



The Mediterranean Diet and Depression

A September 18, 2018 review of research studies shows a traditional Mediterranean diet is associated with reduced risk of depressive symptoms or clinical depression. New Brain Nutrition is leading the way in next steps with Clinical Trials including the Mediterranean diet. READ ON.



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Introduction

In mid-September, 2018, international press covered the release of a new report by Molecular Psychiatry that documents the effectiveness of the Mediterranean diet on reducing symptoms of depression. While there are limits to this observational study, New Brain Nutrition is taking the next steps in research by conducting four clinical trials on the connections between nutrition, lifestyle, and mental health. One of the four studies is focused on the Mediterranean diet.

We are pleased to provide you with our detailed update on these newly published findings and our current and continuing work in this arena.

This special newsletter is provided by the expert researchers, nutritionists and psychiatric professionals of **New Brain Nutrition**. This project has received funding from the **European Union's Horizon 2020** research and innovation programme under grant agreement No 728018, granted to the consortium **Eat2BeNice**.

The Mediterranean Diet - Review and Next Steps



By Jordi Salas-Salvado, MD, PhD

Prof. Jordi Salas Salvadó, MD, PhD completed his PhD in 1985 from Universitat de Barcelona. He is the director of Human Nutrition Unit Research, and Professor of Nutrition and Bromatology at Universitat Rovira i Virgili and Head of the Clinical Nutrition Unit in Sant Joan University Hospital in Reus. He has published more than 389 papers in reputed journals (SCI), has been cited more than 9000 times. He has been the Principal Investigator in many research projects, including New Brain Nutrition, and has directed over 19 Doctoral Theses.

Constantly feeling low mood and blue, losing of pleasure in life and appetite or having difficulties to have good sleep.

These are just some of the symptoms of one of the most prevalent mental conditions worldwide: depression. It affects hundreds of millions people globally, particularly women. Although depression seems to have a genetic component, lifestyle factors like diet have been suggested to play possible roles in the development of this condition and the degree of their symptoms. In fact, many different studies have suggested that different healthy diets may have important benefits for depression.

In a recently published meta-analysis at the prestigious scientific journal *Molecular Psychiatry*, **Lassale and coworkers** aimed to summarize current epidemiological evidence in relation to healthy dietary patterns and depression. They included a total of 41 high quality observational studies conducted in healthy people from different countries, focusing on several types of well-known healthy dietary indices: Mediterranean diet, the Dietary Approaches to Stop Hypertension (DASH) diet, the Healthy Eating Index (HEI) and Alternative HEI (AHEI), and the Dietary Inflammatory Index.

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These healthy dietary indices score favorably for the consumption of different “healthy” foods, such as fruits and vegetables, nuts, cereals, legumes and healthy fats; and they penalize the consumption of “unhealthy” foods, such as processed foods.

The main findings of the Lassale meta-analysis revealed that those persons following more closely the Mediterranean diet, and those following less the pro-inflammatory diet, showed lower risk of depression and depressive symptoms. Similar beneficial results were observed with a high adherence to the HEI and AHEI diets, yet the evidence was not as strong as with the Mediterranean diet. Indeed, the dietary patterns evaluated in this study contain foods and nutrients which may modulate important biological processes related with depression. For example, healthy diets may reduce oxidative stress and inflammation processes, improve insulin sensitivity and blood circulation in the brain.

These important findings give a strong basis to the role of healthy dietary patterns like the Mediterranean diet in preventing depression and depressive symptoms, and they contribute to build future dietary recommendations to prevent this mental condition.

However, as the authors comment, it is important to keep in mind that **all the studies included are observational, meaning, it is not possible to establish causal effects between diet and depression.**



To establish causality that can be used to directly translate the knowledge into clinical practice, science needs specific intervention studies. In these studies, a healthy diet is followed for a long time and depression incidence is evaluated. The PREDIMED-PLUS trial, a multicenter study, is being conducted in Spain for the primary prevention of cardiovascular disease using an intensive lifestyle intervention. It will be possible to confirm these results and have new knowledge in the field of depression.

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With PREDIMED-PLUS, the investigators will be able to evaluate whether an energy-restricted Mediterranean diet, with promotion of physical activity, may be effective for reducing the risk of depression in elders at high cardiovascular risk. In case of our Eat2BeNice study, we plan to analyse the effect of PREDIMED-PLUS interventions not only on depression but also on mood and especially on impulsivity and compulsivity, two important domains related to brain function.

