

## Is diet modification an effective adjunct to use when treating mental illness?

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### Abstract

The aim of this article is to highlight that the modification of patients' diets could be used as tool to combat milder symptoms of mental illness, which have been shown to be less responsive to pharmaceutical treatments traditionally used. The article talks about the role of the gastrointestinal microbiota in this process and aims to explain how the food we consume interacts with these microbes, and the consequences these interactions have on mental wellbeing. The article is important because mental illness is a significant public health concern, and more holistic approaches to treating it could be beneficial.

### Abbreviations

*LPS* – lipopolysaccharide  
*PUFAs* – polyunsaturated fatty acids  
*SCFAs* – short chain fatty acids  
*WHO* – World Health Organization

### Introduction

The human gut microbiome is an emerging area for clinical research, with the importance of the flora in our gastrointestinal tracts and relation to mood only being recently acknowledged. Mental health illnesses are an important concern for public health, with approximately one billion people globally managing a mental health

condition in 2019. According to the World Health Organization (WHO), this number was exacerbated by the COVID-19 pandemic as rates of depression and anxiety rose by 25% throughout it.<sup>1</sup>

The type of diet and micronutrients consumed has consequences on mental wellbeing, which is defined as the ability to manage everyday stressors and to have a positive view of self.<sup>2</sup> These consequences are partially due to how the food eaten interacts with the gut microbiome. Although much of this research is still developing, it is suggested that these interactions can be utilised to treat illnesses like depression. However, current approaches to managing mental health conditions have little emphasis on diet with 74% of doctors in the UK giving nutritional advice less than once a month.<sup>3</sup> Additionally, the advised management for depression in adults contains little about diet, with the major focus for adult treatment involving medications and encouraging patients to attend talking therapies.<sup>4</sup>

Pharmaceutical approaches to treating depression are effective. A meta-analysis analysed the efficacy of 21 anti-depressants on depression and found all of them to have higher efficacies than the placebo.<sup>5</sup> However, anti-depressants are not as effective for all individuals, and they are arguably more useful for more severe presentations. For example, one study demonstrated that the efficacy for anti-depressants decreased as the extent of depressive symptoms became less severe.<sup>6</sup> Other sources have reported that approximately 40% of individuals noticed no improvement in their symptoms after taking an anti-depressant<sup>7</sup> and research has cited that around 30-40% of patients do not respond adequately to "pharmacological or psychological treatment".<sup>8</sup> Therefore, whilst anti-depressant use may

be effective for those with more severe depressive symptoms, other interventions may be needed to improve the health outcomes for those with milder presentations of the illness or for those who do not respond well to the management strategies currently provided. Clinicians could take a more holistic approach when treating less severe mental health illness and one such method could be by paying closer attention to patient diet.

## How are diet, the gut microbiome and mood linked?

Diet alters the type of bacteria present in our gut, which in turn influences the level of inflammation occurring there. One study analysed the effect of high polyphenol intake and consumption of a Mediterranean-like diet on the type of bacteria and compounds found in participants' faecal samples. Higher levels of certain species of bacteria, such as *F.prausnitzii*, were found in those who had a higher compliance to the Mediterranean diet.<sup>9</sup> In addition, higher levels of benzoic and 3-hydroxyphenylacetic acids were observed. These compounds are derived from microbial metabolism of the food we consume and are known to have anti-inflammatory properties. Although these results are less generalisable because the study primarily observed older individuals with an average age of 71.3 years, the paper still provides a base of evidence to show how diet influences the composition of the gut microbiome and how this composition influences gut inflammation.

