https://doi.org/10.1080/23794925.2021.1875342

Routledge
Taylor & Francis Group

Nutrition Provides the Essential Foundation for Optimizing Mental Health

Julia J. Rucklidge[a], Jeanette M. Johnstone[b], and Bonnie J. Kaplan[c]

[a]School of Psychology, Speech, and Hearing, University of Canterbury, Christchurch, New Zealand; [b]School of Medicine, Child and Adolescent Psychiatry, Oregon Health & Science University, Portland, USA; [c]Cumming School of Medicine, University of Calgary, Alberta, Canada

ABSTRACT

Although current evidence confirms the importance of diet for mental health, many psychologists avoid discussing dietary intake with clients, questioning whether this information is within their scope of practice. This article provides psychologists with a review focused on the connection between what we eat and how we feel. Eating a healthy, whole-foods-based diet is an important tool to promote mental health recovery and maintenance. We begin by reviewing several mechanisms by which nutrients maximize brain health, including enabling metabolic reactions to occur, supporting mitochondrial function, reducing inflammation and assisting with detoxification. Understanding the vital role of nutrients for brain health will aid clients in understanding the importance of optimizing their intake of a range of nutrients in order to maximize their mental health: no single nutrient is sufficient. Next, we summarize evidence relating diet to mental health, followed by a consideration of circumstances that may contribute to a client requiring additional nutrients, such as chronic stress, medication use, individual biochemistry, and consuming nutrient-depleted food. The evidence base for treating psychological problems in children with supplementary nutrients is then reviewed, and a case study of a child whose self-regulatory skills improved with broad-spectrum multinutrients is used to illustrate this treatment. The breadth and consistency of the research highlights the importance of children receiving a good foundation of nutrients for optimizing brain health. Finally, we offer practical suggestions for psychologists to incorporate this information into their clinical practice and discuss these suggestions within the context of informed consent.

KEYWORDS
Vitamins; minerals; nutrition; nutrients; treatment; mental health

Many clinical psychologists routinely focus on lifestyle factors in their therapeutic work with clients, providing recommendations about exercise, stress management, and strengthening relationship networks. In the *American Psychologist* (Walsh, 2011) Walsh identified eight therapeutic lifestyle changes (exercise, diet, time in nature, relationships, enjoyable activities, stress management, spirituality, service) within psychologists' scope of practice, suggesting that each warranted greater utilization in clinical treatment. Of those eight factors, this review focuses on the one which the authors believe is *foundational* to them all – nourishing the brain by eating a whole-foods diet.

Historically, scientific studies have focused on physical health and its relationship to nutrient intake, demonstrating improved health from healthy eating and/or nutrient supplementation. Dietary changes often focus on the large molecule macronutrients: fats, carbohydrates and proteins that are required in large amounts. The media extols the virtues of eating a nutritional diet to reduce the risk of heart disease, Type II diabetes, and certain cancers, raising the awareness of the importance of nutrition for myriad of *physical health* symptoms. Given the emerging and consistent evidence demonstrating the importance of a healthy diet for *mental health*, psychologists are in a good position to incorporate this basic information into their clinical practices, talking with clients about dietary choices and, where needed, raising the possibility of multinutrient supplementation by educating clients about the research.

In this article, we begin by reviewing several of the mechanisms by which nutrients maximize brain health. Next, we summarize the evidence base relating diet to mental health, followed by a consideration of the circumstances that may predispose an individual to require additional nutrients beyond what they can get from food. The evidence base for treating psychological problems in children with supplementary

CONTACT Julia J. Rucklidge julia.rucklidge@canterbury.ac.nz School of Psychology, Speech and Hearing, University of Canterbury, Private Bag 4800, Christchurch, New Zealand.

nutrients is then reviewed and we illustrate the potential benefits of multinutrient supplementation with a case study. Finally, we offer practical suggestions for psychologists who want to incorporate this information into their clinical practice.

Nutrition is essential for maintaining a healthy brain

The term "nutrition" encompasses many substances that contribute to development and maintenance of cellular function. In this paper, we focus primarily on the approximately 30 minerals and vitamins that humans need for optimal health.

Minerals are stable chemical substances listed in the periodic table of elements. Plants absorb minerals from the soil and use them to synthesize vitamins, which are organic molecules (meaning they contain carbon). Humans must eat the plants (or eat animals that eat the plants) to obtain the vast majority of the vitamins and minerals required for our health.

There are other components of nutrition that are important for brain health, such as the essential fatty acids (especially omega 3s) that are particularly critical for brain development in children's early years (Huffman et al., 2011; McNamara & Carlson, 2006), amino acids (building blocks of proteins), carbohydrates (for energy) that North Americans usually consume in sufficient quantities, and thousands of phytonutrients (plant-based nutrients), which help prevent disease. The reason for focusing on minerals and vitamins is, in part, because they are generally taken for granted, in spite of their vital daily influence on mental health. Also, their importance for brain function has been understood for decades yet surprisingly, this information is not yet part of standard educational curricula for psychologists and mental health professionals.

The following summary describes four ways in which minerals and vitamins contribute to healthy brain functioning.

Enabling the brain's metabolism to function

In adults, every minute their hearts are beating, a quart of blood passes through their brains. That quart represents 15–20% of the entire blood supply, but the brain is only about 2% of adult body weight. The brain "punches above its weight," needing to be fed as much as 10 times the amount of blood you would expect for an organ so small. Similar numbers apply to children, depending on their age and weight. In general, the brain consumes 20–40% of the nutrients and energy we ingest, which is disproportionately higher than its weight (Leonard et al., 2003). The key message is that even though humans need to eat nutrient-dense food to build strong bones and muscles, when we eat, we are primarily feeding the brain to support its very dynamic metabolism.

Metabolism is the transformation of one compound to another (see Figure 1). Enzymes are required for the brain to convert chemical A to chemical B, and enzymes require a steady supply of cofactors to do this work. Micronutrients (minerals and vitamins) are those cofactors. Because humans cannot make minerals, or many vitamins, we have evolved to get them from our food supply.

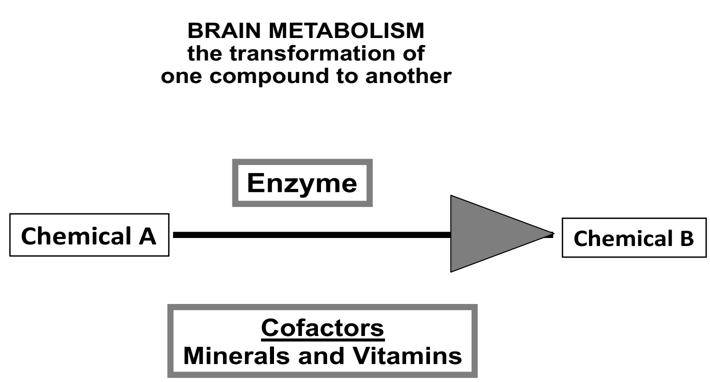

Figure 1. Brain metabolism involves the conversion of one chemical to another with the assistance of enzymes whose activity is dependent on an adequate supply of cofactors.

Metabolism responsible for neurotransmitter synthesis and breakdown illustrates the critical role played by micronutrients. Figure 2 shows a few of the steps by which tryptophan is converted to serotonin, and how they are both broken down into other by-products. Every arrow represents a metabolic step controlled by enzymes. The nutrients required as the cofactors for those enzymes are in dashed-line boxes. This figure represents a tiny portion of the tryptophan-serotonin pathway, showing a few metabolic steps out of thousands.

In this very small portion of brain metabolism, the brain needs five different vitamins and seven different minerals for optimal function. These same types of metabolic steps are necessary for all neurotransmitters (dopamine, adrenaline, GABA, etc.), demonstrating why a broad spectrum of nutrients is necessary for brain metabolism: no single nutrient is capable of optimizing brain function by itself. The figure shows the breadth of the nutrients that are needed to work synergistically, a phenomenon also demonstrated in our food. When we eat whole fruits and vegetables, the nutrients that are required together for best absorption are consumed together.

Enabling mitochondria to function

Every cell in the brain and body contains multiple mitochondria, often called the "energy factories." Mitochondria take in nutrients, go through many metabolic steps, and produce ATP (adenosine triphosphate) – the energy molecule essential for life (Karp, 2012). Energy production takes place using the chemical processes of the Krebs cycle (also known as the citric acid cycle) and the electron transport chain.

The entire sequence of Krebs cycle function and the electron transport chain is *nutrient dependent*. As with the metabolism of serotonin, many nutrients are required; there is no single special nutrient.

