Diet and the microbiota–gut–brain-axis: a primer for clinical nutrition

Gabriela Ribeiroa, Aimone Ferria, Gerard Clarkea,b and John F. Cryana,c

Purpose of review
Diet is an essential modulator of the microbiota–gut–brain communication in health and disease. Consequently, diet-induced microbiome states can impact brain health and behaviour. The integration of microbiome into clinical nutrition perspectives of brain health is sparse. This review will thus focus on emerging evidence of microbiome-targeted dietary approaches with the potential to improve brain disorders.

Recent findings
Research in this field is evolving toward randomized controlled trials using dietary interventions with the potential to modulate pathways of the microbiota–gut–brain-axis. Although most studies included small cohorts, the beneficial effects of Mediterranean-like diets on symptoms of depression or fermented foods on the immune function of healthy individuals shed light on how this research line can grow. With a clinical nutrition lens, we highlight several methodological limitations and knowledge gaps, including the quality of dietary intake information, the design of dietary interventions, and missing behavioural outcomes.

Summary
Findings in diet–microbiome–brain studies can have groundbreaking implications in clinical nutrition practice and research. Modulating brain processes through diet via the gut microbiota raises numerous possibilities. Novel dietary interventions targeting the microbiota–gut–brain-axis can offer various options to prevent and treat health problems such as mental disorders. Furthermore, knowledge in this field will improve current nutritional guidelines for disease prevention.

Keywords
clinical nutrition, diet, mental health, microbiota–gut–brain-axis

INTRODUCTION

The gut microbiota refers to the trillions of micro-organisms residing within the gut, with the microbiome referring to the full collection of genes of these gut microbes. It is now established that this community of bacteria is an essential determinant of key set points across multiple aspects of human physiology [1], including critical functions in energy metabolism [2**] and immunity [3**], extending from gastrointestinal health to brain function and behaviour [1,4,5,6*]. A central question is whether ‘feeding the microbiome’ modulates brain function and human behaviour [7]. The beneficial effects of diet can be moderated or mediated via processes involving the communication pathways between the gut microbiome and the brain (i.e., the microbiota–gut–brain-axis) [8].

Although clinical evidence is limited, recent systematic reviews and meta-analyses of the available evidence have shed light on microbiota signatures in psychiatric disorders [9,10**,11,12]. These findings led to novel research in microbiome-targeted therapies termed ‘psychobiotics’, including administration of live organisms (i.e., prebiotics, synbiotics, postbiotics), faecal microbial transplants, and dietary interventions to reshape microbiome composition and function to a protective profile with beneficial effects on brain and behaviour [7,13,14]. Among psychobiotic therapies, the administration of probiotic organisms (mostly *Bifidobacterium* and...
**KEY POINTS**

- The microbiota–gut–brain-axis comprises several pathways and mechanisms prone to dietary modulation and is of vital interest in clinical nutrition.

- A healthy dietary pattern with varied sources of fibres, phytochemicals and beneficial live bacteria is health-promoting through physiological modulation of the microbiota–gut–brain-axis.

- A western-like diet can lead to altered microbiota composition and low-grade systemic inflammation, as observed in mental illness.

- The use of randomized controlled trials to test microbiota-target dietary approaches with the potential to improve brain disorders is increasing.

- Despite promising findings, methodological limitations in diet–microbiome–brain studies remain to be addressed.

Although most of this knowledge comes from pre-clinical studies, there is emerging interest in translating diet–microbiome–brain findings into clinical research [7,12,13,16]. The bidirectional communication between the gut microbiome and the brain, known as the microbiota–gut–brain-axis, comprises neuroendocrine-immune pathways [15]. The most studied microbial-derived metabolites are short-chain fatty acids (SCFAs – acetate, propionate, and butyrate), resulting from microbial processing of dietary indigestible fibres [15,17]. SCFAs act on enterendocrine L cells secreting glucagon-like peptide-1 (GLP-1) and peptide Y.Y. (PYY). These anorexigenic peptides act on hypothalamic centres to control feeding behaviour and energy balance [5,15,18,19]. Additionally, bacteria-derived secondary bile acids and bacterial lipopolysaccharide (LPS) can enhance GLP-1 secretion in L cells. SCFAs also have immune functions, for example, by promoting host intestinal barrier integrity (e.g., stimulation of mucus production and tight junction assembly) [15]. Other actions of SCFAs include regulating the suppression of cytokine production from myeloid cells and differentiating T regulatory and T helper cell differentiation [15].