Gut inflammation is a significant variable with regards to mood because it has been demonstrated that higher levels of inflammation is associated with experiencing depressive symptoms. For example, one study compared the levels of inflammatory biomarkers in individuals with major depressive disorders alongside healthy individuals.<sup>10</sup> Evidence of raised systemic inflammation was observed with those experiencing depressive symptoms alongside increased levels of lipopolysaccharide (LPS) binding protein. LPS is a structural component to the cell walls of certain types of bacteria to which the binding protein is synthesised by human cells as part of an immune response. Higher levels of LPS-binding protein are associated with increased gut epithelial damage and movement of gut microbes across the intestinal barrier. This suggests there is microbial involvement in the inflammatory process, which in turn affects mood. Secondly, long term inflammatory conditions are associated with low mood with sources citing that around 49% of patients with inflammatory bowel disease experience depressive symptoms.<sup>11</sup> Cross-sectional studies have also shown that an inflammation-inducing diet corresponds with a raised chance of experiencing depressive symptoms.<sup>12</sup> However, a limitation of all of these studies is that they do not provide evidence for a causal relationship between inflammation and depressive symptoms. In fact, other studies have demonstrated no correlation between diets thought to be pro-inflammatory and depressive symptoms.<sup>13</sup> Future studies should aim to develop an understanding on the mechanisms that link inflammation and low mood.

## Implementation of certain dietary patterns to alter mood

Despite the inconsistencies in the evidence relating diet and microbiome-mediated inflammation, changes in diet can be implemented to have beneficial effects on patients' mood, and evidence proposes that the microbiome plays a role in this process. One randomised controlled trial compared the impacts of two types of diet on individuals' self-reported depression scores and the composition of their intestinal microbiome.<sup>14</sup> One diet was classed as a low-fat diet and the other as an almond-based low-carbohydrate diet. Results showed that the almond-based diet was more beneficial to patients as it showed a greater significant decrease in participants' depression scores that was lower than average scores in the general population. The average score for individuals in the UK is between 51-53<sup>15</sup> and by the third month of the study, participants on the almond-

based diet had an average score of 42.07. The number of bacteria that secrete short chain fatty acids (SCFAs) was also significantly higher, and the secretion levels of GLP-1 were maintained to a significantly higher level than those on the low-fat diet. SCFAs decrease the permeability of the intestinal wall and hence reduce inflammation within the intestine,<sup>16</sup> and GLP-1 has been demonstrated to possess anti-anxiety and anti-depressant effects on rodents.<sup>17</sup>

Whilst this research seems promising, it has a few limitations. For example, the participants of the study all had a diagnosis of type 2 diabetes so results may differ in healthy individuals. Moreover, the participants were not diagnosed with clinical depression. Therefore, the results cannot be used to justify the prescription of these diets as a therapeutic for depression. However, as the forms used to assess depression scores were not disease specific the results can be applied more widely to the population, and they suggest that this diet could be used to improve the mental wellbeing of people in general. Furthermore, the proportion of each macronutrient in the almond-based diet are similar to that of the Mediterranean diet, and this dietary pattern has been suggested to also have positive effects on mood, although the evidence is conflicting. A greater intake of olive oil, fruits and legumes alongside a reduced consumption of red meat are characteristics of a Mediterranean diet.<sup>18</sup> Initially, a meta-analysis of cohort studies found no correlation between a Mediterranean diet and improved depressive symptoms.<sup>19</sup> However, when this same review analysed 9 cross-sectional studies, it revealed a significant beneficial relationship. The inconsistencies in the results of these studies emphasise the need for more and larger observational studies to determine the correlation between this type of diet and incidence of depression. The meta-analysis also highlights the importance of conducting consistent studies so that comparisons between them can be more easily made. For instance, the assessment of outcome (level of depression) differed between the studies ranging from use of anti-depressants, self-assessed questionnaires or interviews.

Whilst the literature is unclear on the efficacy of supplementing a Mediterranean diet as a treatment strategy for depressive episodes, there is strong evidence to suggest that it could be instead used as a prophylaxis for its development. One study demonstrated an inverse relationship between adherence to this diet and self-reported depression.<sup>20</sup> Another study also demonstrated that this dietary pattern was associated with less severe depression in a large cohort of women.<sup>21</sup> Therefore, it is suggested that a Mediterranean diet could be used to reduce both occurrence and severity of depression. This second study also highlighted a potential group who may benefit more from this diet as the protective effects were shown to increase alongside age. It is possible that clinicians could tailor advice to patients depending on their age to provide more personalised care in depression.