Modifying genetic expression

Methylation is one of many essential biochemical processes involved in gene regulation, whereby a methyl group (one carbon and three hydrogen atoms) is transferred to a molecule such as DNA. These newly methylated compounds are essential for a number of functions including: DNA synthesis and repair, neurotransmitter production (like serotonin), energy production, detoxification, gene regulation, hormone regulation, cell membrane repair, myelination, and immune function. The methylation-folate cycle, sometimes known as one carbon metabolism, requires specific nutrients (e.g., vitamins B_2, B_6, B_{12}) acting as cofactors in order for the metabolic reactions to occur. Without an adequate supply, methylation will be impaired, which in turn may affect genetic expression and result in poor physical and mental health. Increasing the supply of nutrients has been

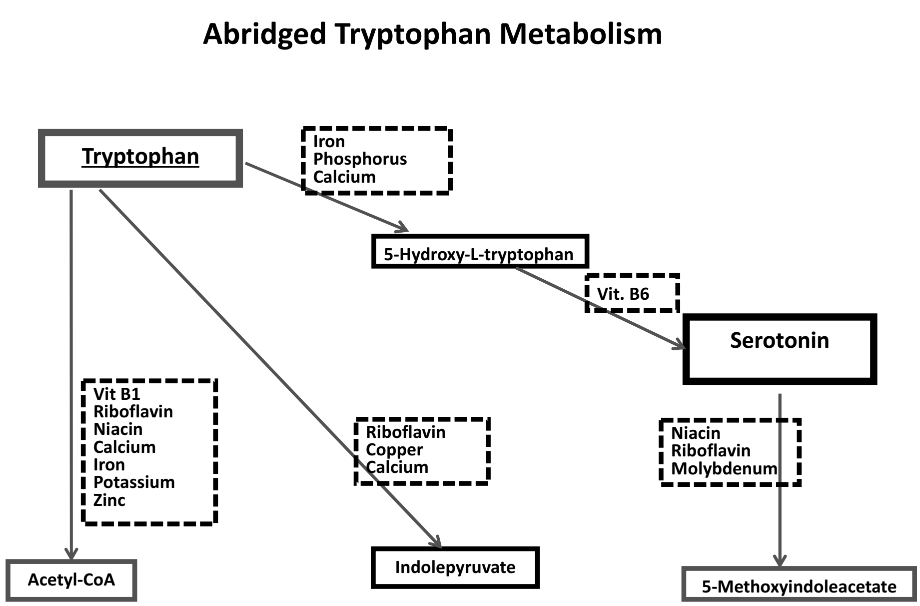

Figure 2. A part of the tryptophan-serotonin pathway, illustrating just a few metabolic steps out of thousands.

shown to modestly increase methylation of the genome, illustrating the role that nutrients might play in gene modification (Stevens et al., 2018).

The methyl groups can be considered to function like a dimmer switch: genes can be turned *up or down* just like a ceiling light. In other words, the act of methylation can modify gene regulation. The presence or absence of a methyl group can influence whether the DNA will be tightly coiled up such that a gene cannot be decoded (or read) or whether it is uncoiled and therefore easily readable. The biggest category of gene-modifying variables appears to come from the environment, especially the nutritional environment. There is preliminary evidence that nutrients may be epigenetic modifiers in mental health (Stevens et al., 2018), but one of the best illustrations of the role that nutrition can play in genetic expression comes from honeybees.

Honeybees have very complex societies with sterile worker bees and a single fertile queen. What is fascinating, though, is that worker bees and honeybees begin life as *genetically identical* larvae. They develop into entirely different bees and behave very differently (called a *phenotypic difference*) due to different nutritional environments. A colony selects a single larva to be fed a diet high in royal jelly, and that bee develops ovaries and becomes the queen. Larvae destined to be worker bees are largely fed pollen, nectar, honey and beebread (Mao et al., 2015). Nutrition modifies the honeybees' genetic expression.

Fighting excess inflammation and protecting from environmental toxins

Inflammatory reactions are essential every time our immune system has to fight off an infection or the invasion of some foreign substance (an antigen). However, sometimes inflammation can become excessive, causing physical health problems, even though there are homeostatic mechanisms that help maintain levels of inflammation within a restricted range. The mitochondria generate a small number of inflammatory molecules called reactive oxygen species (ROS), but mitochondria also produce ATP, which is one of our best weapons against excessive inflammation (Kaplan, Rucklidge, Romijn, McLeod, et al., 2015; Karp, 2012). As discussed, nutrients are essential for production of ATP.

In addition to fighting excessive inflammation, proper nutrition is also essential for protecting us from environmental toxins, including those that may pose a risk to brain health. A workshop review of the research on human health and environmental pollution concluded that nutrition is such an important modulator of toxicity from environmental chemicals that all risk assessment methodologies ought to include dietary intake as a component of risk evaluation (Hennig et al., 2012). Poor dietary habits appear to increase vulnerability to environmental chemicals throughout life. In contrast, a diet rich in antioxidants may reduce that vulnerability. This is especially important for pregnant women and children, as there is strong evidence, for example, of prenatal exposure to plastics (phthalates) increasing the risk of neurodevelopmental problems in children, such as lower IQ, and problems with attention, hyperactivity, and social communication (Ejaredar et al., 2015).

Research on dietary patterns and mental health

We have reviewed how important nutrients are for optimal brain function, from making neurotransmitters, to modifying gene expression, to ensuring adequate ATP production. We now turn to the evidence base that links nutrition and mental health, with an emphasis on data collected in children.

A wealth of research demonstrates an *association* between eating a nutrient-dense diet and better mental health, with the strength of the association confirmed through meta-analyses (Firth, Marx et al., 2019; O'Neil et al., 2014; Rios-Hernandez et al., 2017; Sanchez-Villegas et al., 2009). However, over and above these observational studies, prospective longitudinal studies and randomized controlled trials (RCTs) support a causal relationship (Francis et al., 2019; Jacka et al., 2011, 2017; Li et al., 2017; Nanri et al., 2013; Opie, O'Neil et al., 2015; Parletta et al., 2019): consuming a whole-foods diet rich in micronutrients can improve resilience, reduce the risk of suicide, lower the risk of developing a mental health problem, and can be used to treat mental health problems, in particular, depression. In addition, a number of these studies also show that an ultra-processed diet, characterized by packaged foods containing manufactured chemicals, and typically high in salt, poor quality fats, and sugar, seems to *precede* poor mental health.

As an example of prospective longitudinal research conducted with children, a Canadian study (Loewen et al., 2019) evaluated more than 3,000 children aged ten and eleven for the number of positive health behaviors they were practicing: six health behaviors were related to diet, and the other three involved exercise and daily screen time. Two years later, government data were used to determine which children had been seen by a physician for treatment of a mental health disorder. Not only did children who engaged in more of the positive health behaviors remain mentally healthier, but for every single additional health guideline children adhered to, there were 15% fewer visits for medical treatment of mental health problems. These results were adjusted for gender, body weight, parental educational attainment, household income, and region of residence. Further analyses of their data revealed a significant association between fewer ADHD diagnoses and meeting dietary guidelines for fruit and vegetable, meat, saturated fat, and sugar intake (Loewen et al., 2020).

An earlier study evaluated the diets of more than 3,000 Australian adolescents aged 11–18 years (Jacka et al., 2011). As expected, the highest intake of unhealthy (ultra-processed) foods was correlated with poorer mental health functioning, while the highest intake of healthy whole-foods was associated with better mental health functioning. The progression over time was also revealing: those who improved their diet over two years also improved their mental health, while those whose diet got worse had poorer psychological functioning. The authors adjusted for gender, socio-economic status, body mass index, physical activity and dieting behaviors. This study's implications for prevention are important because adolescence is a time when parents find it very difficult to supervise their children's diet, and it is also a vulnerable time for developing mental health problems.

However, not all studies show these associations. A study of almost 4,000 adolescents (17 years), after adjusting for relevant factors, did not find that fruit and vegetable consumption were associated with the development of depression twelve years later, showing that prediction of these disorders over a long period of time is challenging and multifactorial (Hoare et al., 2018).

When people learn how to eat a healthier diet, mental health improves

At least three RCTs have investigated whether eating a nutrient-dense diet can improve symptoms of depression in adults. The first, called the SMILES trial (Supporting the Modification of Lifestyle Interventions in Lowered Emotional States), was carried out in Australia over twelve weeks (Jacka et al., 2017). To be included in the study, participants had to have previously experienced a Major Depressive Episode and had to report that they ate a typical unhealthy diet with a high intake of sweets, processed meats, and salty snacks. They were randomly assigned to receive either Dietary Support (DS) consisting of seven hours of training with a dietitian to eat foods consistent with the Mediterranean diet (fruits and vegetables, nuts, grains, olive oil, some dairy, meat and eggs (Opie et al., 2018)), or Social Support (SS), with a similar amount of time in a "befriending arrangement." Improvement in mood was significantly greater in the DS group compared to the SS group, with between group effect size (ES) estimated at 1.16. Further, a third of the DS group went into remission for their depression (compared to 8% of the SS group; NNT = 4.1). Also, the participants who improved their diets the most were the ones who experienced the greatest improvement in mood.

The SMILES trial was followed very quickly by two replications. The first one was the HELFIMED trial (Healthy Eating for LiFe with a MEDiterranean-style diet) that had similar results (depression scores dropped by 45% in the DS group and 27% in the SS group; p = .027) using group rather than individual cooking lessons for twelve weeks (Parletta et al., 2019). The third study, targeting depressed young adults aged 17–35, taught participants about a whole-foods diet across three weeks (Francis et al., 2019) and also showed greater mental health improvement in those receiving nutritional information compared to no change in those on the waitlist (between group ES for depression = 0.75). What was especially interesting about this last study was that the diet intervention was done via a 13 minute video, with no direct contact with dieticians, demonstrating that people can be taught how to improve their diets in a short amount of time, no matter where they live, as long as they can access the internet. Other research shows that giving fruit to university students (aged 18–25 years) can improve their feeling of vitality, flourishing, and motivation in comparison with people who are just told to eat more fruit (Conner et al., 2017). Although these types of dietary studies cannot blind participants to the treatment, the replication across different research groups lends confidence that the findings are robust.

