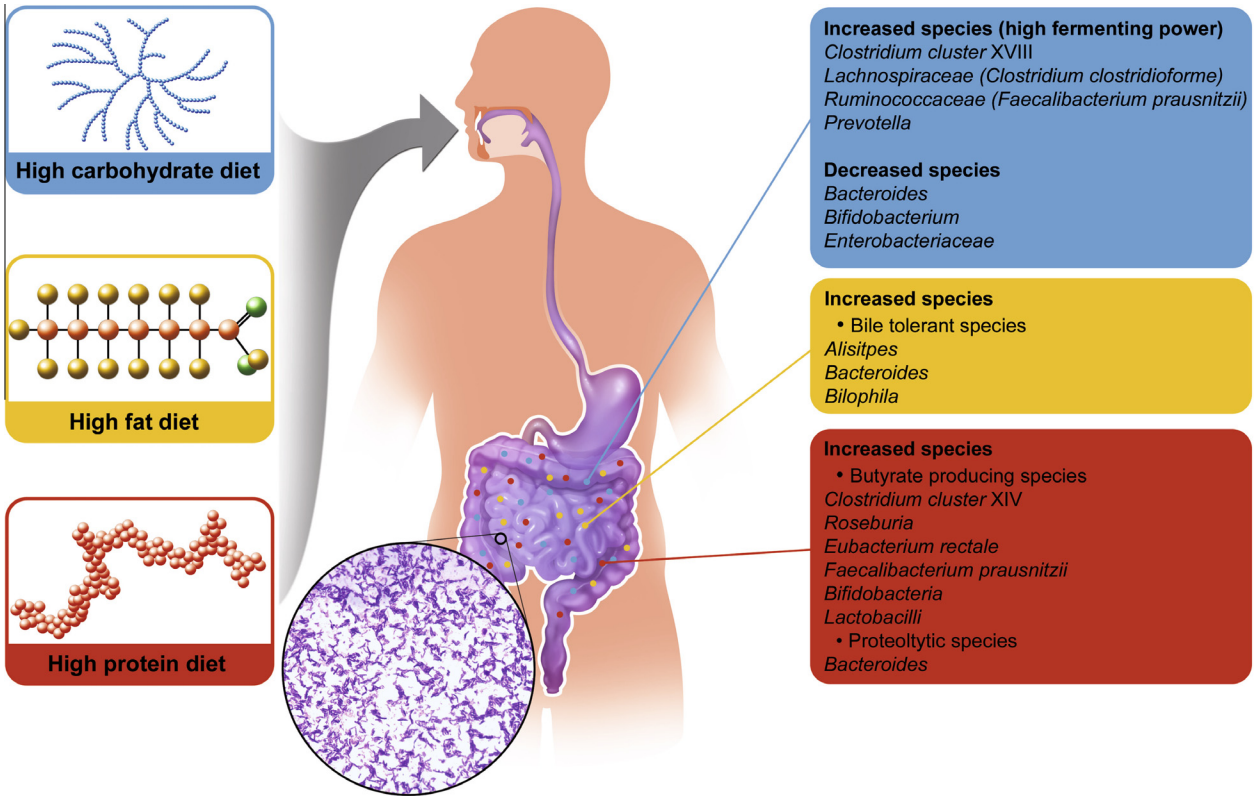

Fig. 3. Diel influences the composition of the gut microbiota. Depending on the major macronutrient in a diet type, the composition of the gut microbiota can be transiently altered to adapt to the digestion pattern for the specific macronutrient. Specific bacterial populations and functions are stimulated accordingly.

Table 1
Nutritional disorders: definition, diagnosis and prevalence.

Nutritional disorder	Type of cellular imbalance	Diagnosis	Prevalence
Obesity and overweight	Positive	• Adults: BMI $\geqslant$25 • Children: BMI-for-age > +1SD	• 1.9 billion adults (2014) • 41 million children (2014)
Undernutrition	Negative	• Stunting: HAZ < −2SD • Wasting: WAZ < −2SD • Underweight: WHZ < −2SD	• 29 million children under five are severely malnourished • 1–6 million deaths every year
Anorexia nervosa	Negative	• BMI <18.5 • Body weight <85% of ideal body weight • Over-evaluation of shape and weight	• 0.3% of adolescents between 15 and 19 years old

HAZ: height-for-age z-score. WAZ: weight-for-height z-score. WHZ: weight-for-height z-score.

of diet with the aforementioned prebiotics [2,23,26]. Several foods are being currently tested for prebiotics capacity [29,30] and testing should continue in order to find probiotics, prebiotics and synbiotics that can modulate the gut microbiota composition and be easily available to the general population.