Overall, following a healthy diet, like Mediterranean diet, not only has important benefits for different aspects of human health but also it is likely that the diet prevents depression, depressive-related symptoms and possible other mental related conditions. For this reason, a healthy diet nourishes a healthy mind.

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The Mediterranean Diet and Depression - Next Steps in New Brain Nutrition

Jeanette Mostert, PhD

Jeanette Mostert, PhD specializes in Cognitive Neuroscience and Biological Psychiatry. She taught at the Bachelor-programme Psychobiologie at the University of Amsterdam, and now works as Dissemination Manager for for two horizon2020 projects that are sponsored by the European Union: CoCA and Eat2BeNice (New Brain Nutrition.)



"Mediterranean diet could prevent depression, new study finds" [CNN]; "Mediterranean diet 'may help prevent depression'" [BBC].

The **publication of Lassale** and her colleagues in the prestigious scientific journal *Molecular Psychiatry* on the association between Mediterranean Diet and depression, received a lot of attention in the media last week.

So, can diet really influence your mental health? The publication of Lassale shows that there are indications that what you eat is related to how you feel. But because this study is an observational study, we can't conclude anything yet about causation. In other words, we don't know yet whether eating healthy causes you to feel less depressed, or whether feeling depressed causes you to eat unhealthy.



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Causal links between diet and mental health

The researchers of the European consortium **Eat2beNICE**. The way we do this is through clinical trials. In this way, we first let chance decide whether a person receives a particular diet or is part of the control group. Through this randomization we can be sure that the differences that we find between the two groups are really due to the dietary intervention that people received, because all other factors are the same between the two groups.

Specifically for the effects of the Mediterranean diet on behaviour, in the Eat2beNICE project we are using the information and measurements available from the **PREDIMED-PLUS** trial. In this study, we are looking specifically for the effect of a calorie-restricted Mediterranean diet, combined with physical activity, on several behavioral outcomes related with several psychiatric diseases of adults at high cardiovascular risk.

At the same time, we are conducting three other clinical trials:

1. In Nijmegen (The Netherlands), we investigate the effects of a very strict, hypo-allergenic diet on behavioural problems in children with ADHD.
2. We are investigating the effects of vitamin supplements in a clinical trial that will be conducted in Mannheim(Germany) and Groningen(The Netherlands).
3. Researchers in Barcelona (Spain) and Frankfurt (Germany) are investigating the effects of probiotics (i.e. bacteria that are good for you) on mental health in adults that are highly impulsive and/or aggressive.

Through these studies we hope to be able to identify if these types of food improve mental health and in which circumstances. This can have big implications for psychiatry, where putting someone on a specific, personalised diet may be a way to improve treatment. Also, people who are at a risk for developing mental health problems may benefit from specific diets to reduce this risk. But before this can be put into action, we first need good scientific data on what really works.



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How can food drive human behaviour?

A second aim of our large research consortium is to identify the mechanisms between nutrition and the way the brain works. We think that the bacteria that live in your gut play a large role in this, as they interact with other systems in your body, including your brain. So we are collecting poop samples of the people that are participating in our clinical trials to identify which bacteria are more or less common in our participants compared to the control population.

We are also measuring our participants' behaviour and we will scan their brains. We hope that this will help us understanding better why certain types of food can be beneficial for mental health, and why some others increase the risk for mental health problems. This too will help to elucidate, and understand, the causal links between food and behaviour.

In short, we are very thankful for the study of Lassale and her colleagues, for backing up the evidence that what you eat is related to how you feel and behave. Now there's work for us to do to prove the causal and mechanistic links. We'll keep you posted here!

Authors Jeanette Mostert and Alejandro Arias-Vasquez work at the department of Genetics at the Radboud University Medical Center in Nijmegen, The Netherlands. Alejandro Arias-Vasquez is the project coordinator of the Eat2beNICE project. Jeanette Mostert is the dissemination manager.

Further reading

Lassale C, Batty GD, Baghdadli A, Jacka F, Sánchez-Villegas A, Kivimäki M, Akbaraly T. **Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies.** Mol Psychiatry. 2018 Sep 26. doi: 10.1038/s41380-018-0237-8.