Research going back to the 1980s suggests a dietary component that may be a culprit in contributing to poor mental health: food preservatives and artificial colors can affect the behavior of some children (Jacobson & Schardt, 1999). In a meta-analysis of 15 RCTs examining the impact of artificial food coloring (AFCs) on hyperactivity in children with attention-deficit/hyperactivity disorder (ADHD ($N = 219$)), Schwab and Trihn reported ES between 0.21 and 0.28, demonstrating the small negative impact of AFCs on hyperactivity (Schab & Trinh, 2004).

Overall, it appears that about one third of children with ADHD respond to a dietary intervention based on elimination of additives like colors and preservatives as well as other foods that cause adverse effects (Ly et al., 2017; Nigg et al., 2012). However, based on the existing literature, it is not possible to interpret whether children improve because of the removal of processed foods with artificial additives, or do they improve because the diet that replaced the ultra-processed foods contained more nutrient-dense, whole-foods? More research is needed.

Diet during pregnancy and mental health of the offspring

Research on the offspring of women who have had their diet monitored during pregnancy is another avenue for learning about the importance of diet for children's mental health. The two large-scale famines that have been most thoroughly studied both demonstrated the importance of a pregnant mother being well-nourished: the Dutch Hunger Winter 1944–1945 and a severe famine in China 1959–1961. In both settings, women who were malnourished in pregnancy had over twice the risk of producing offspring who were later diagnosed with schizophrenia or depression (Brown & Susser, 2008; Li et al., 2018).

While these are extreme examples of dietary restriction, other maternal eating habits can influence their child's development, such as eating a highly processed diet during pregnancy. A study based on more than 23,000 Norwegian mother-child pairs found a relationship between the mothers eating more processed foods during pregnancy and behavioral problems in their children at age five (Jacka et al., 2013). Potential confounders controlled for included gender, paternal and maternal age, gestational age, maternal education attainment, household income, maternal smoking, maternal depression, marital status and maternal locus of control. Similarly, a study of more than 3,000 children in the Netherlands analyzed maternal consumption of what they referred to as the traditional Dutch Diet: lots of fresh and processed meat and potatoes, a relatively high intake of margarine and a very low intake of eggs, vegetables, fish and dairy products. This Dutch Diet was found to be associated with more aggression in the offspring (Steenweg-de Graaff et al., 2014), even after controlling for maternal pre-pregnancy body mass index (BMI), maternal smoking, parental educational level, maternal age, marital status and family income. A French study with about 1,200 mother-child pairs found that a typical Western diet during pregnancy was associated with increased likelihood of detecting problems with hyperactivity and inattention at ages three, five and eight years (Galera et al., 2018). Confounds included dietary pattern at two years of age, maternal stress and depression, gestational diabetes, and socioeconomic variables. The positive side of dietary intake was revealed in a study of about 700 mother-infant pairs in Norway: increased fruit consumption during pregnancy was associated with better cognitive development of the infant at one year (Bolduc et al., 2016), controlling for gender, gestational age, family income, ethnicity, and gestational diabetes.

When might people need additional nutrients?

The research reviewed so far highlights the importance of eating a whole-foods diet to optimize mental health. We will now explore some situations that may require an increased intake of nutrients above the usual dietary reference ranges.

Individual differences

Aside from the metabolic pathways' requirements for an abundance of nutrients for efficiency, individual differences may contribute to an individual's need for higher intake of nutrients. Some individuals may have inherited a need for unusually high amounts of nutrient cofactors, a phenomenon known for decades in the area of physical health. In 2002, Ames summarized 50 genetic mutations associated with slowed metabolic pathways due to an excessively high need for certain vitamin cofactors (Ames et al., 2002).

In other words, research has identified that some people inherit the need for an above-average supply of nutrients for metabolic pathways to work efficiently for optimal physical health. It is possible that some psychiatric symptoms may also result from metabolic dysfunction caused by insufficient vitamin and mineral cofactors in the brain, an idea first proposed by Nobel Laureate Linus Pauling in the 1960s (Pauling, 1968). As many mental disorders run in families, Pauling hypothesized that the genes for mental illness may be the ones involved in the regulation of essential nutrients for brain metabolism. If so, bringing these nutrient levels back up to sufficient levels with supplementation could be helpful. As the Ames paper showed, restoring near-normal physical functioning is possible when enzymes with drastically reduced activity become supersaturated with the necessary co-factors through nutrient supplementation (Ames et al., 2002).

Stress

Stress, an inevitable part of life, exacerbates health problems. Chronic stress, with extended activation of the fight/flight response, can lead to chronic nutrient depletion. There are many "threats" that exist for children: school pressures, family and friend relationship challenges, and even worry about existential threats, like climate change and COVID-19. All of these stressors can deplete their bodies and *brains* of micronutrients.

Nature ensures that micronutrient-dependent functions required for short-term survival (like the fight/flight response) are protected at the expense of longer-term functions (like concentration) (McCann & Ames, 2009). Managing the flight/fight response takes priority over other functions, a preferential sequence referred to as the "Triage Theory" (McCann & Ames, 2009). In this situation, supplementing with broad-spectrum multinutrients has been shown to be an effective way to replenish nutrients, and alleviate stress (Kaplan, Rucklidge, Romijn, Dolph, et al., 2015; Rucklidge et al., 2012; Young et al., 2019). However, to date, there have been no controlled studies on general resilience in children, so caution is recommended in extrapolating these data to a younger age group.

Taking certain medications long-term

Another factor that can increase the need for nutrients is the use of various medications. For example, mood stabilizers deplete folic acid, vitamin D, vitamin B_6 and vitamin B_{12}, as well as minerals such as copper, selenium and zinc (Kaplan & Shannon, 2007). Metformin reduces B_{12}; contraceptives decrease B_6, folate, magnesium, vitamin C and E; and aspirin negatively affects vitamin C levels (Mohn et al., 2018). When working with children, we need to be aware that these medications could be affecting nutrient stores and impacting brain health. Increasing an individual's nutrient supply through multinutrient supplementation may reverse the depletion caused by these medications, and possibly result in needing a lower dose of some psychotropic medication (Mehl-Madrona & Mainguy, 2017; Rucklidge et al., 2010).

Dysbiosis

The association between digestive problems and low mood has been known for centuries (Phillips, 1910). Now that we have some understanding of the human gut microbiome, it is recognized that digestive problems can by caused by dysbiosis, or an imbalance in the gut microbial communities that is associated with disease.

Over the last decade, there has been a growing interest in the role of the gut microbiome in the expression of mental illness (Cryan et al., 2019). This idea was brought to international attention when animal studies showed that transplanting gut microbes can change behavior. In one noteworthy study, where mice modeled for autism spectrum disorder had their gut microbes replaced by ones typical of normal mice, their autism-like behaviors improved (Hsiao et al., 2013). Other research showed that certain emotional traits (like anxiety) can be transferred between mice through transplanting gut microbes (Collins et al., 2013).

In human research, an increasing number of studies are beginning to investigate how the gut microbiota might affect behavioral symptoms (Szopinska-Tokov et al., 2020). When gut microbiota of individuals with and without ADHD were transplanted into mice, those mice showed differential brain structure and function depending on which microbiota they received (Tengeler et al., 2020). Another line of research, which is very preliminary and based on rodent research, implicates the microbiome in teen distress (McVey Neufeld et al., 2016) and child misbehavior (Flannery et al., 2020), although the applicability to humans is not yet clear.

There appear to be a number of communication channels through which the microbiome can influence neural pathways in the brain, including changes in immunity, metabolism, and endocrine function (Cenit et al., 2017; Mathee et al., 2020). Responsible for much of the communication between the gut and the brain, the vagus nerve plays a role in the regulation of emotional responses, and controls the autonomic nervous system (Breit et al., 2018). This communication link between the gut and the brain may explain why a less diverse microbiome is associated with poorer mental health (Bastiaanssen et al., 2019).

Some research has suggested an association between certain bacterial strains and disorders like ADHD, schizophrenia, and depression, but the results of these studies have been inconsistent (Cryan et al., 2019). Some studies have reported the complete absence of some microbes (*Coprococcus* and *Dialister*) in people who are depressed (Valles-Colomer et al., 2019), but it is not yet known whether this absence is a cause of the depression, or whether the microbial changes are caused by depression treatment, or other variables. Preliminary research showed that multinutrient supplementation increases bacterial diversity, which was associated with symptom improvement in children with ADHD (Stevens et al., 2019).

Unfortunately, the science cannot yet define what constitutes a healthy gut microbiome for optimal brain function. Based on the studies just cited, diversity appears to be important (Bastiaanssen et al., 2019), and the less optimal the microbiome, the more likely there could be mental health problems. Several factors may negatively impact gut microbial diversity (e.g., antibiotics, stress, infection, environmental toxins) while a diet rich in plant-based foods supports microbial diversity (Cryan et al., 2019; Robertson et al., 2017). As such, one of the first recommendations for improving gut health is to improve the quality of the foods eaten and reduce the consumption of ultra-processed foods. These recommendations require little nutritional expertise, and clinical psychologists are well-positioned to convey the information, as will be discussed below.