Gut microbes synthesize key neuroactive molecules such as the γ-aminobutyric acid (GABA), catecholamines (noreadrenaline, norepinephrine, dopamine), serotonin (5-HT) and tryptophan metabolites and precursors. However, the relative effects of bacterial-derived catecholamines in host physiology are mainly unknown [5,15,18,19]. Gut bacteria can convert neurotransmitters precursors into active forms, such as the amino acid glutamate to GABA by *Escherichia* spp., while *Lactobacillus* spp. can stimulate the conversion of dietary tryptophan into 5-HT by enterochromaffin cells [15]. These neuroactive molecules can interact with the autonomic nervous system or stimulate vagal sensory neurons in the gut leading to neuronal activation in the *nucleus tractus solitarius* (NTS) [5,15,18,19]. The NTS then conveys information to other brain structures, such as the hypothalamus, nucleus accumbens, and ventral tegmental area, thus controlling homeostatic and reward-related feeding behaviour [5,15,18,19].

The composition of the diet can impact these pathways through several factors [16] (Fig. 1). For example, a healthy diet (with varied sources of dietary fibre [20,21], phytochemicals [22], or live bacteria [3,23]) can promote increased microbial diversity and production of SCFA and other bioactive compounds with beneficial physiological effects from gastrointestinal and metabolic health to brain processes [3,13,16,20,21,23]. On the contrary, a western-like pattern comprising processed foods lacking the recommended quantity of

*Lactobacillus* strains, alone or combined) has been the most tested, for example, in clinical depression [14]. In contrast, dietary therapies, either using specific dietary factors (e.g., dietary fibre supplements) or whole dietary interventions (e.g., Mediterranean diet), are much less studied in terms of their impact on the gut microbiome, at least in part, due to their methodological challenges. Compared with other psychobiotic interventions, the effect of diet is ubiquitous, extending across the entire lifespan with implications for neurodevelopment and neurodegeneration [7,13]. Therefore, modulating the microbiota–gut–brain-axis through diet is a promising approach to preventing and treating mental health disorders. However, dietary gut microbiota–target interventions are in their early stage of research. Although more randomized clinical trials (RCTs) are emerging, it is crucial to address methodological limitations inherent to dietary intervention studies and collect high-quality microbiome, brain, and behavioural data simultaneously. Thus, this opinion review will focus on recent studies that used dietary gut microbiota–target interventions, emphasizing those with behavioural data in the context of mental health. In addition, we will discuss recommendations for establishing more informative and robust dietary assessment protocols and interventions in diet–microbiome studies.

**THE MICROBIOTA–GUT–BRAIN-AXIS**

There are many pathways through which the gut–microbiota communicates with the brain that are prone to dietary modulation [1,5,7,13,15,16].
dietary fibre and with higher content of saturated fats, salt and sugars can result in suboptimal gut microbiota composition and a low-grade systemic inflammation associated, for example, with mental illness, gastrointestinal pathology and metabolic disorders [11] and obesity [24,25] (Fig. 1).

**EVIDENCE FROM GUT–MICROBIOME TARGETED DIETARY INTERVENTIONS IN MENTAL HEALTH**

Recent systematic reviews and meta-analyses have supported the role of the gut microbiome in mental health [9,10,11]. For example, there is evidence of...
a lower relative abundance of SCFA-producing genera and a higher relative abundance of lactic acid-producing bacteria genera across different psychiatric disorders [9,10]. And, increased circulating levels of the tight-junction protein zonulin, the endotoxin LPS and gut-related systemic inflammatory markers have been shown in patients with severe mental illness and chronic fatigue relative to controls [11]. In addition, recent RCTs have raised attention to the efficacy of dietary interventions in outcomes relevant to mental disorders, such as improvement of depression symptoms [3**,26*,27–29]. This section will provide a nonextensive discussion of recent findings of diet–microbiome studies, highlighting those with behavioural outcomes whenever possible.

