MINI REVIEW

The effects of diet, exercise, good microbes, and fecal microbiota transplant on health improvement

Sophia Wesley

Wesley S. The effects of diet, exercise, good microbes, and fecal microbiota transplant on health improvement Curr. Res.: Integr. Med. 2023;8(3):31-34

ABSTRACT

Studies on how to influence bacteria in favour of health outcomes have been prompted by the realisation that germs are essential to human life. The consumption of dietary substances that can support the ingested organisms in terms of producing an improved health result has not yet received a joint recommendation. The purpose of this paper is to explore how health management practises utilise helpful bacteria in the form of probiotics, fermented foods, and donor faeces. Additionally, we look at the logic behind choosing healthy microbial strains and designing diets to support their growth in the gut. The most prevalent inborn mistake of amino acid metabolism, Phenylketonuria (PKU), is a condition that necessitates lifetime dietary intervention. A pilot clinical trial design is described to investigate the effects of probiotics and exercise in patients with PKU. The purpose of the example design is to highlight the significance of using omics technology to determine whether the intervention elevates neuroactive biogenic amines in the plasma, increases the abundance of *Eubacterium rectale*, *Coprococcus eutactus*, *Akkermansia muciniphila*, or Butyricicoccus, and increases *Escherichia/Shigella* in the gut, all of which are considered indicators of improved health.

Key Words: *Diet; Gut microbiota; Fecal microbiota transplant; Probiotics; health*

INTRODUCTION

By metabolising food, releasing significant metabolites, removing or detoxifying specific compounds, and regulating host responses, the gut microbiota plays a critical role in human health immunity. Age, physical activity, food, and antibiotic use are only a few of the many variables that have an impact on the microbiota The gestational age (term vs. preterm), mode of delivery (vaginal vs. caesarean), and nutritional status (breastfed vs. formula fed) of newborns have all been shown to have a substantial impact on the gut microbiome . Although we are learning more about the connection between microbes and health, there are still many unanswered questions [1].

The goal of this review is to explain how existing understanding of health-promoting microorganisms may influence future investigations and therapeutic applications in this area. We highlight a few noteworthy findings that mostly concern nutrition and physical activity [2]. For the aforementioned reason, the PubMed database was searched for pertinent publications using keywords relating to diet, exercise, microorganisms, and health. The keywords were then concatenated with Boolean operators.

Fecal Microbiota Transplant (FMT)

FMT has been used to treat recurrent C. *difficile* infections with success, including in individuals with inflammatory bowel disease. Donors are chosen after a thorough examination of their health status, during which numerous individuals are disqualified for a variety of reasons. Although locating a donor is expensive, healthcare systems are not currently footing the bill. Therefore, hospital sources and private clinics only typically offer FMT in research settings. Despite the fact that the absence of pathogens is a key inclusion criterion for donors, the microbiota's exact composition and the presence of specific species are now irrelevant. This is mostly due to a lack of equipment or an expensive process, but there has also been minimal data to suggest that this matters clinically for treating recurring C. *difficile* infections[3].

This is a serious issue with FMTs because the same FMT concept has now been used to treat a variety of illnesses without changing the make-up of the donor sample or requiring the recipient to maintain a diet more similar to the donor's. For instance, FMT has been used to treat multiple sclerosis, non-alcoholic fatty liver disease, ulcerative colitis, and Sjogren syndrome (dry mouth) in addition to those who have immune-mediated dry eye. The faecal microbiota in the donor is mostly a product of that person's diet because the mix of food consumption impacts microbial metabolism [4]. However, there hasn't been much effort made to have the recipient follow the donor's diet after FMT in order to preserve a healthy and stable microbiota. It is unknown to what extent this failure demands repeat FMT therapy, however a recent study has shown that this may not be as serious of a problem as once thought. In particular, 80% of the pre-FMT strains in the recipient were eliminated 5 years after FMT in a small cohort of 13 patients who had received the procedure to treat recurrent C. *difficile*, despite no

Editorial Office, Current Research : Integrative Medicine , UK

Correspondence: Sophia Wesley, Editorial Office, Current Research : Integrative Medicine,Uk e-mail: integrativemedicine@medicineinsights.com

Received:- 4 May 2023, Manuscript No. pulcrim-23-6398; Editor assigned: 6 May2023, Pre-QC No.- pulcrim-23-6398 (PQ); Reviewed:- 15 May 2023, QC No. pulcrim-23-6398 (Q); Revised:-25 May 2023; Manuscript No. - pulcrim-23-6398 (R); Published:-28 May 2023, DOI:10.37532. pulcrim.23.8 (3) 31-34.

attempt to match the recipient's diet with that of the donor.