When food is nutritionally depleted

Neither plants nor humans can synthesize minerals. As explained above, plants absorb minerals from the soil and then use those minerals to synthesize vitamins. Over the last seventy years, it is concerning for human health that research suggests our food supply has been decreasing in nutrient density (Davis et al., 2004). Criticisms of the methodology used to compare nutrient content across time have been raised (Marles, 2017), such as crops have several varieties and may be sampled in different ways, or stored differently, with variable amounts of heat and humidity, but fairly significant changes being reported across several countries suggests there is cause for concern.

Several causes of nutrient depletion of our food have been identified. Modern agriculture has sought to increase the yield for many crops to increase financial margins, which creates a "dilution effect" of lower nutrient levels (Marles, 2017). Many years of tilling the soil, even with rotating crops, depletes minerals. Food producers use fertilizer, the primary components of which are nitrogen, phosphorous, and potassium (NPK). While these three are important, plants require 15–16 essential minerals for best growth, defense against insects, and the ability to synthesize vitamins (Datnoff et al., 2007).

Another possible contributor to nutrient depletion of crops is the heavy use of glyphosate, an herbicide and principal ingredient of Roundup®. Glyphosate, initially patented in the United States in 1964 as a descaling agent to get rid of mineral deposits in pipes and boilers, is now applied to crops to kill weeds. A 2019 study showed that glyphosate disturbs the human blood-brain barrier, making it more permeable (Martinez & Al-Ahmad, 2019). Permeability means that some molecules that the blood-brain barrier intended to exclude might be able to pass through, causing adverse effects in the brain. It is also relevant that while there is still debate on the topic, concerns have been raised about whether glyphosate can make dietary minerals like iron, manganese, and nickel *less* available for the body to absorb (Zobiole et al., 2010) as well as decreasing soil health (Kanissery et al., 2019), factors that could also affect plant nutrient density.

Another possible cause of decreased crop nutrients is the presence of high levels of carbon dioxide in the atmosphere. Although carbon helps plants grow, increased levels of atmospheric carbon dioxide also leads to plants containing more sugars and fewer micronutrients. While the plants are bigger and the food may taste sweeter, they provide fewer nutrients needed for brain health. One study of eight strains of rice exposed to increased carbon dioxide found that the exposed rice had lower levels of vitamins, minerals, and protein (Zhu et al., 2018). Another study looked at nutrient balance in spring wheat grown for three consecutive seasons (Hogy et al., 2009). Higher carbon dioxide levels led to larger plants and a higher yield resulting in an increase in carbohydrates, but protein declined by more than 7%, and iron and manganese both decreased. Similar results have been found in studies of other crops.

As our planet heats up, it is possible that our crops will become higher in carbohydrates and lower in protein and micronutrients. These issues have vital importance for human brain health and warrant more research.

How supplementary nutrients might improve mental health

We have reviewed several reasons why dietary change may not be sufficient for everyone. Individual differences, stress levels, medication use, and gut health, all provide plausible reasons why nutrient requirements may vary, resulting in a greater need for nutrients in some individuals than what can be obtained from diet alone. In addition, environmental factors such as depleted soil minerals, and climate change can influence the nutrient density of the food we consume. This leads to the question of whether there is evidence for treating mental health problems with supplementary nutrients, especially (but not exclusively) in children.

Scientists first tackled this question by studying one nutrient at a time (e.g., zinc or magnesium or vitamin B_{12}). While some studies revealed small positive effects (Benton & Cook, 1991; Benton et al., 1997; Thys-Jacobs et al., 1998), most of the research was largely negative. A number of systematic reviews and meta-analyses have highlighted the concentrated effort to find a single nutrient that would alleviate symptoms associated with complex psychiatric issues such as mood (Kaplan et al., 2007; Sarris et al., 2011), psychosis (Firth et al., 2017), ADHD (Rucklidge et al., 2009) or antisocial behaviors (Benton, 2007), reporting modest to low benefit from a single nutrient approach, with many single nutrients found to be ineffective as a primary treatment of mental illness (Firth, Teasdale, et al., 2019). The complex interplay of nutrients working together for brain metabolism likely explains why the search for a single nutrient to resolve complex psychiatric symptoms is unrealistic. Therefore, in reviewing the evidence base for nutrient supplementation for mental health, we will focus on the studies of nutrients given *in combination* as the treatment strategy.

Aggression

The ability of supplementary nutrients to reduce antisocial behaviors has been demonstrated with case studies, open-label studies and multiple RCTs. A broad spectrum of minerals and vitamins (sometimes combined with omega 3s) can reduce aggression and violent incidents. The results have been reported across a range of populations, from aggressive children to incarcerated adults (Gesch et al., 2002; Hambly et al., 2017; Kaplan et al., 2004; Kaplan, Hilbert, et al., 2015; Rucklidge et al., 2018; Schoenthaler et al., 1997; Schoenthaler & Bier, 2000; Tammam et al., 2016; Zaalberg et al., 2010). The earliest randomized trial was more than 20 years ago, when researchers conducted a fully blinded three-month RCT in 62 incarcerated youth aged 13–17. Those randomized to receive a broad array of minerals and vitamins exhibited a 28% greater decrease in rule violations compared with those receiving the placebo, both violent (ES = 0.52), and nonviolent (ES = 0.70) offenses (Schoenthaler et al., 1997).

Another RCT conducted by these researchers found school children aged 6–12 who received a broad spectrum of nutrients for one school year also improved (Schoenthaler & Bier, 2000). The 40 children in the experimental group who were randomized to receive the multinutrient supplement exhibited 47% fewer antisocial behaviors requiring discipline than the 40 children who received a placebo. The antisocial behaviors monitored in the study included threats, fighting, vandalism, defiance, endangering others and disorderly conduct.

Studies have also reported the same impact in incarcerated adults (Gesch et al., 2002; Zaalberg et al., 2010). Evidence for the benefit of multinutrients has continued to emerge from studies of children with explosive rage, conduct disorder, and ADHD with mood dysregulation (Hambly et al., 2017; Kaplan et al., 2004; Kaplan & Leung, 2011; Rucklidge et al., 2018). These human studies complement the long-standing literature on lab animals, which supports the relationship between poor nutrition and aggression (Valzelli, 1984). In summary, there is ample evidence that supplementation with a broad spectrum of micronutrients can reduce aggression.

Autism spectrum disorders (ASD)

A pilot RCT involving 20 children with ASD found that those taking a multinutrient supplement showed improvements in sleep and gastrointestinal problems, along with some suggestive trends for improved behavior, eye contact, and receptive language (Adams & Holloway, 2004). These same researchers followed up with a larger RCT in 141 children and adults with autism, and reported positive effects from a modified version of the formula over a placebo in reducing tantrums (ES = 0.51) and hyperactivity (ES = 0.37) as well as improving receptive language (ES = 0.40) and overall functioning (ES = 0.46), with no significant effects on expressive language, play, sociability, cognition, sleep, and eye contact (Adams et al., 2011). The formulas in both these studies contained 29 nutrients and participants were monitored for three months. Next, the researchers conducted an effectiveness trial comparing multinutrients combined with a variety of other therapies (including essential fatty acids, Epsom salts, carnitine, digestive enzymes, and a gluten-free/dairy-free diet) versus no treatment over a twelve-month period. There was significant improvement in those who received the comprehensive treatment approach, including non-verbal IQ, symptoms of ASD, social responsiveness, sensory profile, and aberrant behavior (Adams et al., 2018).

A case-control study (Mehl-Madrona et al., 2010) systematically followed 44 children and adults (age range was 2–28 years) taking multinutrients, some for up to two years, for the treatment of ASD. These individuals were later matched by age, gender, and symptom severity to 44 children and adults from the same clinic whose families had chosen conventional medications to treat the symptoms. The clinician was blinded to the treatment the participant received. On the Aberrant Behavior Checklist, averaged for parent and caregiver scores, the micronutrient formula was superior to medications overall. The subscales for irritability and hyperactivity showed significant benefit for the micronutrient group over placebo groups, with between group ES about 0.6. In addition, the clinician-rated Yale-Paris Self-Injurious Behavior Scale revealed a significant benefit of the nutrients: Self-Injurious Behavior intensity was lower post-treatment, with no change in the medication group. The roughly 50% decrease in the intensity of self-injurious behavior in the micronutrient group was unexpected and warrants further clinical studies, as this is among the most disturbing behaviors for families.

ADHD

The historical evidence for the use of multinutrients in the treatment of ADHD has been surrounded by controversy, given that early studies tended to utilize either very small doses, resulting in nonsignificant effect, or mega-doses, resulting in toxicity and adverse effects (Heilskov Rytter et al., 2015). In the past two decades, several studies have employed broad-spectrum multinutrients to treat core ADHD symptoms, at doses sufficient to be beneficial "therapeutic doses," but below potentially toxic levels (known as the Tolerable Upper Intake Level (UL)). Although the open-label trials varied in length and multinutrient composition, all of them resulted in significant improvements in behavioral functioning, including core ADHD symptoms and/or emotion regulation (Gordon et al., 2015; Kaplan et al., 2004; Rucklidge et al., 2011).

The first RCT (Rucklidge, Frampton, et al., 2014) followed 80 medication-free adults diagnosed with ADHD, randomized to receive either broad-spectrum multinutrients or placebo for eight weeks. Greater improvement on ADHD rating scales compared with placebo was found for observer (ES = 0.59) and self-report ratings (ES = 0.61) (but not clinician (ES = 0.23)). Clinicians rated 48% of those taking the nutrients as "much" or "very much" improved compared with 21% of the placebo group (X^2 = 6.189, p = .013, OR = 3.4; Figure 3). Those randomized to multinutrients, who entered the trial with a moderately to severely low mood, showed a greater improvement in mood compared with the placebo group (between group ES = 0.64).