The Mediterranean diet, which has long been recognized as health-promoting [30], was first tested as an adjunct to conventional antidepressant therapy in the ‘SMILES’ trial [29,31]. This 12-week Mediterranean diet-like intervention showed a significant improvement in depression symptomatology compared with befriending support (control intervention) for patients with major depressive disorder. The beneficial effects of the Mediterranean Diet on mood were corroborated in a cohort of young males with clinical depression in which 12 weeks of dietary intervention resulted in decreased symptoms of depression relative to befriending therapy [26*]. In adults with depression, a Mediterranean-like diet combined with fish oil (i.e., omega-3) supplementation improved symptoms of depression relative to controls that received social support [32]. However, most studies focused on the impact of diet on behavioural outcomes and did not provide data on the gut microbiome. On another side, in a multicountry cohort of elderly subjects, adherence to a Mediterranean-like intervention for 1 year was associated with enriched microbial taxa and multiple markers of decreased frailty and improved cognitive function [27].

Fermented foods such as yoghurt, kefir and kombucha obtained from microbial growth and enzymatic conversions of food components [33] have been associated with improved gastrointestinal and metabolic health [13,16*,34]. However, studies reporting brain and behaviour outcomes are few. For example, a prospective RCT in healthy participants showed that a diet high in fermented foods (4–6 portions per day) led to increased microbiome’s diversity and reduced pro-inflammatory cytokines such as serum interleukin (IL)-6 [3**]. Another RCT with a double-blind placebo-controlled design showed that daily consumption of a fermented milk beverage improved symptoms of depression and decreased serum IL-6 in patients with depression. However, an improved mood was also observed in the placebo group [35].

Moreover, a randomized crossover trial in healthy volunteers demonstrated that consuming a kefir beverage did not change mood outcomes but resulted in improved memory performance and increased relative abundance of Lactobacillus [36]. Finally, in a prospective study of healthy medical students under psychological stress (academic exams), higher fermented foods consumption was associated with the severity of depressive and anxiety symptoms [37], which was not found for food-derived prebiotics. In contrast, higher consumption of fermented foods was associated with lower severity of depressive symptoms in medical students with psychiatric illness, while no association was found for anxiety symptoms [23]. These results suggest that interventions with fermented foods can modulate brain processes through changes in the gut microbiome and gut–brain-axis pathways, which are worthy of further investigation. Nevertheless, larger trials in healthy and clinical populations, such as those including patients with mood and anxiety disorders, are needed to establish a role for fermented foods as dietary interventions to target the microbiota–gut–brain-axis.

Other diet-related approaches to target the microbiota–gut–brain-axis include even less explored avenues such as ketogenic diets and intermittent fasting. For example, there is preclinical evidence that gut microbiota mediates the effects of ketogenic diets in rodent models of epilepsy [38]. Additionally, evidence comes primarily from studies in children where those with epilepsy showed different microbiota relative to healthy controls, with either increased or decreased diversity depending on the disease status and the response to drugs or ketogenic diets [39]. Furthermore, children that benefited from ketogenic diets had increased butyrate levels and decreased relative abundance of specific genera such as Bifidobacterium, Akkermansia, Enterococcaceae and Actinomyces [39].

Intermittent fasting has gained attention mainly in weight management and improved metabolic outcomes, although the underlying mechanisms are not yet clarified. The gut microbiome may have a potential role in those outcomes. However, diet–microbiome studies in humans have been limited to Ramadan fasting. For example, 1-month intermittent fasting in Ramadan induced an increased relative abundance of butyric acid-producing Lachnospiraceae and improved body mass index and blood glucose relative to nonfasting controls [40]. But, since Ramadan fasting results in decreased energy intake and a profound dietary modification [41], it does not necessarily reflect the more common intermittent fasting approaches. Energy consumption and dietary macronutrient distribution are not necessarily modified in
the latter. Thus, controlled studies using fasting as an intervention are needed, accounting for energy intake, dietary composition, gut microbiota, and behavioural data.

**KEY POINTS FOR DESIGNING A DIET–MICROBIOME–BEHAVIOUR STUDY**

Human studies aiming to assess diet–microbiome–behaviour effects face several levels of complexity, from intra-individual variability in the microbiome [42] to limitations inherent in diet studies (e.g., difficulty in assessing dietary intake and adherence to diet) [42]. One major challenge is the lack of standardized protocols for dietary assessment or interventions in microbiome studies [43]. This section will provide a nonexhaustive critical review of fundamental aspects for designing diet–microbiome–behaviour studies, including selecting dietary assessment methods and implementing dietary interventions.

