Food and mood: how do diet and nutrition affect mental wellbeing?

Poor nutrition may be a causal factor in the experience of low mood, and improving diet may help to protect not only the physical health but also the mental health of the population, say **Joseph Firth and colleagues**

Depression and anxiety are the most common mental health conditions worldwide, making them a leading cause of disability.[1] Even beyond diagnosed conditions, subclinical symptoms of depression and anxiety affect the wellbeing and functioning of a large proportion of the population.[2] Therefore, new approaches to managing both clinically diagnosed and subclinical depression and anxiety are needed.

In recent years, the relationships between nutrition and mental health have gained considerable interest. Indeed, epidemiological research has observed that adherence to healthy or Mediterranean dietary patterns—high consumption of fruits, vegetables, nuts, and legumes; moderate consumption of poultry, eggs, and dairy products; and only occasional consumption of red meat—is associated with a reduced risk of depression.[3] However, the nature of these relations is complicated by the clear potential for reverse causality between diet and mental health (fig 1). For example, alterations in food choices or preferences in response to our temporary psychological state—such as "comfort foods" in times of low mood, or changes in appetite from stress—are common human experiences. In addition, relationships between nutrition and longstanding mental illness are compounded by barriers to maintaining a healthy diet. These barriers disproportionality affect people with mental illness and include the financial and environmental determinants of health, and even the appetite inducing effects of psychiatric medications.[4]

While acknowledging the complex, multidirectional nature of the relationships between diet and mental health (fig 1), in this article we focus on the ways in which certain foods and dietary patterns could affect mental health.

KEY MESSAGES

- Healthy eating patterns, such as the Mediterranean diet, are associated with better mental health than "unhealthy" eating patterns, such as the Western diet
- The effects of certain foods or dietary patterns on glycaemia, immune activation, and the gut microbiome may play a role in the relationships between food and mood
- More research is needed to understand the mechanisms that link food and mental wellbeing and determine how and when nutrition can be used to improve mental health

Mood and carbohydrates

Consumption of highly refined carbohydrates can increase the risk of obesity and diabetes.[5] Glycaemic index is a relative ranking of carbohydrate in foods according to the speed at which they are digested, absorbed, metabolised, and ultimately affect blood glucose and insulin levels. As well as the physical health risks, diets with a high glycaemic index and load (eg, diets containing high amounts of refined carbohydrates and sugars) may also have a detrimental effect on psychological wellbeing; data from longitudinal research show an association between progressively higher dietary glycaemic index and the incidence of depressive symptoms.[6] Clinical studies have also shown potential causal effects of refined carbohydrates on mood; experimental exposure to diets with a high glycaemic load in controlled settings increases depressive symptoms in healthy volunteers, with a moderately large effect.[7]

Although mood itself can affect our food choices, plausible mechanisms exist by which high consumption of processed carbohydrates could increase the risk of depression and anxiety—for example, through repeated and rapid increases and decreases in blood glucose. Measures of glycaemic index and glycaemic load can be used to estimate glycaemia and insulin demand in healthy individuals after eating.[8] Thus, high dietary glycaemic load, and the resultant compensatory responses, could lower plasma glucose to concentrations that trigger the secretion of autonomic counter-regulatory hormones such as cortisol, adrenaline, growth hormone, and glucagon.[5 9] The potential effects of this response on mood have been examined in experimental human research of stepped reductions in plasma glucose concentrations conducted under laboratory conditions through glucose perfusion. These findings showed that such counter-regulatory hormones may cause changes in anxiety, irritability, and hunger.[10] In addition, observational research has found that recurrent hypoglycaemia (low blood sugar) is associated with mood disorders.[9]

The hypothesis that repeated and rapid increases and decreases in blood glucose explain how consumption of refined carbohydrate could affect psychological state appears to be a good fit given the relatively fast effect of diets with a high glycaemic index or load on depressive symptoms observed in human studies.[7] However, other processes may explain the observed relationships. For instance, diets with a high glycaemic index are a risk factor for diabetes,[5] which is often a comorbid condition with depression.[4 11] While the main models of disease pathophysiology in diabetes and mental illness are separate, common abnormalities in insulin resistance, brain volume, and neurocognitive performance in both conditions support the hypothesis that these conditions have overlapping pathophysiology.[12] Furthermore, the inflammatory response to foods with a high glycaemic index[13] raises the possibility that diets with a high glycaemic index are associated with symptoms of depression through the broader connections between mental health and immune activation.