A replication was published four years later, with 93 medication-free children aged 7–12, randomly assigned to either broad-spectrum multinutrients or placebo capsules for ten weeks (Rucklidge et al., 2018). Clinician-rated inattention (ES = 0.41) and overall functioning (ES = 0.48) improved significantly more in children who took the nutrients than those who took the placebo. There were no group differences in clinician-rated hyperactivity/impulsivity (ES = 0.11) nor in parent and teacher-rated ADHD symptoms. Across all raters (parents, teachers, and clinicians), there was significantly greater improvement in emotion regulation (ES = 0.66) and aggression (ES = 0.52) for those children who took the multinutrients compared to the placebo group. A meta-analysis confirms the consistency of findings across these two RCTs, noting a significant effect on clinician-rated inattention, global functioning, CGI-I and CGI-I-ADHD (Johnstone et al., 2020).

The participants in both RCTs were followed for one year after the study began. The results from both follow-ups were remarkably similar (Darling et al., 2019; Rucklidge et al., 2017). About 20% of the participants in both studies continued taking the nutrients, and were identified as having better mental health than those who chose to stop taking the nutrients or who switched to medications. Indeed, about 80% of those taking the nutrients were identified as being in remission from their ADHD symptoms, versus 40% of those on medications, and 20% of those who had stopped all treatments. The two main reasons cited for stopping the nutrients in both studies were cost and the number of pills to take. Side effects and ineffective control of symptoms did not feature as strongly as the other two reasons. Continued symptom improvement over time was reported for participants who stayed on the nutrients, suggesting that the benefit of the multinutrient treatment takes time to reach its full potential. Further, those who switched from nutrients to stimulant medications were more likely to have problems with mood or anxiety compared to those who stayed on nutrients at the one-year follow-up assessment (Darling et al., 2019).

In summary, open label pilot studies and two RCTs provide promising data for multinutrient supplementation in ADHD populations. Replication at other geographical centers is underway, with a larger

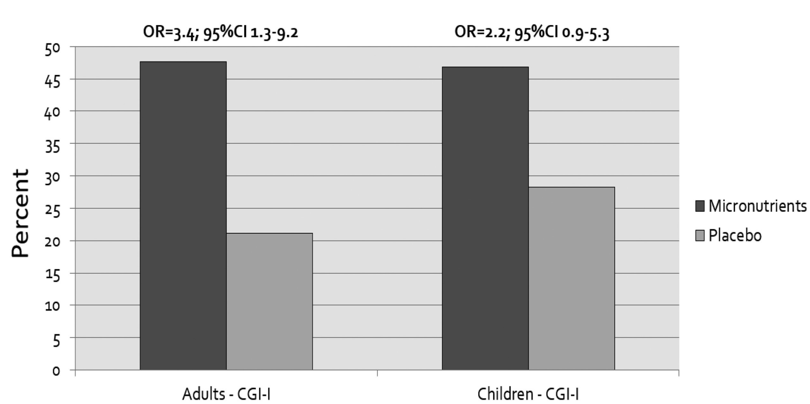

Figure 3. Responders (1 or 2 on CGI-I) across the two ADHD RCTs for micronutrients and placebo. CGI-I = Clinical Global Impression-Improvement.

trial of emotionally dysregulated kids with ADHD involving three centers (two in the US and one in Canada) completed in July 2020 (Johnstone et al., 2019); study results are expected in 2021.

Mood dysregulation

There have been numerous clinical observations and open-label trials of broad-spectrum multinutrients (Frazier et al., 2013; Kaplan, Hilbert, et al., 2015; Kaplan et al., 2001; Popper, 2001), as well as case studies (Kaplan et al., 2002), and database analyses in adults (Gately & Kaplan, 2009) and children (Rucklidge et al., 2010) with bipolar disorder, all showing significant improvement in symptoms and the need for a reduced amount of medication to maintain symptom control for most of the participants.

As mentioned in the ADHD RCT with 93 children, participants were evaluated one year after baseline. Of the 93 children, 62 were classified as mood dysregulated at baseline (≥20 on the Child Mania Rating Scale (CMRS) (West et al., 2011)), and ten of them met full criteria for Disruptive Mood Dysregulation Disorder (DMDD; based on DSM-5 criteria). At one year follow-up, those who stayed on micronutrients were significantly less dysregulated (based on the CMRS) compared to those children who switched to stimulant medication and those who discontinued all treatment, with very large (ES = 1.5–1.7) *between* group effect sizes (Rucklidge, 2019). When the children were classified as to whether their dysregulated mood was in remission (<20 on the CMRS), 100% of those on nutrients were classified as remitters, compared with 38% of those on medications and 48% of those receiving no treatment. When considering responder status, based on receiving a score of "much" or "very much" improved on the Clinical Global Impression – Improvement scale (CGI-I), 85% of those on nutrients were responders, versus 62% of those on medications and 22% of those receiving no treatment (Figure 4).

Dysregulated mood in ADHD is very hard to treat (Carlson, 2020) and medications can result in ADHD symptoms getting worse in the presence of emotion dysregulation (Masi et al., 2020). In contrast, several of the open-label case series and case reports cited above reported that a broad-spectrum multinutrient approach seems especially effective for the treatment of mood dysregulation and explosive rage. Although the follow up data from the ADHD study are limited by bias that can creep in with a naturalistic follow-up, the results highlight an untapped area for exploration.

As a means to illustrate the emotional and behavioral changes experienced by one boy, the following clinical vignette documents the child's progress while taking a broad spectrum micronutrient formula, as recorded by one of the authors (JMJ).

Clinical vignette

Calvin (pseudonym), an 8 year-old boy, had a difficult start in life due to poly-drug exposure in utero. His birth mother was a teenager who experienced homelessness during her pregnancy; she left him in the care of a friend days after giving birth. Calvin was hospitalized soon after for malnutrition and dehydration, and adopted as an infant. As a toddler, he was emotionally dysregulated, banging his head against the wall when upset, and screaming for hours. In primary school, Calvin was behind in all subjects and prone to temper tantrums that resulted in the other students

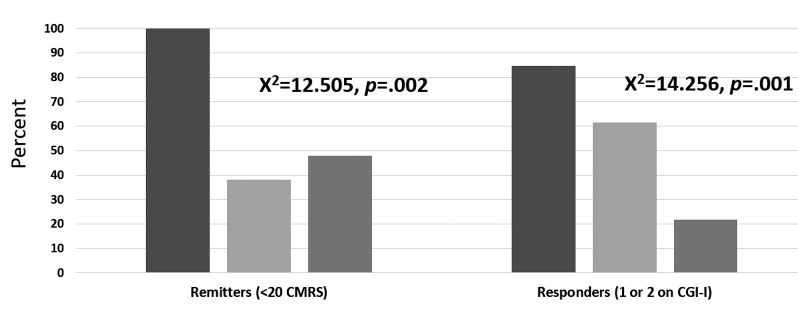

Figure 4. Percentage of remitters (Child Mania Rating Scale (CMRS)<20) and responders ("much" or "very much" improved on the Clinical Global Impression–Improvement scale [CGI-I]) at 1 year follow-up for those children with ADHD identified as emotionally dysregulated at baseline (CMRS>20).

vacating the classroom so that the teacher could help him calm down. Based on a thorough neuropsychological evaluation, Calvin met criteria for Other Specific Neurodevelopment Disorder, associated with known in utero polydrug exposure, and ADHD. Since the evaluation, additional data have clarified that Calvin meets criteria for Fetal Alcohol Spectrum Disorder.

At the request of his adoptive mother who was reluctant to try stimulant medication for ADHD, Calvin was given one of the multinutrient formulas used in the studies described above for mood and ADHD. Over the course of two months, he learned to swallow the capsules. After eight weeks of taking the formula at a therapeutic dose, Calvin and his parents reported dramatic improvements. Calvin began to regulate his behavior and emotions, self-soothe and use his words when upset. When Calvin got upset, the strong emotion lasted a few minutes, rather than 30 minutes or longer. The school stopped calling the parents regularly concerning Calvin's emotional and behavioral issues. He became able, for the first time, to follow his teacher's directions, and by the end of the school year, he was caught up to grade level in reading and math. Best of all for Calvin, he was finally able to slow down and concentrate to read and complete the directions to his Lego sets, which enabled him to build the models on his own. Commenting on his improvements, Calvin's mother volunteered her surprise that her son's dietary preferences had changed as well. He did not crave soda and ultra-processed fast foods with the same frequency and urgency that he did before taking the nutrients. Whereas prior to taking nutrients, Calvin threw a temper tantrum if he did not get soda or ultra-processed fast food *daily*, after the nutrients, he became less upset when his mom denied him these foods. Gradually, his intake of fast food reduced to less than once-per-week, and when he was allowed these foods, they were "a treat" for him, rather than a craving.