**ESTABLISHING AN APPROACH FOR DIETARY INTAKE ASSESSMENT**

The assessment of dietary intake in free-living settings is a major challenge in nutrition research [44], extending to diet–microbiome studies. In brief, dietary intake can be evaluated using direct methods, comprising direct observation, duplicate diets, and nutritional biomarkers [45,46]. More commonly, indirect (self-report) methods, such as food diaries (weighed or estimated), 24-h dietary recalls and Food Frequency Questionnaires (FFQs) [45,46], are used due to their lower cost and burden [45]. However, all subjective techniques rely on the participant’s self-report and, thus, on memory, past experiences, and perceptions [46]. Therefore, all self-report methods are prone to systematic bias and misreporting issues [44,46].

Conversely, more objective methods such as nutritional biomarkers, despite being more expensive and complex to measure, are less susceptible to misreporting [44,45]. Examples of nutritional biomarkers in dietary assessment are total energy intake measured by doubly-labelled water and omega-3 and -6 fatty acids evaluated by blood fatty acid concentration or tissue lipid compartment [45]. Other examples are concentrations of minerals and vitamins in urine (e.g., potassium, iodine), serum (e.g., calcium, phosphorus, magnesium, iron, zinc, vitamins D, E and C) and plasma (e.g., selenium, zinc, vitamin K, folate and vitamin B12) [45]. Specific nutritional biomarkers include phytochemicals, carotenoids, caffeine metabolites, flavones, isoflavones and phytosterols [45]. Despite the potential of biomarkers for assessing dietary intake, particularly given the specificity of diet–microbiome studies, they do not replace self-reported data entirely [44]. Thus, ideally, both methods should be combined for optimal results [44].

In the microbiome literature, indirect methods have been primarily used, particularly Food Frequency Questionnaire (FFQs). The latter provided insight into the relationship between dietary patterns and gut–microbiome features, such as the microbial genera abundance [47]. FFQs have several strengths: lower participant burden, lower cost than other dietary assessment methods, and relatively quick and automated data analysis. However, the self-report intake in FFQs is memory dependent and limited to items comprised by the food list [46]. Thus, it may not capture specific foods relevant to diet–microbiome studies (e.g., fermented foods) or ethnic differences since they are developed for particular populations [43]. On the other side, food diaries provide reasonable estimates of energy intake and most nutrients, foods, and food groups.

Furthermore, FFQs may lead to higher misreport when compared to other tools such as food diaries. For example, in a 12-month study including over 1000 participants, energy intake was more underestimated by FFQs than automated self-administered 24-h recalls or unweighted 4-day food diaries when compared against its biomarker (i.e., energy intake assessed by doubly labelled water) [48]. Additionally, the validity of the assessment tool can depend on the nutrient being evaluated. For example, the EPIC-Norfolk Study showed that a 7-day food diary performed consistently better than the FFQ for vitamin C (both urinary and plasma measures). At the same time, consistent results were found for polyunsaturated fatty acid intakes [45].

However, food diaries can result in a higher participant burden, data entry requires substantial time, and human resources with expertise in dietetics are necessary [45]. Technology assistance (e.g., smartphone applications) can attenuate these limitations, decreasing researcher burden in data collection and entry and improving standardization across multiple assessments [45]. For example, mobile app-recorded food diaries were successfully applied in a gut–microbiota–targeted dietary intervention study in healthy volunteers [3**]. Furthermore, among other digital-based dietary programs, the app version had higher engagement and lower nonusage attrition in patients with depression [49], reinforcing the utility of digital-based dietary assessment in future diet–microbiome–behaviour studies.

In summary, direct and self-report methods have advantages and disadvantages, and there is not a one-size fit solution for dietary assessment methods. However, according to the study design and research question, researchers can decide which
Micronutrient supplementation and functional foods

instruments to include based on available toolkits (see Dao et al. [46] for details). Furthermore, in diet–microbiome–behaviour studies, nutritional biomarkers can be an asset to address food composition variability and the effects of food processing and cooking methods [44]. Although this approach needs further validation [44], it has the potential to change current dietary assessment practices. Lastly, using digital-based options is also recommended [44], mainly when the software uses validated databases and calculation methods [44].