Probiotic organisms, which are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host", have been used in addition to other methods to modify the gut microbiome. Too infrequently, though, have strains been chosen with traits that are appropriate for the problems the target host faces, such as the capacity to alter transit time, lessen inflammation, produce specific neurotransmitters, or boost anti-oxidant activity .

Aging and the gut microbiome

We have a better understanding of the factors that affect the makeup and function of the gut microbiota as more research on this topic is published. These investigations have ramifications for the method used to choose donors for FMTs. For instance, a sizable study of more than 1000 Chinese individuals showed that the microbiota of the centenarian cohort was strikingly similar to people over the age of 30, indicating that it is possible to maintain a gut microbiota that promotes health throughout life [5].

Age itself may therefore not be as important a determinant as food and staying in one place all of one's life. Given this, there may be creatures essential for longevity in the guts of centenarians. If these organisms were discovered, FMT donors may include a cohort that possesses these strains or those over 30 whose gut microbiota contains these strains. Can studies of the microbiomes of healthy elderly people be instructive if organisms are to be chosen for administration to the gut? Age-related reductions in Faecalibacterium, Bacteroidaceae, and Lachnospiraceae may aid to identify FMT criteria or strains that could be transferred because to the increased abundance of Akkermansia [6]. The results of one study demonstrated how a Mediterranean diet can change the gut flora in the elderly, leading to higher levels of short/branch-chained fatty acids and lower levels of harmful chemicals, which lower markers of inflammation and frailty and boost cognitive performance.

The microbiota gut-brain connection and physical activity

Exercise that is difficult and strenuous, especially when it's hot outside, might reduce intestinal permeability and heighten inflammatory reactions. As shown in an interventional trial where insulin-resistant participants were randomised to do sprint intervals or moderate-intensity, continuous training, this depended on the type of activity. Training sessions led to advantageous gut microbial adjustments. Two weeks following the training, it was found that the ratio of Firmicutes/Bacteroidetes, Clostridium, and Blautia had reduced and the ratio of Bacteroidetes had grown.

Strenuous exercise may decrease intestinal permeability and increase inflammatory responses, especially in hot weather. This was dependent on the type of exercise, as demonstrated in an interventional trial in which patients with insulin resistance were assigned to either sprint interval training or moderate-intensity continuous training [7].

Training sessions produced positive microbial changes in the stomach. The ratio of Firmicutes/Bacteroidetes, Clostridium, and Blautia had all decreased two weeks after the training, whereas the ratio of Bacteroidetes had increased.

To demonstrate that the animals could run more quickly, the authors injected single species into germ-free mice. The authors failed to provide evidence that these species are common in Olympic or other elite athletes, as would be predicted, despite the fact that this experimental approach is not specifically suited to human investigations. The results also go against those of Motiani et al. , who demonstrated that physical exercise decreased the number of Firmicutes, a phylum that includes *E. rectale and C. eutactus.*

With the purpose of immunological stimulation, endurance athletes are known to consume a variety of ergogenic aids, some of which include minerals and chemical compounds known as zeolites. The intestinal barrier protein zonulin, however, decreased after 12 weeks of treatment, according to a study of 52 endurance athletes . In a smaller research, when compared to placebo, male athletes who took a six-strain probiotic for 14 weeks demonstrated improved gut barrier function and a drop in the pro-inflammatory marker Tumour Necrosis Factor Alpha (TNF-).trials are needed in order to inform clinical practice guidelines for athletes. Adherence to the definition of prebiotics (“a substrate that is selectively utilized by host microorganisms conferring a health benefit” and using appropriate prebiotic amounts are important [8].