Before starting the multinutrients, the clinician's rating of the severity of Calvin's symptoms, the CGI-Severity (CGI-S) based on all available information, was a 6 "severely ill" (range 1–7); two months after starting a therapeutic dose of multinutrients, his CGI-S was a 3 "mildly ill," and he was rated a treatment responder based on a CGI-I of 1 "very much improved." His parent ratings on the Child and Adolescent Symptom Inventory-5 (CASI-5), using item means were a 3 for ADHD hyperactivity, and 2.8 for the inattentive (range is 0–3, with 2 or higher as the clinical cutoff). Both scores dropped to a 1 after two months, based on his mother's report. Because of Calvin's behavioral and emotional improvements, his adoptive parents believed he could, for the first time, stay in his seat and watch a movie, so four months after he started a therapeutic dose of the multinutrients, his father took him to the theater to see Dumbo the Flying Elephant. Calvin sat through the whole movie, without impulsively interrupting or getting up. It was a memorable experience for both Calvin and his dad.

One year later, at the annual follow-up phone call with Calvin and his mother, the clinician-rated CGI-S was still "mildly ill," and his CGI-I was "much improved." Calvin's mother reported slight increases in hyperactivity and inattention compared to his functioning two months after starting a therapeutic dose of the multinutrients, with item means of 1.6 and 1.5 respectively, but both scores were still much improved compared to baseline, and below the clinical cutoff. See Table 1 for additional clinical data.

Psychosis

Other than two case studies, one in a child and one in an adult successfully treated with multinutrients (Kaplan et al., 2017; Rodway et al., 2012), the only research that has been conducted specifically on micronutrients and psychosis involved 19 patients with psychosis who gradually reduced their medications as they added a broad-spectrum multinutrient formula (Mehl-Madrona & Mainguy, 2017). The study started as an RCT with a one month lead-in, when everyone received the nutrients. At the end of the month, they were due to be randomized, with a 50% chance of receiving a placebo, but not one of the participants was willing to risk the chance of being in the placebo group; all stated they were feeling better with the nutrients. The researchers were forced to change their study design and monitor these participants over two years instead, comparing their progress to thirty-one patients who had chosen not to be in the trial.

Table 1. Symptom changes in an 8-year-old boy pre- and post-multinutrient treatment.

	Timepoint		
Measure	Baseline: Pre-multinutrients	Two-months on nutrients	One-year* on nutrients
CGI-S[a]	6 "severely ill"	3 "mildly ill"	3 "mildly ill"
CGI-I[b]	n/a	1 "very much improved"	2 "much improved"
Hyperactivity[c]	3	1	1.6
Inattention[c]	2.8	1	1.5
ODD[c,d]	2.4	0.8	1.6
DMDD[c,e]	2	0.5	1.8

*Boy was 9 years old at this rating point
[a]Clinician-rated Clinical Global Impression (CGI) – Severity
[b]CGI-Improvement (CGI-I)
[c]Based on parent-report on the Child and Adolescent Symptom Inventory-5 (CASI-5)
[d]Oppositional Defiant Disorder
[e]Disruptive Mood Dysregulation Disorder

At fifteen months, the group taking reduced medications plus the multinutrient formula showed significantly fewer psychosis symptoms than the medication-only group. This difference was even stronger at the two-year mark. The researchers concluded that a broad-spectrum multinutrient formula was a beneficial long-term adjunct strategy for people with psychotic disorders. When participants took the nutrients, they needed smaller doses of their medication to be effective, and they experienced fewer medication side effects.

Safety and side effects of broad-spectrum multinutrients

To date, no serious adverse effects have been attributed to the broad-spectrum multinutrient formulas which have been studied. Several of the studies have collected safety data (via blood tests, heart rate, blood pressure) before and after exposure to the nutrients, typically over two or three months, some over several years. In all of these studies, amounting to several hundred blood tests before and after multinutrient use, no evidence of clinically meaningful short-term or long-term harm has emerged (Adams et al., 2018; Rucklidge, Eggleston, Ealam, et al., 2019; Rucklidge et al., 2018; Rucklidge, Frampton et al., 2014; Simpson et al., 2011).

The most commonly reported side effects are headaches and stomach aches, although they are typically mild, transitory, and can be avoided by taking capsules on a full stomach and with plenty of water. A minority of study participants report feeling more agitated, and lowering the dose tends to reduce agitation for many. In randomized controlled trials, these minor side effects in the multinutrient group have not occurred more frequently than in those taking a placebo (Rucklidge et al., 2018; Rucklidge, Frampton et al., 2014).

It is important to note these results are based mostly on studies conducted with people *not concurrently taking psychiatric medications*. In the Mehl-Madrona study, the participants were monitored by a psychiatrist. Taking the nutrients with medications needs to be monitored carefully by the prescriber and doses may need to be adjusted (Popper et al., 2017).

Another consideration is that study participants report fewer adverse effects from multinutrient treatment relative to medications. For instance, in the study comparing nutrients to medications for the treatment of autism-related symptoms, the 44 people with autism taking prescription medications experienced 6.5 times as many adverse events as the 44 people with autism taking multinutrients (Mehl-Madrona et al., 2010).

Alongside considering safety, clinicians often wonder about whether the nutrient interventions are applicable only to people who have an identified deficiency in a particular nutrient, like zinc or vitamin D. A number of studies have revealed that a deficiency, as indicated by blood nutrient levels examined thus far, has not been useful for identifying who would benefit from supplementation. The two ADHD RCTs described also looked at predictors of response to nutrient treatment and while a few nutrients modestly predicted outcome (Rucklidge, Eggleston, Darling, et al., 2019;

Rucklidge, Johnstone, et al., 2014), the three main findings were that: 1) the vast majority of the nutrient levels fell in the normal range across both studies (72% of the samples had nutrient levels in the "normal" range) and pre-treatment nutrient levels were not associated with any of the ADHD symptoms, 2) nutrient levels before treatment did not reliably predict who would respond to the treatment, meaning that people who had "normal" range nutrient levels had a similar response rate as those who had "abnormal" nutrient levels, and 3) change in a nutrient biomarker did not correlate with mental health improvement (Rucklidge, Eggleston, Boggis, et al., 2019). Other researchers have also found serum levels of specific micronutrients (e.g., vitamin D, folate and B12) are poor predictors of response to nutrient interventions for people with mood and psychotic disorders (Van der Burg et al., 2019). The term "nutrient deficiency" may be misleading as it suggests that individuals must be deficient relative to the average population. If an individual's nutritional needs are higher than the average population, then nutrient levels will not be able to assist in identifying who is deficient relative to their own, individual metabolic needs. Therefore, extensive nutrient testing is not a necessary prerequisite to considering nutrient treatment.

Suggestions for clinical application

Clinicians may be reluctant to incorporate nutrition education and guidance into clinical practice because of their own lack of education regarding how nutrients influence brain function. This educational deficiency is the reason for devoting the first section of this paper to explanations of what nutrients do in the brain. Such information should not be limited to clinicians: we suggest that the role of nutrients in brain health should be part of educational curricula across the board, down to the elementary school level, and certainly part of a mental health clinician's training.

Clinicians may think that talking about diet is outside their scope of practice, although many behavioral activation strategies to treat low mood include increasing or decreasing food intake and as mentioned above, Walsh (2011) included nutrition as one of the within-scope tools that psychologists should be utilizing. Reducing caffeine or alcohol are often common suggestions made by psychologists for addressing mood or anxiety issues (Tenore et al., 2015).

The scientist-practitioner model encourages psychologists to evaluate the evidence, stay abreast of new treatments and present this information in a digestible and balanced way to clients. Based on the burgeoning research in the field of nutritional psychology, psychologists are well placed to discuss with clients the connection between diet and mental health, highlighting some of the nutritional psychology research studies. Providing such information, including pros and cons of such an approach relative to other treatments, would be aligned with obtaining full informed consent.

One way to start the conversation is to ask parents and/or children about their understanding of what nutrients do in the body. Given that most dietary guidelines focus on fats, carbohydrates and proteins, many individuals may have concluded that these are the important dietary elements on which to focus. While they are essential for the brain to develop and function (carbohydrates provide glucose, proteins provide amino acids, and fats are required for overall brain structure), the focus on these three macronutrients should not overshadow the essential micronutrients – minerals and vitamins. As we have highlighted in this article, micronutrients in sufficient amounts are required to synthesize and break down neurotransmitters.

Clinicians may be reluctant to ask clients about their diets for fear of being intrusive, or perhaps out of concern that their own diet is not ideal. One way to address this is to use the following introduction: "There is an increasing amount of scientific data showing that what we eat influences how we feel. *Let's talk about your diet.*"

Although there are various quantitative tools available, clinicians may want to take a more conversational approach by following that introduction with some of the Start the Conversation questions proposed by Paxton from the University of North Carolina (Paxton et al., 2011). The following four questions, adapted from Paxton's questionnaire, provide virtually all the information needed to help a clinician focus a first discussion.

(a) How many times a week do you eat fast food meals or snacks?Ho
(b) How many sodas or sweetened drinks do you have each day?
(c) How many servings of fruit do you eat each day?
(d) How many servings of vegetables do you eat each day?

While these items are not scored, and there are no right or wrong answers, a client's responses may lead to a discussion about setting goals. Clients may volunteer that they know they should drink less soda, or eat more vegetables, for instance; these comments will provide the opportunity to discuss goals, and how they can work toward them. The following are additional suggestions to strengthen the conversation.