Nutritional disorders associated with a dysbiosis of the gut microbiota

Classification of nutritional disorders

WHO defines malnutrition as the "cellular imbalance between supply of nutrients and energy and the body's demand for them to ensure growth, maintenance and specific functions" [31]. According to the positive or negative energy balance observed several types of malnutrition are defined. Obesity represents a positive energy balance [32] and is the most prevalent nutritional disorder in western countries; it is also highly prevalent in developing countries, representing a heavier burden on public health than undernutrition worldwide [33]. In fact, according to WHO, the prevalence of obesity has doubled in the last 30 years. In 2014, worldwide 1.9 billion adults were overweight among which 600 million adults were obese while 41 million children under five are obese or overweight [34,35]. WHO defines overweight and obesity in adults with a BMI (Body Mass Index) $\geqslant$ 25 and a BMI $\geqslant$ 30 respectively [34,36]. Obesity can also be defined by the measure of a BMI over 120% of ideal body weight (Table 1) [33]. In children under five, overweight is defined +2 standard deviation (SD) from the median of child growth standards [37] while obesity is defined by +3SD from the aforementioned median. For children aged from 5 to 19 years, WHO recommends to consider as overweight, children with a BMI-for-age >1SD above the WHO growth reference median and as obese, children with a BMI-for-age >2SD above the aforementioned median. Another measure of obesity in children involve a BMI over the 95th percentile which is based on the child's age and sex (Table 1) [36,38]. Common comorbidities include cardiovascular diseases, hypertension, type 2 diabetes,

Table 2
Characteristics of the gut microbiota associated with nutritional disorders.

Nutritional disorder	Diversity alterations	Metabolic alterations
Obesity	Lower global diversity Increase of the *Firmicutes*: *Bacteroidetes* ratio Increase of *Methanobrevibacter smithii* Increase of *Lactobacillus* Decrease of *Bifidobacteria* Decrease of *Escherichia coli*	Increase of genes involved in carbohydrate metabolism Increase of genes involved in phosphotransferase system and membrane transport Decrease of genes involved in transcription and nucleotide metabolism Decrease of genes involved in cofactors and vitamin metabolism
Severe acute malnutrition	Lower global diversity Increase in aerobic species (*Proteobacteria* and pathogenic species) Decrease in anaerobic species (*Bacteroidetes*) Absence of *Methanobrevibacter smithii*	Increase of virulence factor homologs Increase of genes involved in motility and chemotaxis, respiration, membrane transport and virulence Decrease of genes implicated in nutrient uptake and metabolism Inhibition of enzymes implicated in the tricarboxylic acid cycle
Anorexia nervosa	Lower global diversity Increase of *Methanobrevibacter smithii* Decrease of *Lactobacillus*, *Streptococcus* Decrease of the *Clostridium coccoides* and *Bacteroides fragilis* groups	Decreased concentrations of the SCFA acetate and propionate

hypercholesterolemia, non-alcoholic fatty liver disease, cancer and some immune related disorders [33,36,39].

Undernutrition consists of stunting (height-for-age (HAZ) < −2SD), wasting (weight-for-age (WAZ) < −2SD) and underweight (weight-for-height (WHZ) < −2SD). Chronic malnutrition is characterized by stunting while acute malnutrition is characterized wasting, underweight [40,41] and/or nutritional oedema [40,42]. Severe acute malnutrition (SAM) (WHZ < −3SD) affects 29 million under five children and is responsible for the death of 1–6 million children every year (Table 1) [43]. It is mostly prevalent in developing countries of sub-Saharan Africa, Central America and South Asia [44]. Symptoms include, besides nutritional oedema in some cases, diarrhea [45], hepatic steatosis, skin rashes, ulceration, anorexia [46], delayed growth and deficiencies in macronutrients and micronutrients [47]. This type of malnutrition represents a negative energy balance [32] associated with a deficit of macronutrients, more specifically a deficit of protein, quantitative in marasmus and qualitative in kwashiorkor [31,42].