Blog by Jolanda van der Meer on hypo-allergenic diet (TRACE study): <http://newbrainnutrition.com/adhd-and-food-elimination-diet/>

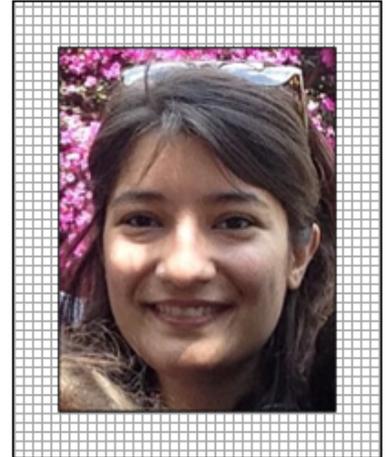
Blog by Julia Rucklidge on trials with vitamin supplements: <http://newbrainnutrition.com/micronutrients-and-mental-health/>

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The Gut-Brain Axis: How the Gut Relates to Psychiatric Disorders

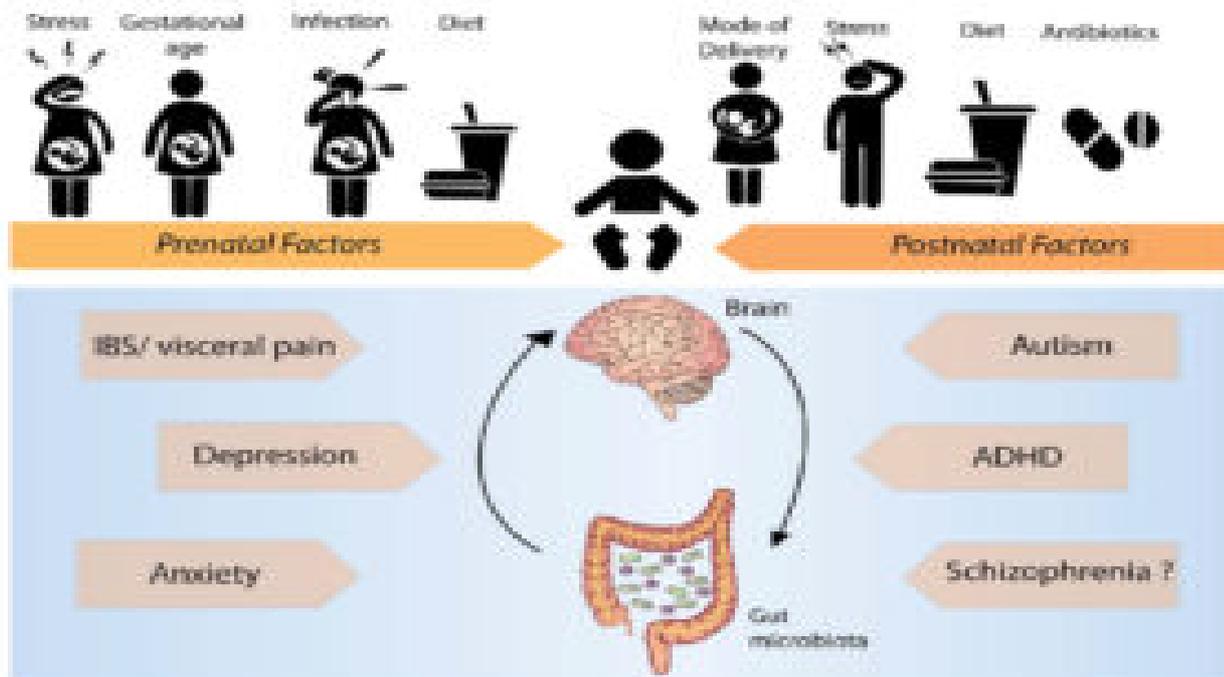
Judit Cabana Dominguez, PhD

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The human gut is colonized by microorganisms in a similar number as the cells of the human body.

“Microbiota” refers to these microorganisms, and it maintains a symbiotic relationship with the host, contributing to essential functions such as food digestion, energy harvest and storage, the function of the intestinal barrier, and the immune system and protection against pathogenic organisms. Prenatal and postnatal factors can alter the composition of the microbiota, such as stress and diet or the use of antibiotics (see image).



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For instance, stress during pregnancy can alter the composition of vaginal microbiota, which affects the composition of the microbiota of the newborn and is related to gastrointestinal (GI) symptoms and allergic reactions. Interestingly, there is a bidirectional communication between the GI tract and the central nervous system (the gut-brain axis) that involves neuronal and metabolic pathways, immune and endocrine mechanisms. Changes in the composition of the microbiota can lead to altered development of the brain and increased risk of psychiatric and neurodevelopmental disorders, such as **anxiety**, **depression** and **autism** (see image).