Diet, immune activation, and depression

Studies have found that sustained adherence to Mediterranean dietary patterns can reduce markers of inflammation in humans.[14] On the other hand, high calorie

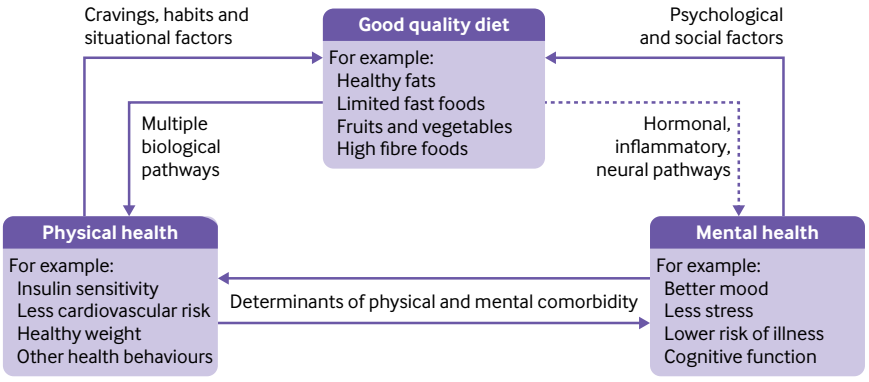

Fig 1 | Hypothesised relationship between diet, physical health, and mental health. The dashed line is the focus of this article.

meals rich in saturated fat appear to stimulate immune activation.[13 15] Indeed, the inflammatory effects of a diet high in calories and saturated fat have been proposed as one mechanism through which the Western diet may have detrimental effects on brain health, including cognitive decline, hippocampal dysfunction, and damage to the blood-brain barrier.[15] Since various mental health conditions, including mood disorders, have been linked to heightened inflammation,[16] this mechanism also presents a pathway through which poor diet could increase the risk of depression. This hypothesis is supported by observational studies which have shown that people with depression score significantly higher on measures of "dietary inflammation,"[3 17] characterised by a greater consumption of foods that are associated with inflammation (eg, trans fats and refined carbohydrates) and lower intakes of nutritional foods, which are thought to have anti-inflammatory properties (eg, omega-3 fats). However, the causal roles of dietary inflammation in mental health have not yet been established.

Nonetheless, randomised controlled trials of anti-inflammatory agents (eg, cytokine inhibitors and non-steroidal anti-inflammatory drugs) have found that these agents can significantly reduce depressive symptoms.[18] Specific nutritional components (eg, polyphenols and polyunsaturated fats) and general dietary patterns (eg, consumption of a Mediterranean diet) may also have anti-inflammatory effects,[14 19 20] which raises the possibility that certain foods could relieve or prevent depressive symptoms associated with heightened inflammatory status.[21] A recent study provides preliminary support for this possibility.[20] The study shows that medications that stimulate inflammation typically induce depressive states in people treated, and that giving omega-3 fatty acids, which have anti-inflammatory properties, before the medication seems to prevent the onset of cytokine induced depression.[20]

However, the complexity of the hypothesised three way relation between diet, inflammation, and depression is compounded by several important modifiers. For example, recent clinical research has observed that stressors experienced the previous day, or a personal history of major depressive disorders, may cancel out the beneficial effects of healthy food choices on inflammation and mood.[22] Furthermore, as heightened inflammation occurs in only some clinically depressed individuals, anti-inflammatory interventions may only benefit certain people characterised by an "inflammatory phenotype," or those with comorbid inflammatory conditions.[18] Further interventional research is needed to establish if improvements in immune regulation, induced by diet, can reduce depressive symptoms in those affected by inflammatory conditions.

Brain, gut microbiome, and mood

A more recent explanation for the way in which our food may affect our mental well-being is the effect of dietary patterns on the gut microbiome—a broad term that refers to the trillions of microbial organisms, including bacteria, viruses, and archaea, living in the human gut. The gut microbiome interacts with the brain in bidirectional ways using neural, inflammatory, and hormonal signalling pathways.[23] The role of altered interactions between the brain and gut microbiome on mental health has been proposed on the basis of the following evidence: emotion-like behaviour in rodents changes with changes in the gut microbiome,[24] major depressive disorder in humans is associated with alterations of the gut microbiome,[25] and transfer of faecal gut microbiota from humans with depression into rodents appears to induce animal behaviours that are hypothesised to indicate depression-like states.[25 26] Such findings suggest a role of altered neuroactive microbial metabolites in depressive symptoms.