Another example of negative energy balance is anorexia nervosa. Anorexia nervosa is the first described and officially recognized eating disorder with two subtypes, the restricting type and the binge/purging type [48–50]. It has a low prevalence of 0.3% and is observed in developed and developing countries mostly in adolescents aged from 15 to 19 years old [48,49]. Eating disorders have a core symptomatology which consists in over-evaluation of shape and weight. Other symptoms include a significantly low body weight highlighted by a BMI under 18.5 or a body weight under 85% of ideal body weight and in some cases, amenorrhea (Table 1) [48–51]. Given these symptoms, it is clear that anorexia nervosa is a mental disorder that has a physical impact through its manifestation [49,50].

All these nutritional disorders have been proven to be linked to a disruption of the gut microbiota with specific characteristics in the shifting of the bacterial diversity observed in each of the aforementioned nutritional disorders (Table 2).

Alterations of the gut microbiota associated with nutritional disorders

As well described, the gut microbiota is implicated in the regulation of energy metabolism through the digestion of indigestible polysaccharides for the host which fermentation by the microbiota leads to the production of SCFA (propionate, butyrate and acetate); SCFA represent 10% of the daily energy supply in humans [39,52]. They serve as energy supply for the colonocytes as well as ligand for G Coupled Protein Receptors (GCPR) thus influencing insulin sensitivity in adipocytes and peripheral organs, reducing fat accumulation, improving gut motility and nutrient absorption and activating host immunity [39,52,53]. The gut microbiota also regulates energy metabolism by stimulating triglyceride deposition in adipocytes as well as triglycerides and cholesterol synthesis and lipogenesis. Conversely, the gut microbiota inhibits fatty acid oxidation, ketogenesis and glucose consumption [39]. As such, energetic imbalance is linked to gut microbiota alteration.

Alterations of the gut microbiota associated with obesity and the metabolic syndrome

In obese individuals, the gut microbiota alteration stimulates monosaccharides absorption through an increased capillary density in the small intestine epithelium [54] and leads to a greatly improved capacity for harvesting additional energy from diet with an increase of species implicated in indigestible polysaccharide fermentation in the colon [39,55]. In fact, a lower diversity is observed in obese individuals in most studies [35,54–56] with an increase of the *Firmicutes*: *Bacteroidetes* ratio [39,52–54,56,57] alongside an increase in methanogenic archaea such as *M. smithii* which presence improve polysaccharides fermentation by removing H_2 in the gut environment [52,58]. As a result, two major SCFA are found increased in obese subjects [54]: butyrate is the main energy supply for the colonocytes and is negatively correlated with intestinal permeability while acetate is a substrate for hepatic cholesterol synthesis and de novo lipogenesis [57] leading to an increase in adiposity and body weight [59]. Nevertheless, other data suggest a decrease of *M. smithii* in obese subjects compared to lean individuals [60]. A change in the diversity of Lactic Acid Bacteria (LAB) is also observed with a described increase in *Lactobacillus* species [58] and *Lactobacillus reuteri* in particular and low levels of bifidobacteria and *Escherichia coli* [56,60]. Obesogenic species also include *Blautia hydrogenotrophica*, *Coprococcus catuss*, *Eubacterium ventriosim*, *Ruminococcus broomii* and *Ruminococus obeum*. These *Firmicutes* species are known to improve energy harvesting from the diet [56]. The alteration of the gut microbiota associated with obesity composition also leads to a low grade inflammation negatively correlated with the gut microbiota gene count. Obese individuals with a HGC present an increase of anti-inflammatory species such as *F. prausnitzii* [39,52] and *A. muciniphila* and a higher production of organic acids [61] while a decrease in pro-inflammatory species such as *Bacteroides* spp is observed [39]. On the other hand, LGC obese subjects gut microbiota is associated with a higher prevalence of potentially pro-inflammatory species and genes implicated in oxidative stress response [61]. Species which diversity is modified in obesity-associated gut microbiota seem to have

specific functions linked to the physiopathology of obesity. Therefore, the role of the gut microbiota in obesity is more likely due to the genes and metabolites produced by the microbiota. An increase of genes involved in phosphotransferase system, carbohydrate metabolism and membrane transport is observed whereas a decrease in genes mediating transcription and nucleotide metabolism alongside a decrease in cofactors and vitamin metabolism [52].