Depression is one of the most recurrent stress-related disorders that highly impacts the quality of life. *Fecal samples of patients with depression have a decreased microbial richness and diversity than controls.* The use of probiotics have been shown to help with sad mood and negative thoughts, which may be a potential preventive strategy for depression.

Autism is characterized by impaired communication, poor social engagement and repetitive behaviours, with frequent GI symptoms. *We know that the bacteria composition is more diverse in autistic individuals than in unaffected subjects.*

For other psychiatric disorders, such as Attention deficit/hyperactivity disorder (**ADHD**) and **Schizophrenia**, there is indirect evidence for a role of the microbiota, but more studies are needed.

This connection between the gut and brain is two way communication, and is known as **“The Gut-Brain Axis.”**

Our knowledge of the impact of gut microbiota on brain function is growing fast, which may pave the way to possible applications for the treatment of psychiatric and neurodevelopmental disorders.

Authors Judit Cabana, Bru Cormand, and Noelia Fernandez Castillo are in the Department of Genetics, Microbiology & Statistics, University of Barcelona, Catalonia, Spain

More information can be found in: Felice VD, O’Mahony SM. The microbiome and disorders of the central nervous system. (2017) *Pharmacol Biochem Behav.* Sep;160:1-13. <https://www.ncbi.nlm.nih.gov/pubmed/28666895>

Nutrition, Gut Microbiota and Behaviour



Yvonne Willemsen, MSc

Yvonne Willemsen MSc does her PhD research at the Psychobiology lab, within the Developmental Psychology department of Radboud University in Nijmegen (the Netherlands). She is specialized in molecular nutrition and her main interest lies in nutrition and child health, especially the molecular mechanisms behind the associations between nutrition and gut microbiota.

The reason why I look at impulsive behavior is because mental disorders are the single largest contributors to disease burden in Europe. Impulsivity and compulsivity increase the risk of psychiatric disorders, especially Attention Deficit Hyperactivity Disorder, alcohol and drug abuse disorders, conduct disorder and antisocial disorders (including aggression). The urgency of addressing impulsivity and compulsivity is additionally strongly supported by the fact that these problems increase the risk for mortality.

My name is Yvonne Willemsen and I have started my PhD track at Radboud University in the Netherlands in October 2017. For my project I will assess the association between nutrition, gut microbiota composition and impulsive behavior in toddlers and young adolescents. In the following paragraphs, I will explain the first study that I am currently conducting.

Many previous studies have examined the association between nutrition and executive functions. Executive functions are cognitive processes in the brain that contribute to regulating thoughts and behaviors.

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Executive functions can be roughly divided into three core functions, namely: inhibitory control, working memory, and cognitive flexibility. Inhibitory control, which can be interpreted as the opposite of impulsivity, is necessary to suppress impulses. It is also an important core function of executive functions, as it supports working memory and cognitive flexibility.

To date, studies have examined the association between nutrition and executive functions in general

(1). Whether nutrition is related to inhibitory control specifically (in toddlers and young adolescents) is something that still needs to be investigated. The next step of my study is to understand how nutrition is associated with inhibitory control. To explain a possible mechanism, we will look at the gut microbiota. The reason why the gut microbiota is a point of interest is because gut microbiota can secrete molecules that may influence brain function, and thus may influence inhibitory control

(2). This connection between the gut and the brain is also known as the gut-brain axis. Gut microbiota composition can change according to nutritional intake, and can therefore play a role in the gut brain axis (3). To assess the association between nutrition, gut microbiota and behavior in toddlers and young adolescents, we will use questionnaires and different behavioural measures.

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Nutrition and the Mental Health Crisis



About Julia Rucklidge, PhD

Award-winning clinical psychologist Professor Julia Rucklidge, PhD is Director of the Mental Health and Nutrition Research Group at the University of Canterbury, Christchurch, New Zealand. Originally from Canada, she specialises in research on the impact of nutrition and nutrients on psychological symptoms and has given a TEDx talk on "The surprisingly dramatic role of nutrition in mental health".

Nutrition as part of the solution to the mental health crisis!

Mental illness affects one in five people globally and, despite the wide availability of solid empirically supported therapies, these statistics are not getting any better. We appear to have reached an impasse improving outcomes, despite improvements in other areas of medicine.