DESIGNING MICROBIOME-TARGETED DIETARY INTERVENTIONS

Several aspects must be considered when designing a dietary intervention in a microbiome study. One critical question is the optimal duration of the dietary intervention [43]. Preclinical evidence showed rapid diet-induced changes in the gut–microbiome, consistent with results from different dietary interventions in humans that resulted in microbiome composition changes within days [28,50]. However, there is also evidence of gut–microbiota resilience as shown in long-term dietary interventions for weight loss [51]. The initial shift in the microbiota was followed by a return to baseline characteristics even though the participants maintained the prescribed diet and weight loss [51]. Accordingly, the length of a dietary intervention required to induce changes at the host level is suggested to be weeks or months, depending on the outcomes of interest and the study design (longer for crossover design) [43]. In addition, other factors such as baseline microbiota composition and extent of change in a dietary intervention (e.g., increasing fibre intake vs. switching to vegetarian from a meat-based diet) will probably play a role. Also, the impact of dietary interventions on the habitual diet and overall feeding behaviour in diet–microbiome studies has not been consistently assessed and reported to the best of our knowledge. For example, increasing dietary fibre intake or introducing novel foods can impact satiety and satiation [21], and thus habitual dietary intake regarding energy content and macronutrient composition. Therefore, diet–microbiome studies would benefit from assessing the participants’ baseline diet and feeding behaviour characteristics (e.g., hunger, satiety and fullness) and monitoring the relationship between these parameters throughout the follow-up.

Furthermore, participants must be willing to comply with the changes in diet that can comprise novel foods, unusual textures, cooking methods,

| Table 1. Critical points for designing diet–microbiome–brain and behaviour studies | Assessment of dietary intake types of methods | Planning | Dietary Intervention | Follow-up |
| --- | --- | --- | --- | --- |
| Domain | Subjective | Objective | | | |
| General advice | Food diaries | Direct observation | Characterize baseline diet using a representative time frame | Conduct structured visits to address difficulties in diet records or diet compliance |
| | 24 h dietary recalls | Duplicate diets | Estimate energy requirements and energy expenditure to define the diets’ caloric value | Monitor anthropometric measures and nutritional biomarkers |
| | FFQs | Nutritional biomarkers | Conduct assessment of nutritional status, including anthropometry | Assess diet-related side effects |
| | Diet checklists | Develop measures to reduce attrition | Individualize diet according to baseline preferences | Evaluate potential changes in habitual diet, appetite, or lifestyle |
| | Diet histories | | | |
| | Technology-assisted dietary assessment | Consult dietary assessment toolkits to guide selecting and implementing the most appropriate diet assessment protocol | | |
| | | | | |
| | Preferred validated methods that allow for data comparability and harmonization of nutritional databases | | | |
| Challenges | Find a balance between the burden of the participants and researchers and data accuracy and specificity | Define a sufficiently specific intervention without compromising feasibility | Personalize the intervention according to specificities | Deal with attrition and compliance |
| Solutions | Use web-based methods such as smartphone apps for dietary intake registering and data processing. The latter can be validated with conservative software and databases | Anticipate barriers to diet compliance in the target population and specific outcomes | Provide varied and equivalent food alternatives to high-fibre or high fermented foods | Use behaviour change techniques (e.g., goal setting, problem-solving, feedback and monitoring) |
| | Consider combining subjective measures with objective measures such as nutritional biomarkers | Examples: lower acceptance for specific textures and tastes (e.g., high-fibre foods) Motivation to consume novel foods (e.g., fermented foods) | Use motivational strategies such as motivational interview to deliver information | Potential need to utilize different methods for delivering the intervention that does not require in-person attendance (e.g., telehealth) |
| | | Consider providing prepared meals or a laboratory setting if the budget allows | Use a nonstigmatizing approach | Measure and analyse both usage and intensity of use of measures of web-based interventions |
and shopping habits. In this context, knowledge acquired from lifestyle programs (e.g., diabetes prevention) [52], including behavioural change techniques and strategies to promote engagement and attenuate retention, can be translated into diet–microbiome–behaviour studies, particularly relevant when studying individuals with mental disorders [52]. Thus, researchers must design dietary interventions, considering available resources and the specificities of the targeted population, among other relevant factors such as assessment of compliance to diet, as shown in Table 1.