Alterations of the gut microbiota associated with SAM

Acute malnutrition is associated with wasting in which the gut microbiota seems to have an effect since it has been associated with weight gain and in skeletal growth [62]. SAM-associated gut microbiota is described as immature [63,64], presenting a loss of diversity [65] with an enrichment in *Proteobacteria*, among which aerobic and pathogenic species [45,47,66,67], confirmed by an increase in the number of virulence factors homologs [47] and protein encoding genes functionally related to motility and chemotaxis, respiration, membrane transport and virulence [45]. Aerobic bacterial overgrowth in the small intestine has previously been associated with SAM [67,68]. A decrease in anaerobic species, is also observed [67,69] and moreover, a total absence of *M. smithii*, one of the most oxygen sensitive species in the human gut [69]. The decrease of anaerobic species is consistent with the decrease of the *Bacteroidetes* phylum described by Monira *et al.* which consists mostly of anaerobic species [40,65]. Enriched genera include *Bilophila* [46], *Klebsiella* [65], *Escherichia*, *Streptococcus*, *Shigella*, *Enterobacter*, *Veillonella* and a depletion in genera associated with health such as *Roseburia*, *Faecalibacterium*, *Butyribrio* and the *Synergistetes* phylum [47]. Gupta *et al.* also described an increase of the families *Bacteroidaceae* and *Porphyromonadaceae* [45]. Some depleted species such as *F. prausnizii* have previously been associated with weight gain in gnotobiotic mice colonized with healthy infant microbiota [63]. Depletion in genes implicated in nutrient uptake and metabolism is also observed in the microbiome consistently with the fact that depleted species are members of the *Firmicutes* phylum which are polysaccharides fermenters and SCFA producers [47]. In fact, SCFA availability is reduced in the gut of SAM patients [45]. A selective inhibition by the kwashiorkor-associated gut microbiota of one or more tricarboxylic acid cycle enzymes was observed by Smith *et al.* [46].

Alterations of the gut microbiota associated with anorexia nervosa

Only a few studies have explored the gut microbiota of anorexic patients. Since anorexia nervosa is a nutritional disorder, alterations must be observed in the gut microbiota of anorexic subjects. Studies have reported an increase of the prevalence of *M. smithii* [58,68] and a decrease of the prevalence of *Lactobacillus* species [58] notably a decrease of *Lactobacillus plantarum* alongside a decrease of *Streptococcus* spp., the *Clostridium coccoides* group and the *Bacteroides fragilis* group [70] associated with decreased concentrations of the SCFA, acetate and propionate. Moreover, the gut microbiota of anorexic subjects appears to present a lower total diversity [70]. A study exploring the gut microbiota of an anorexic patient described *Firmicutes*, *Actiobacteria* and *Bacteroidetes* as the most abundant phyla respectively with a high prevalence of anaerobic families [71].

Conclusion and perspectives

The gut microbiota is influenced in its taxonomic composition and its functional abilities by the macronutrients proportion in the diet in order to be able to assist the host in the digestion process. The role of the gut microbiota in digestion makes it an instrumental factor in energy imbalance and consequently in nutritional disorders. Dybiosis of the gut microbiota has in fact been observed in nutritional disorders such as obesity, undernutrition and anorexia nervosa with different characteristics of the gut microbiota associated with each disorder. The gut microbiota of anorexic patients has barely been studied and additional studies are required in order to have a better understanding of how the gut microbiota plays a role in this disease. Conversely, the extensive description of obesity and kwashiorkor associated gut microbiota paves the way to more interventional studies where commensals of the gut microbiota are tested as probiotics in order to reestablish a healthy flora and consequently a healthy individual. The era of microbio-therapeutics is here!

Author agreement

All authors have seen and approved the final version of the manuscript. This work has not been published and is not under consideration for publication elsewhere.

Conflict of interest

No conflict of interest to disclose.

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