We need to explore new avenues.

There has been a small explosion in research using nutrients for the treatment of mental illness over the last decade. The general premise is that our brains need nutrients to function and chemicals that are essential for good mental health, like dopamine and serotonin, require micronutrients, like vitamins and minerals.

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Preliminary clinical trials are putting micronutrients and good nutrition on the map as essential for optimal brain health. These trials show that giving more nutrients than what is obtained through diet alone can have a positive impact on serious conditions, like Attention-Deficit/Hyperactivity Disorder (ADHD)(1), autism(2) or anxiety(3). Along a similar vein, other studies are highlighting that improving diet alone can also improve mental health. By showing that manipulation of the amount of nutrients one consumes can influence mental health, the research demonstrates that the nutrients these participants were receiving prior to these interventions were not adequate to meet their mental health needs.

Beyond a 'sledge hammer' solution

This approach of “one size fits all” will only go so far. Some people don't respond. Some people only get marginally better. Why? Can we use genetic and nutrient testing to determine the optimal dose and nutrients that someone may require to get better based on their individualized profile? Can we use microbiome analyses to determine what microbial strains are required to best heal the gut to optimize absorption of nutrients? Current and future technologies should allow us to greatly expand the number of people who benefit from a nutritional approach.



Can this research also be used to target our food choices? To date, nutritional value is not the primary motivator in food processing. Agricultural practices tend to prioritize food storage, growth rates, transportability, shelf life, colour, shape and size above nutrient content. Could scanning of nutrient levels of fruits and vegetables using your mobile phone bring focus to the importance of the nutrient quality of our food such that this becomes the priority of consumers over aesthetic qualities or price?

Food or medicine?

Some challenges lie ahead in access to nutrients. As soon as nutrients are proven to have therapeutic benefit, legislation in some countries requires that they be treated as medicines.

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In other cases, dose alone can affect classification as a supplement or medication. This means as the evidence for efficacy increases, accessibility to the general public will be reduced as the ministry may insist that nutrients be accessible only by prescription.

Based on the medical model, there is a belief that pills that improve health comes with side effects that must be carefully monitored and controlled. To date, our research has shown minimal to non-existent side effects from the nutrient combinations we have studied. Moreover, physicians are currently not well placed to prescribe nutrients because so few have training in nutrition.

Government has the power to ensure legislation allows easy access to nutrients and permits health claims to be made based on good science. Such legislation could ensure that nutrients are easily available due to the very low risk associated with consuming nutrients as compared with pharmaceutical drugs.

Further challenges

Some companies sell nutrient products that optimize profit over health benefit. This may result in cutting corners, not using minerals that have been well chelated, not using the most bioavailable forms of vitamins. This will impact efficacy. It will be a challenge to ensure that nutrients designed for improving mental health are not compromised. Snake oil salesmen are never too far away.

Ensuring good access to nourishing food will also be a challenge. The prevailing mindset is that good food is expensive. However, this is true only if one doesn't count the costs associated with eating poorly. We need attitudes towards food to change from providing calories to providing the essentials of health. Perhaps one day we will all come to realize that so many packaged and highly processed foods are nutritionally depleted. Ideally, if consumers would stop buying these products, changes would follow.

It is encouraging that some people can have better mental health and more fulfilling lives simply by ensuring their brains receive adequate nutrients and that they will not have to experience the side effects associated with so many medications. Perhaps mental illness will be viewed as being at least partially caused by improper nutrition, as our ancestors knew. Could such a shift influence the stigma associated with mental illness?

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Valuing the role of nutrition as part of addressing our mental health statistics is part of our future. How well we can ensure that access is optimized and price is affordable will depend on good legislation, a re-evaluation of our current health care model and ensuring competing market forces don't compromise the acceptability and efficacy of this solution.

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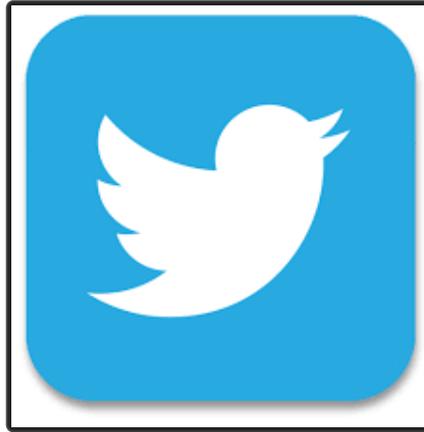
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