**CONCLUSION**

Diet–microbiota–gut–brain-axis is an emerging topic with high potential application for clinical nutrition. Controlled diet–microbiome studies in humans are emerging with promising findings for brain health. However, much work is needed to address current limitations in this field. Future diet–microbiome studies will benefit from standardized methods for dietary assessment based on validated approaches but with sufficient specificity for the microbiome field. In terms of intervention studies, it is critical to determine the optimal length of dietary intervention, to test behavioural approaches to promote compliance with diet specificities and to include behavioural outcomes along with microbiome and nutritional data. Lastly, the resources required for developing technologically assisted methodologies, including mental health populations, should be considered when designing new diet–microbiome studies.

**Acknowledgements**

None.

**Financial support and sponsorship**

Prof. Cryan is funded by Science Foundation Ireland SFI/12/RC/2273_P2, the Saks Kavanagh Foundation, EU H2020 project DLV-848228 DIS-CovERIE, and Swiss National Science Foundation project CRSII5_186346/NMS2068. G.R. was funded by a Postdoctoral Fellowship [Grant number 3932R20789].

**Conflicts of interest**

Prof. Cryan has received research funding from 4D Pharma, Cremo, Dupont, Mead Johnson, Nutricia, and Pharmavite; has been an invited speaker at meetings organized by Alimentary Health, Alkernes, Ordesa, and Yakult; and has served as a consultant for Alkernes and Nestle. This support neither influenced nor constrained the contents of this article.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest

1. Long-Smith C, O’Riordan KJ, Clarke Q, et al. Microbiota–gut–brain axis: new therapeutic opportunities. Annu Rev Pharmacol Toxicol 2020; 60:477–502.
2. Schellekens H, Torres-Fuentes C, van de Wouw M, et al. *Bifidobacterium longum* counters the effects of obesity: partial successful translation from rodent to human. eBioMedicine 2021; 103176. doi:10.1016/j.ebiom.2020.103176.
3. Wastyn HC, Fragiadakis GK, Perelman D, et al. Gut-microbiota-targeted diets modulate human immune status. Cell 2021; 184:4137.e14–4159.e14. This 17-week randomised, prospective multilocus study showed the differential effects of a high-fibre or fermented-food diet on the microbiome’s diversity, with the latter decreasing inflammatory markers and modulating immune responses.
4. Cruz-Pereira JS, Rea K, Nolan YM, et al. Depression’s unholy trinity: dysregulated stress, immunity, and the microbiome. Annu Rev Psychol 2020; 71:49–78.
5. Garcia-Cabrero R, Carbia C, O’Riordan KJ, et al. Microbiota–gut–brain axis: an evaluation of reward processes. J Neurochem 2021; 157:1495–1524.
6. Meyer K, Lulla A, Debroy K, et al. Association of the gut microbiota with cognitive function in middle age. JAMA Netw Open 2022; 5:e2143941–e2143941.
7. Berding K, Cryan JF. Microbiota-targeted interventions for mental health. Curr Opin Psychiatry 2022; 35:3–9.
8. Marx W, Lane M, Hockey M, et al. Diet and depression: exploring the biological mechanisms of action. Mol Psychiatry 2021; 26:134–150.
9. McGuinness AJ, Davis JA, Dawson SL, et al. A systematic review of gut microbiota composition in observational studies of major depressive disorder, bipolar disorder and schizophrenia. Mol Psychiatry 2022; 27:1920–1935.
10. Nikolova VL, Hall MRB, Hall LJ, et al. Perturbations in gut microbiota composition in psychiatric disorders: a review and meta-analysis. JAMA Psychiatry 2021; 78:1343–1354.