Nutrition and the gut microbiome

It is not surprising that nutrition has a major impact on microbiota composition, shape, and function given that gut microorganisms depend on the food we eat for replication and retention.

In a 2014 study, an animal-based diet reduced the amounts of Firmicutes (*Roseburia, E. rectale, and Ruminococcus bromii*), which break down dietary plant polysaccharides. But in light of the previous discussion, these results raise the question of whether food that boosts or depletes the population of organisms like *E. rectale* should be consumed before exercising. The Mediterranean diet has already been discussed. The use of fermented foods as a means of controlling the gut flora was another possibility investigated. It should be highlighted that unless specifically added and documented, fermented foods (described as "foods made through desired microbial growth and enzymatic conversions of food components" are not probiotic and do not contain probiotics. The 17-week, randomised, prospective trial made use of fermented meals and plant-based fibre.

Six servings of kombucha, yoghurt, kefir, buttermilk, kvass, kimchi, sauerkraut, and/or a vegetable brine drink were to be consumed each day as part of the protocol for the fermented foods. This demonstrates that the authors' primary objective—changing the cytokine response score within each arm from baseline (2 weeks prior) to the conclusion of the maintenance phase (week 10)—was not dependent on any particular microbes, but rather on beneficial microbes in general. The authors point out limitations in the causation and processes, but they nevertheless discovered that persons eating a diet high in fermented foods had lower levels of inflammatory markers and higher levels of microbial diversity. Some might argue that it is difficult to draw conclusions that would lead to dietary recommendations or an explanation for any recommendation, except that a variety of fermented foods have apparent immunological benefits, given the wide variation of food types and the organisms within them. Others, however, might counter that Wastyk et al.'s strategy was highly pragmatic given that in a real-world setting, people are typically free to choose from a variety of food products and do not always adhere to a rigid intervention protocol, which is restricted in variety. How sensory elements function is a topic that may be significant for the gut as well as the brain. Food's shelf life, flavour, texture, look, and fragrance all have an impact on what individuals eat and how their bodies process it. People frequently "eat with their eyes" because they appraise food before tasting it . With the help of salt, sugar,

chemicals, and the exclusion of water, the food business has skillfully created foods that are frequently affordable and aesthetically pleasing but nutritionally unbalanced. For a very long time, these sensory aspects have been influenced by additives. How sensory components work is a subject that may be important for both the gut and the brain. Food's shelf life, flavour, texture, appearance, and aroma all affect what people eat and how their bodies digest it. Due to the fact that they evaluate food before tasting it, people frequently "eat with their eyes" .The food industry has expertly manufactured foods that are frequently affordable and aesthetically beautiful yet nutritionally unbalanced with the use of salt, sugar, fats, chemicals, and the absence of water. These sensory aspects have been impacted by additives for a very long time. The latter occurs at the same time that metabolites like butyrate are reduced. In the end, poorly digested proteins cause the intestinal microbiota to ferment them, which results in the generation of harmful compounds such hydrogen sulphide, indole, and ammonia Notably, the rate of worldwide carrageenan use is rising quickly [9].