In addition to genetic factors and exposure to antibiotics, diet is a potentially modifiable determinant of the diversity, relative abundance, and functionality of the gut microbiome throughout life. For instance, the neurocognitive effects of the Western diet, and the possible mediating role of low grade systemic immune activation (as discussed above) may result from a compromised mucus layer with or without increased epithelial permeability. Such a decrease in the function of the gut barrier is sometimes referred to as a "leaky gut" and has been linked to an "unhealthy" gut microbiome resulting from a diet low in fibre and high in saturated fats, refined sugars, and artificial sweeteners.[15 23 27] Conversely, the consumption of a diet high in fibres, polyphenols, and unsaturated fatty acids (as found in a Mediterranean diet) can promote gut microbial taxa which can metabolise these food sources into anti-inflammatory metabolites,[15 28] such as short chain fatty acids, while lowering the production of secondary bile acids and p-cresol. Moreover, a recent study found that the ingestion of probiotics by healthy individuals, which theoretically target the gut microbiome, can alter the brain's response to a task that requires emotional attention[29] and may even reduce symptoms of depression.[30] When viewed together, these studies provide promising evidence supporting a role of the gut microbiome in modulating processes that regulate emotion in the human brain. However, no causal relationship between specific microbes, or their metabolites, and complex human emotions has been established so far. Furthermore, whether changes to the gut microbiome induced by diet can affect depressive symptoms or clinical depressive disorders, and the time in which this could feasibly occur, remains to be shown.

Priorities and next steps

In moving forward within this active field of research, it is firstly important not to lose sight of the wood for the trees—that is, become too focused on the details and not pay attention to the bigger questions. Whereas discovering the anti-inflammatory

properties of a single nutrient or uncovering the subtleties of interactions between the gut and the brain may shed new light on how food may influence mood, it is important not to neglect the existing knowledge on other ways diet may affect mental health. For example, the later consequences of a poor diet include obesity and diabetes, which have already been shown to be associated with poorer mental health.[11 31-33] A full discussion of the effect of these comorbidities is beyond the scope of our article (see fig 1), but it is important to acknowledge that developing public health initiatives that effectively tackle the established risk factors of physical and mental comorbidities is a priority for improving population health.

Further work is needed to improve our understanding of the complex pathways through which diet and nutrition can influence the brain. Such knowledge could lead to investigations of targeted, even personalised, interventions to improve mood, anxiety, or other symptoms through nutritional approaches. However, these possibilities are speculative at the moment, and more interventional research is needed to establish if, how, and when dietary interventions can be used to prevent mental illness or reduce symptoms in those living with such conditions. Of note, a recent large clinical trial found no significant benefits of a behavioural intervention promoting a Mediterranean diet for adults with subclinical depressive symptoms.[34] On the other hand, several recent smaller trials in individuals with current depression observed moderately large improvements from interventions based on the Mediterranean diet.[35-37] Such results, however, must be considered within the context of the effect of people's expectations, particularly given that individuals' beliefs about the quality of their food or diet may also have a marked effect on their sense of overall health and wellbeing.[38] Nonetheless, even aside from psychological effects, consideration of dietary factors within mental healthcare may help improve physical health outcomes, given the higher rates of cardiometabolic diseases observed in people with mental illness.[33]

At the same time, it is important to be remember that the causes of mental illness are many and varied, and they will often present and persist independently of nutrition and diet. Thus, the increased understanding of potential connections between food and mental wellbeing should never be used to support automatic assumptions, or stigmatisation, about an individual's dietary choices and their mental health. Indeed, such stigmatisation could be itself be a casual pathway to increasing the risk of poorer mental health. Nonetheless, a promising message for public health and clinical settings is emerging from the ongoing research. This message supports the idea that creating environments and developing measures that promote healthy, nutritious diets, while decreasing the consumption of highly processed and refined "junk" foods may provide benefits even beyond the well known effects on physical health, including improved psychological wellbeing.

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