Focus first on eating whole foods

Think of our food supply as consisting of three categories: whole foods, slightly processed foods (e.g., canned or frozen), and ultra-processed foods (packaged food with preservatives, added sugars and artificial colors). Government data show that more than 50% of the "stuff" North Americans put into their mouths is from that third category, consisting of packaged products which are mostly nutrient-free (Moubarac et al., 2017). Further, in the US, the Center for Disease Control reported 2015 data that showed only about 9% of the public is consuming the recommended number of daily vegetable servings (Lee-Kwan et al., 2017). Moving our society toward a whole-foods diet would result in an enormous step toward health. In Canada, research has shown that if every Canadian increased their intake of fruits and vegetables by just one serving per day, there would be a health care cost saving of 9.2 billion dollars per year (Ekwaru et al., 2017).

Clients may be curious about specialty diets (e.g., gluten-free, ketogenic), and while those diets can be helpful to some people, they are restrictive and have not yet been shown to conclusively benefit mental health. Individuals who begin with a very restrictive diet and fail to adhere to it may end up feeling discouraged and become reluctant to continue with dietary modifications. For this reason, we suggest dietary changes focus first on moving from ultra-processed products toward eating more whole foods. The research shows that moving toward a whole-foods Mediterranean-style diet can cut depression by at least 25% in just three weeks (Francis et al., 2019), and even more by twelve weeks (Jacka et al., 2017; Parletta et al., 2019). Further, beginning with a whole-foods diet paves the way for success because it offers more food choices instead of food restrictions. If a client is considering a restrictive diet, a referral to a dietician may be required, as elimination diets can be quite complex and it is important to ensure a balanced intake of nutrients is consumed.

Encourage gradual transitions

For a family that consumes mostly packaged, ultra-processed food, attempting to make dramatic and sudden dietary changes may feel overwhelming and lead to inaction or failure. To start slowly, suggest initiating one cook-from-scratch dinner each week. For example, a meatless Monday dinner could be used to encourage experimenting with different types of greens, beans and legumes, or other healthy whole food meals.

Another type of transition that might be useful relates to beverages. Dependence on carbonated sodas is commonly reported by people who eat highly processed "fast foods" (Cantor et al., 2016). Flavored carbonated water can be helpful in weaning down or off sodas. Many carbonated water choices are flavored with fruit, but no sweeteners (either sugar or artificial). Increasing the consumption of plain water or teas is the long-term goal.

Clarify that a Mediterranean diet is possible on a limited budget

While some whole foods are expensive (lobster, steak), the SMILES trial showed that it is possible to eat a whole-foods diet and save money (Opie, Segal, et al., 2015). Frozen vegetables and lentils are nutritious, inexpensive, and convenient, as are canned beans and fish. Introduce your clients or their parents to the millions of online recipes that utilize inexpensive dried beans of various types. If time constraints are an issue, remind your clients that cooking with lentils is very fast. Another way to educate clients about this topic is to ask them to track their costs and create a graph so they can see how they save money.

Encourage clinic patients to take community cooking classes

Based on the three dietary education studies mentioned previously, clinicians could begin by teaching clients about eating a whole-foods diet as an initial intervention, which could lead to more instructive guidance, including ways to replace ultra-processed food with healthier options. For instance, ask clients to record every item they consumed in the meal eaten prior to an appointment, and then to categorize each item or ingredient as either: whole food (1), slightly processed (2), or ultra-processed (3). Finally ask them to write what they might have chosen instead, to move items from category 3 to 2, or to 1. Another option is to connect clients with local classes or websites that teach healthy cooking.

Discuss nutrient supplementation

If change to a healthier diet along with other essential lifestyle modifications and therapeutic interventions are not providing the desired benefits, referring clients to the literature on supplements could be the next step. However, it is important to frame this information as being *in addition* to a whole-food diet, not as a substitute.

Omega-3 supplementation is a good option, especially for people who dislike fish.

However, we are not aware of a sufficient amount of research on any particular brand to provide guidance in that regard. In general, check the manufacturer's purity claims and assertions regarding testing for mercury. We need both EPA and DHA for optimizing mental health, with research using omega-3 supplements for the treatment of depression recommending a 2:1 ratio of EPA:DHA with a minimum of 1 g/day, and research on ADHD recommending a minimum of 500 mg of EPA/day (Chang et al., 2018).

For multinutrient formulas (mineral-plus-vitamin), the majority of the evidence in children that has been described in this article comes from two formulas developed in Canada (EMPowerplus™ and Daily Essential Nutrients™); none of the studies have been funded by the companies. There are now more than 50 peer-reviewed publications on these two formulas (list available on request but many are in the references). In addition, there are combinations of nutrients that have been studied for aggression in Europe (no specific brand used) and for autism in the US (ANRC Essentials Plus™) which have also been tested in controlled trials. Attempts to study other broad-spectrum formulas have not been successful, as the companies producing them have been reluctant to have them evaluated.

It is also noteworthy that the typical over-the-counter multinutrient formulas for children, of which 22 were examined, contain only small doses of the micronutrients compared to the amounts in the formulas for which research has shown mental health benefit (Rucklidge, Harris, et al., 2014). A systematic review and meta-analysis of multinutrients for psychiatric conditions also highlighted the limited ingredient range and low dosage of many studied formulas (Johnstone et al., 2020). Typically, the multinutrients' cost is paid by the family, and healthcare spending accounts may reimburse for qualified expenses such as these. Cost may be an issue for some, which will be part of the consideration in deciding on the best treatment approach. Research indicates that best outcomes emerge in those who stay on the nutrients for at least one year (Darling et al., 2019; Rucklidge et al., 2017). Funding for multinutrient supplements is currently an issue that may be resolved if insurance companies and the public health care system cover the cost. Research from two case studies demonstrate the nutrient treatment cost less than 10% of conventional care (Kaplan et al., 2017; Rodway et al., 2012), which may interest governments with tight budgets. Further studies on cost savings and the efficacy of the multinutrient supplementation are needed to increase the likelihood of insurance or public health reimbursement. Regardless of the weight of the evidence, however, clinicians are well served to be mindful of the advantages of psychiatric medications that may appeal to some families. Those advantages include the existence of insurance coverage, the fact that medications require few pills, and less frequent dosing.

Conclusions

Research evidence underscores the importance of eating a healthy diet for achieving and maintaining optimal mental health. Clinicians have an opportunity to talk to their clients about this connection. This paper supports teaching clients about the importance of eating a whole-foods Mediterranean-style diet as an additional tool to incorporate into routine clinical practice. Good nutrition provides the *foundation* for other interventions such as cognitive-behavior therapy or medication. Attending to nutritional needs *first* may increase the likelihood that subsequent therapies will be more successful – an hypothesis that seems logical, but has not yet been evaluated. For some clients, eating a whole-foods diet is not sufficient. After considering the range of lifestyle and therapy factors, including sleep hygiene, exercise, ongoing relationship difficulties, frequency and type of psychotherapy, as part of informed consent, clinicians may want to consider discussing the research on multinutrient supplementation, including both the pros and cons of this approach.

In any discussion of nutrient supplementation, it is essential that supplements are not viewed as a substitute for a healthy diet. Given this field is rapidly expanding, with studies underway to further investigate mechanisms of action, others replicating and adding greater methodological rigor to the published studies, as well as further RCTs exploring the efficacy of micronutrients in the treatment of a variety of disorders, psychologists will have a wealth of data available to inform their clinical work. This review provides the foundational knowledge as well as resources and readings for further exploration for psychologists and clinicians motivated to educate themselves about the field of nutrition and mental health. In addition, a new mass online open-access course (MOOC) has just been developed for educating professionals and the public on the topic of nutrition and mental health (https://www.edx.org/course/mental-health-and-nutrition).

Disclosure statement

The authors have no disclosures to make or any conflicts to declare.

ORCID

Julia J. Rucklidge http://orcid.org/0000-0003-3793-7342

References

Adams, J. B., Audhya, T., Geis, E., Gehn, E., Fimbres, V., Pollard, E., Mitchell, J., Ingram, J., Hellmers, R., Laake, D., Matthews, J., Li, K., Naviaux, J., Naviaux, R., Adams, R., Coleman, D., & Quig, D. (2018). Comprehensive nutritional and dietary intervention for autism spectrum disorder—A randomized, controlled 12-month trial. *Nutrients*, *10*(3), 369. http://www.mdpi.com/2072-6643/10/3/369

Adams, J. B., Audhya, T., McDonough-Means, S., Rubin, R. A., Quig, D., Geis, E., Gehn, E., Loresto, M., Mitchell, J., Atwood, S., Barnhouse, S., & Lee, W. (2011). Effect of a vitamin/mineral supplement on children and adults with autism. *BMC Pediatrics*, *11*, 111. https://doi.org/10.1186/1471-2431-11-111

Adams, J. B., & Holloway, C. (2004). Pilot study of a moderate dose multivitamin/mineral supplement for children with autism spectrum disorder. *Journal of Alternative and Complementary Medicine*, *10*(6), 1033–1039. http://online.liebertpub.com/doi/abs/10.1089/acm.2004.10.1033

Ames, B. N., Elson-Schwab, I., & Silver, E. A. (2002). High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K(m)): Relevance to genetic disease and polymorphisms. *American Journal of Clinical Nutrition*, *75*(4), 616–658. https://doi.org/10.1093/ajcn/75.4.616