On the other hand, it has also been demonstrated that patients with hypercholesterolemia who consume 250 mg of carrageenans daily for 20 days have lower levels of total cholesterol and low-density lipoprotein cholesterol (p 0.05). Does this imply that carageenans may be introduced to a probiotic strain that lowers cholesterol, and if so, how would its results compare to those of a statin? The latter medications constitute the cornerstone of cardiovascular cholesterol treatment, but they have severe adverse effects and work through cytochrome P450, which means they may interact with other pharmaceuticals. Carrageenans or probiotic strains have not been shown to interact with drugs in this way, to our knowledge. Undoubtedly, this would make for an interesting future research project. It's interesting that human trials have not supported the assertion made in rodent research that non-nutritive sweeteners have a deleterious impact on the gut microbiota. When human participants ingested a dose corresponding to three 355 mL diet beverage cans per day, a recent 14-day intervention research found no alterations in gut bacteria. In a small human investigation, it was shown that the emulsifier carboxymethylcellulose, which is added to meals to enhance texture and lengthen shelf life, reduces the diversity of the gut microbiota and is linked to decreased levels of short-chain fatty acids and free amino acids. To ascertain if particular dietary additives might help or harm the gut flora, more study is required [9]. Exploring the gut flora also needs to take into account food odour in addition to nutrient intake. Food fragrance affects taste, inclination, and craving, but how does the microbiota factor into this? Three olfactory functions—odor threshold, discrimination, and identification—were connected with variations in the nasal microbiota, according to a study. It's interesting that poor olfactory function was linked to butyric acid production. Given that smell affects perception, eating habits, mood, memories, and social interactions, it is reasonable to assume that this may have an impact on a person's diet and gut microbiome. Overall, studies have shown dietary treatments to maintain gut functionality and have shown that nutrition modifies the gut flora. According to one review, a balanced diet with a balance of n-6 polyunsaturated fats, simple carbohydrates, food-derived bioactive peptides, and iron may help to restore intestinal homeostasis. It should also contain protein, phytochemicals, vitamins, minerals, and carbohydrates that are accessible to the microbiota. However, some research is now examining how different foods affect the gut microbiota. For instance, a recent human interventional investigation on mango pulp consumption showed a link between improved gut microbial diversity and cardiovascular outcomes with the abundanceof specific bacterial species. Additionally, the advantages of a Mediterranean diet in terms of general health have been wellestablished. In a pilot trial, four days of either a Westernised fast-food diet or a Mediterranean diet were consumed. When fast food was consumed, the gut's makeup closely resembled that of chronic disease, as opposed to the Mediterranean diet, which revealed the reverse. High protein intake increases the risk of cardiovascular and intestinal diseases, obesity, Type 2 Diabetes Mellitus (T2DM), and disorders of the Central Nervous System (CNS) due to the toxic metabolites of branch-chained fatty acids, ammonia, indoles, phenols, and hydrogen sulphide. Skeletal muscle loss due to protein anabolism can occur in the elderly if probiotics and prebiotics that boost short-chain fatty acids aren't taken into account[10].

FMT and probiotic strain alignment with host health status

A variety of artificial FMTs have been created, building on the ground-breaking work of Allen-Vercoe, who attempted to choose strains from the faeces of a healthy donor and propagate them to replace FMTs. This work aims to separate out strains that may have pathogenic potential or have no role to play in colonising the recipient and out-competing *C. difficile*. It also seeks to avoid the time-consuming and expensive issues associated with identifying and retaining access to donor stool . One of these products, SER-109, still needs donor faeces, which is treated using a unique technology to get rid of viruses, parasites, and vegetative bacteria. A variety of species, including *Bacillus, Clostridium, Eubacterium, Blautia,* and *Roseburia* among many others, are the end result . The treatment has been shown to lessen infection recurrence, which may have happened because bile acid synthesis suppressed the pathogen's spores. It's interesting that the product is not referred to as a probiotic, which may have been done to avoid comparison to other probiotics and facilitate FDA approval; alternatively, it could be because the strains are not documented and vary from batch to batch, failing to meet the definition of a probiotic. Ferring Pharma and NuBiyota have continued their development while a company that was working on another neuroprotective compound, CP101, cancelled the product trials. NuBiyota has succeeded in growing strict anaerobes and encapsulating them into high-quality drugs with optimal stability, with the goal of first treating recurrent *C. difficile*. Due to intellectual property concerns, the specifics of these business's products are not yet publicised, but it is likely that the strains chosen were chosen for their ability to coexist, be safely applied, and hinder infection. To the best of our knowledge, there are no dietary suggestions with their administration.

CONCLUSIONS

It is gradually becoming understood that nutrients consumed and how the microbiota respond to them are related. However, to test specific microbes (probiotic or FMT compositions) with a dietary intake that promotes the growth of desired organisms and metabolites for each person's primary health issue, human interventional studies are required.

These signals may be linked to the heart, the brain, the liver, or the pancreas. Aligning microorganisms with food may help to treat potentially lethal conditions like PKU and *C. difficile* while also improving patient prognosis. The objective is that with more research in this area, clinical practise guidelines may eventually be able to suggest particular microorganisms to treat a range of illnesses/conditions.

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