## Implementation of specific supplements to alter mood

Supplementation of specific micronutrients such as omega-3 polyunsaturated fatty acids (PUFAs) could be a way of treating depression. A meta-analysis that evaluated 13 randomised control trials found that consumption of this compound had a positive effect on depressive symptoms.<sup>22</sup> Additionally, a second meta-analysis found a "small but significant" positive impact on perinatal depression as a result of omega-3 PUFA consumption.<sup>23</sup> However, the results of this second study are not as generalisable as the previous one because the outcomes may not be the same for other types of depression. Moreover, neither of these studies provide explanations for the mechanisms behind these observations. However, it may be due to the anti-inflammatory properties of omega-3 PUFAs. Their anti-inflammatory properties have been explained in some studies as a consequence of their interactions with gut flora.<sup>24</sup>

Finally, intake of probiotics could aid in the treatment and prevention of depression. For example, a meta-analysis analysed a sample of 5 randomised control trials that evaluated the effect of probiotic

consumption on mood.<sup>25</sup> Interestingly, it found a significant decrease in depression scores was observed in both those with major depressive disorder and healthy subjects. This suggests that the intake of probiotics may be beneficial for preventing the development of depressive symptoms. Other randomised controlled trial have yielded similar results with a second randomised control trial showing the consumption of a probiotic yoghurt alongside a probiotic capsule improved the state of mental wellbeing in participants.<sup>26</sup> Despite providing significant evidence for the benefits of probiotics, these studies have a few notable limitations. For example, different depression rating scales and types of probiotics were used between the studies mentioned. Therefore, it is hard to draw completely reliable comparisons. Additionally, all of these studies have small sample sizes and are not carried out over long periods of time. Longer and larger randomised control trials with a baseline continuity in their methods are needed to progress this area of research further.

## Conclusion

The literature linking diet modification, the human microbiome and mood suggests that alterations to dietary patterns may have beneficial effects on depressive symptoms. However, the mechanisms underlying how diet, the microbiome and inflammation are connected remains unclear and more extensive randomised control trials are needed to clarify this relationship. There is stronger evidence to suggest that certain diets have preventative effects on mood as opposed to using dietary advice as a therapeutic. The therapeutic benefits are minimal and so should be used in conjunction with the current treatment methods already used, or for those who have 'milder' depression which is often treatment resistant. There are numerous documented risk factors for developing dysthymia such as low dietary intake and low socioeconomic status.<sup>27</sup> These are all potential future targets of research regarding the holistic treatment of depression.

This article only covers diet in regard to the holistic treatment of depression, where there are in fact numerous factors to consider. Exercise levels, sleep quality and even Mediterranean lifestyles<sup>28</sup> are all potential factors that can influence a person's mood. More research is needed to investigate the usefulness of adjusting these variables when trying to treat depression holistically. As mentioned previously, clinicians are hesitant to provide nutritional advice to patients. If advising alterations to diet in the treatment of depression is to become mainstream in clinical practice, future doctors need to feel confident at providing nutritional advice. Some proposed reasons for this hesitancy are the lack of teaching hours dedicated to nutrition in medical schools.<sup>29</sup> A proposed idea for effectively including more nutritional education into medical school curricula is by incorporating interprofessional learning activities<sup>30</sup> and altering the way fundamental biomedical concepts are taught.<sup>31</sup> Implementation of these methods could hopefully increase the confidence of doctors to provide nutritional advice, which could ultimately improve the outcomes of patients with depression.

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### Benjamin Craig

My name is Ben and I am a third-year medical student at Plymouth. I have had an interest in nutrition since starting medical school and was really pleased to be able to explore this in my first SSU. I hope you enjoy the rest of the articles in this journal and consider submitting one too!

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