This systematic review and meta-analysis showed that gut microbiota perturbations (i.e., depletion of certain anti-inflammatory butyrate-producing bacteria and enrichment of pro-inflammatory bacteria) were shared by distinct psychiatric disorders, namely depression, bipolar 375 disorder, schizophrenia, and anxiety.
11. Safadi JM, Quinton AMG, Lennox BR, et al. Diet-induced enrichment of pro-inflammatory bacteria were shared by distinct psychiatric populations (i.e., depletion of certain anti-inflammatory butyrate-producing bacteria and enrichment of pro-inflammatory bacteria) were shared by distinct psychiatric disorders, namely depression, bipolar 375 disorder, schizophrenia, and anxiety.
12. Safadi JM, Quinton AMG, Lennox BR, et al. Diet-induced enrichment of pro-inflammatory bacteria were shared by distinct psychiatric populations (i.e., depletion of certain anti-inflammatory butyrate-producing bacteria and enrichment of pro-inflammatory bacteria) were shared by distinct psychiatric disorders, namely depression, bipolar 375 disorder, schizophrenia, and anxiety.
13. Spichak S, Bastiaanssen TFS, Berding K, et al. Mining microbes for mental health: determining the role of microbial metabolic pathways in human brain health and disease. Neurosci Biobehav Rev 2021; 126:698–781.
14. Berding K, Vickova K, Marx W, et al. Diet and the microbiota–gut–brain axis: sowing the seeds of good mental health. Adv Nutr 2021; 12:1259–1285.
15. Horn J, Mayer DE, Chen S, Mayer EA. Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders. Transl Psychiatry 2022; 12:164.
16. Arnet AM, Deehan EC, O’Sullivan AF, et al. Rethinking healthy eating in light of the gut microbiome. Cell Host Microbe 2022; 30:764–785.
17. Spichak S, Bastiaanssen TFS, Berding K, et al. Mining microbes for mental health: determining the role of microbial metabolic pathways in human brain health and disease. Neurosci Biobehav Rev 2021; 126:698–781.
18. Arnet AM, Deehan EC, O’Sullivan AF, et al. Rethinking healthy eating in light of the gut microbiome. Cell Host Microbe 2022; 30:764–785.
19. Spichak S, Bastiaanssen TFS, Berding K, et al. Mining microbes for mental health: determining the role of microbial metabolic pathways in human brain health and disease. Neurosci Biobehav Rev 2021; 126:698–781.
20. Arnet AM, Deehan EC, O’Sullivan AF, et al. Rethinking healthy eating in light of the gut microbiome. Cell Host Microbe 2022; 30:764–785.
21. Berding K, Carbia C, Cryan JF. Going with the grain: fibre, cognition, and the microbiota–gut–brain–axis. Exp Biol Med 2021; 246:796–811.

1363-1950 Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. www.co-clinicalnutrition.com 449
28. Zhu C, Sawrey-Kubicek L, Beals E, O’Neil A, Berk M, Itsiopoulos C, (befriending therapy). Mediterranean diet intervention led to significant decreases in symptoms of depression and anxiety in young males (the “AMMEND” study): a randomized control trial. Am J Clin Nutr 2022; 126:730–737.

29. In this 12-week, parallel-group, open-label, randomized control trial, a Mediterranean diet intervention supplemented with fish oil improves diet quality and mental health in young males compared to a control intervention (befriending therapy).

30. Ghosh TS, Rampelli S, Jeffery IB, et al. Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries. Gut 2020; 69:1218.

31. Dong TS, Guan M, Mayer EA, et al. Obesity is associated with a distinct brain-gut microbiome signature that connects Prevotella and Bacteroides to the brain’s reward center. Gut Microbes 2022; 14:2051999–12051999.

32. Dong TS, Mayer EA, Osadchy V, et al. A distinct brain–gut–microbiome profile exists for females with obesity and food addiction. Obesity 2020; 28:1477–1486.

33. Bayes J, Schloss J, Sibbritt D. The effect of a Mediterranean diet on the symptoms of depression in young males (the “AMMEND” study): a randomized control trial. Am J Clin Nutr 2022; 126:730–737.

34. In this 12-week, parallel-group, open-label, randomized control trial, a Mediterranean Diet intervention led to significant decreases in symptoms of depression and increased quality of life in young males compared to a control intervention (befriending therapy).

35. Ghosh TS, Rampelli S, Jeffery IB, et al. Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries. Gut 2020; 69:1218.

36. Parretta N, Zamowicki D, Cho J, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomized controlled trial (HELPIXED). Nutr Neurosci 2019; 22:474–487.

37. Marco ML, Sanders ME, Gänzle M, et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods. Nat Rev Gastroenterol Hepatol 2021; 18:196–208.

38. Rocks T, West M, Hockey M, et al. Possible use of fermented foods in rehabilitation of anorexia nervosa: the gut microbiota as a modulator. Prog Neuropsychopharmacol Biol Psychiatry 2021; 107:112021.

39. Zhang X, Chen S, Zhang M, et al. Effects of fermented milk containing Lactococcus lactis subsp. cremoris on plasma lipoprotein levels in postmenopausal women. J Nutr Biochem 2022; 132:2338.

40. Cannavale CH, Mysorekar AR, Bailey MA, et al. Consumption of a fermented dairy beverage improves hippocampal-dependent relational memory in a randomized, controlled cross-over trial. Nutr Neurosci 2022; 13:1–10.

41. Karbownik MS, Mokros L, Dobiesla M, et al. Association between consumption of fermented food and food-derived prebiotics with cognitive performance, depressive, and anxiety symptoms in psychologically healthy medical students under psychological stress: a prospective cohort study. Front Nutr 2022; 9:850249.

42. Mu C, Choudhary A, Mayengbam S, et al. Seizure modulation by the gut microbiota and tryptophan-kynurenine metabolism in an animal model of infantile spasms. eLifeMedicine 2022; 7:103833.

43. Gong X, Cai Q, Liu X, et al. Gut flora and metabolism are altered in epilepsy and partially restored after ketogenic diets. Microb Pathog 2021; 155:104899.

44. Su J, Wang Y, Zhang X, et al. Remodeling of the gut microbiome during Ramadan-associated intermittent fasting. Am J Clin Nutr 2021; 113:1332–1345.

45. Ali I, Liu K, Long D, et al. Ramadan fasting leads to shifts in human gut microbiota structured by dietary composition. Front Microbiol 2021; 12:642989.

46. Wilkinson JE, Franzosa EA, Everett C, et al. A framework for microbiome science in public health. Nat Med 2021; 27:766–774.

47. Johnson AJ, Zheng JJ, Kang JW, et al. A guide to diet-microbiome study design. Front Nutr 2020; 7:79.

48. de la Hunty A, Buttriss J, Draper, et al. UK Nutrition Research Partnership (NRP) workshop: forum on advancing dietary intake assessment. Nutr Bull 2021; 46:228–237.

49. Medical Research Council, National Institute for Health Research. Diet, Anthropometry and Physical Activity (DAPA) measurement toolkit. Available at: https://dapatoolkit.mrc.ac.uk/ [Accessed June 15, 2022]

50. Dao MC, Subar AF, Warthon-Medina M, et al. Dietary assessment toolkits: an overview. Public Health Nutr 2019; 22:404–418.

51. Shikany JM, Demmer RT, Johnson AJ, et al. Association of dietary patterns with the gut microbiota in older, community-dwelling men. Am J Clin Nutr 2019; 110:1003–1014.

52. Park Y, Dodd KW, Kipnis V, et al. Comparison of self-reported dietary intakes from the automated self-administered 24-h recall, four food records, and food-frequency questionnaires against recovery biomarkers. Am J Clin Nutr 2018; 107:80–93.

53. Young CL, Mohabib M, Staudacher HM, et al. Optimizing engagement in an online dietary intervention for depression (My Food & Mood version 3.0): cohort study. JMIR Ment Health 2021; 8:e24871.

54. Gutthu L, Spencer SP, Perelman D, et al. Impact of a 7-day homogeneous diet on interpersonal variation in human gut microbiomes and metabolomes. Cell Host Microbe 2022; 30:863.e4–874.e4.

55. Fragiadakis GK, Wastyn HC, Robinson J, et al. Long-term dietary intervention reveals resilience of the gut microbiota despite changes in diet and weight. Am J Clin Nutr 2020; 111:1127–1138.

56. This study analysed data from a randomised intervention study of participants consuming a healthy low-carbohydrate or low-fat diet. While each diet resulted in significant changes in the microbiota composition shortly after the intervention, the microbiota returned to its original baseline state, despite participants maintaining their diet and weight loss for the remaining intervention. These results suggest a resilience of the microbiota’s perturbation.

57. Opie RS, Jacka FN, Marx W, et al. Designing lifestyle interventions for common mental disorders: what can we learn from diabetes prevention programs? Nutrients 2021; 13: doi: 10.3390/nu13113766.