Bastiaanssen, T. F. S., Cowan, C. S. M., Claesson, M. J., Dinan, T. G., & Cryan, J. F. (2019). Making sense of … the microbiome in psychiatry. *International Journal of Neuropsychopharmacology*, *22*(1), 37–52. https://doi.org/10.1093/ijnp/pyy067

Benton, D. (2007). The impact of diet on anti-social, violent and criminal behaviour. *Neuroscience and Biobehavioral Reviews*, *31*(5), 752–774. https://doi.org/j.jaac.2011.10.015/j.neubiorev.2007.02.002

Benton, D., & Cook, R. (1991). The impact of selenium supplementation on mood. *Biological Psychiatry*, *29*(11), 1092–1098. https://doi.org/10.1016/0006-3223(91)90251-G

Benton, D., Griffiths, R., & Haller, J. (1997). Thiamine supplementation mood and cognitive functioning. *Psychopharmacology*, *129*(1), 66–71. https://doi.org/10.1007/s002130050163

Bolduc, F. V., Lau, A., Rosenfelt, C. S., Langer, S., Wang, N., Smithson, L., Lefebvre, D., Alexander, R. T., Dickson, C. T., Li, L., Becker, A. B., Subbarao, P., Turvey, S. E., Pei, J., Sears, M. R., Mandhane, P. J., & Investigators, C. S. (2016). Cognitive enhancement in infants associated with increased maternal fruit intake during pregnancy: Results from a birth cohort study with validation in an animal model. *EBioMedicine*, *8*, 331–340. https://doi.org/10.1016/j.ebiom.2016.04.025

Breit, S., Kupferberg, A., Rogler, G., & Hasler, G. (2018). Vagus nerve as modulator of the brain-gut axis in psychiatric and inflammatory disorders. *Frontiers in Psychiatry*, *9*, 44. https://doi.org/10.3389/fpsyt.2018.00044

Brown, A. S., & Susser, E. S. (2008). Prenatal nutritional deficiency and risk of adult schizophrenia. *Schizophrenia Bulletin*, *34*(6), 1054–1063. https://doi.org/10.1093/schbul/sbn096

Cantor, J., Breck, A., & Elbel, B. (2016). Correlates of sugar-sweetened beverages purchased for children at fast-food restaurants. *American Journal of Public Health*, *106*(11), 2038–2041. https://doi.org/10.2105/AJPH.2016.303427

Carlson, G. A. (2020). Presidential address: Emotion dysregulation in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, *59*(1), 15–19. https://doi.org/10.1016/j.jaac.2019.11.004

Cenit, M. C., Sanz, Y., & Codoner-Franch, P. (2017). Influence of gut microbiota on neuropsychiatric disorders. *World Journal of Gastroenterology*, *23*(30), 5486–5498. https://doi.org/10.3748/wjg.v23.i30.5486

Chang, J., Su, K.-P., Mondelli, V., & Pariante, C. (2018). Omega-3 polyunsaturated fatty acids in youths with attention deficit hyperactivity disorder: A systematic review and meta-analysis of clinical trials and biological studies. *Neuropsychopharmacology*, *43*(3), 534–545. https://doi.org/10.1038/npp.2017.160

Collins, S. M., Kassam, Z., & Bercik, P. (2013). The adoptive transfer of behavioral phenotype via the intestinal microbiota: Experimental evidence and clinical implications. *Current Opinions in Microbiology*, *16*(3), 240–245. https://doi.org/10.1016/j.mib.2013.06.004

Conner, T. S., Brookie, K. L., Carr, A. C., Mainvil, L. A., & Vissers, M. C. (2017). Let them eat fruit! The effect of fruit and vegetable consumption on psychological well-being in young adults: A randomized controlled trial. *PloS One*, *12*(2), e0171206. https://doi.org/10.1371/journal.pone.0171206

Cryan, J. F., O'Riordan, K. J., Cowan, C. S. M., Sandhu, K. V., Bastiaanssen, T. F. S., Boehme, M., Codagnone, M. G., Cussotto, S., Fulling, C., Golubeva, A. V., Guzzetta, K. E., Jaggar, M., Long-Smith, C. M., Lyte, J. M., Martin, J. A., Molinero-Perez, A., Moloney, G., Morelli, E., Morillas, E., O'Connor, R., & Dinan, T. G. (2019). The microbiota-gut-brain axis. *Physiological Reviews*, *99*(4), 1877–2013. https://doi.org/10.1152/physrev.00018.2018

Darling, K. A., Eggleston, M. J. F., Retallick-Brown, H., & Rucklidge, J. J. (2019). Mineral-vitamin treatment associated with remission in attention-deficit/hyperactivity disorder symptoms and related problems: 1-year naturalistic outcomes of a 10-week randomized placebo-controlled trial. *Journal of Child and Adolescent Psychopharmacology*, *29*(9), 688–704. https://doi.org/10.1089/cap.2019.0036

Datnoff, L. E., Elmer, W. H., & Huber, D. M. (Eds.). (2007). *Mineral nutrition and plant disease*. American Phytopathological Society.

Davis, D. R., Epp, M. D., & Riordan, H. D. (2004). Changes in USDA food composition data for 43 garden crops, 1950 to 1999. *Journal of the American College of Nutrition*, *23*(6), 669–682. https://doi.org/10.1080/07315724.2004.10719409

Ejaredar, M., Nyanza, E. C., Ten Eycke, K., & Dewey, D. (2015). Phthalate exposure and childrens neurodevelopment: A systematic review. *Environmental Research*, *142*, 51–60. https://doi.org/10.1016/j.envres.2015.06.014

Ekwaru, J. P., Ohinmaa, A., Loehr, S., Setayeshgar, S., Thanh, N. X., & Veugelers, P. J. (2017). The economic burden of inadequate consumption of vegetables and fruit in Canada. *Public Health Nutrition*, *20*(3), 515–523. https://doi.org/10.1017/S1368980016002846

Firth, J., Marx, W., Dash, S., Carney, R., Teasdale, S. B., Solmi, M., Stubbs, B., Schuch, F. B., Carvalho, A. F., Jacka, F., & Sarris, J. (2019). The effects of dietary improvement on symptoms of depression and anxiety: A meta-analysis of randomized controlled trials. *Psychosomatic Medicine*, *81*(3), 265–280. https://doi.org/10.1097/PSY.0000000000000673

Firth, J., Stubbs, B., Sarris, J., Rosenbaum, S., Teasdale, S., Berk, M., & Yung, A. R. (2017). The effects of vitamin and mineral supplementation on symptoms of schizophrenia: A systematic review and meta-analysis. *Psychological Medicine*, *47*(9), 1515–1527. https://doi.org/10.1017/S0033291717000022

Firth, J., Teasdale, S. B., Allott, K., Siskind, D., Marx, W., Cotter, J., Veronese, N., Schuch, F., Smith, L., Solmi, M., Carvalho, A. F., Vancampfort, D., Berk, M., Stubbs, B., & Sarris, J. (2019). The efficacy and safety of nutrient supplements in the treatment of mental disorders: A meta-review of meta-analyses of randomized controlled trials. *World Psychiatry*, *18*(3), 308–324. https://doi.org/10.1002/wps.20672

Flannery, J. E., Stagaman, K., Burns, A. R., Hickey, R. J., Roos, L. E., Giuliano, R. J., Fisher, P. A., & Sharpton, T. J. (2020). Gut feelings begin in childhood: The gut metagenome correlates with early environment, caregiving, and behavior. *mBio*, *11*(1), e02780–02719. https://doi.org/10.1128/mBio.02780-19

Francis, H. M., Stevenson, R. J., Chambers, J. R., Gupta, D., Newey, B., & Lim, C. K. (2019). A brief diet intervention can reduce symptoms of depression in young adults - A randomised controlled trial. *PloS One*, *14*(10), e0222768. https://doi.org/10.1371/journal.pone.0222768

Frazier, E. A., Gracious, B., Arnold, L. E., Failla, M., Chitchumroonchokchai, C., Habash, D., & Fristad, M. A. (2013). Nutritional and safety outcomes from an open-label micronutrient intervention for pediatric bipolar spectrum disorders. *Journal of Child and Adolescent Psychopharmacology*, *23*(8), 558–567. https://doi.org/10.1089/cap.2012.0098

Galera, C., Heude, B., Forhan, A., Bernard, J. Y., Peyre, H., Van der Waerden, J., Pryor, L., Bouvard, M. P., Melchior, M., Lioret, S., de Lauzon-guillain, B., & Group, E. M.-C.-C. S. (2018). Prenatal diet and children's trajectories of hyperactivity-inattention and conduct problems from 3 to 8 years: The EDEN mother-child cohort. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *59*(9), 1003–1011. https://doi.org/10.1111/jcpp.12898

Gately, D., & Kaplan, B. (2009). Database analysis of adults with bipolar disorder consuming a multinutrient formula. *Clinical Medicine: Psychiatry*, *4*, 3–16.

Gesch, C. B., Hammond, S. M., Hampson, S. E., Eves, A., & Crowder, M. J. (2002). Influence of supplementary vitamins, minerals and essential fatty acids on the antisocial behaviour of young adult prisoners. Randomised, placebo-controlled trial. *British Journal of Psychiatry*, *181*(1), 22–28. https://doi.org/10.1192/bjp.181.1.22

Gordon, H. A., Rucklidge, J. J., Blampied, N. M., & Johnstone, J. M. (2015). Clinically significant symptom reduction in children with attention-deficit/hyperactivity disorder treated with micronutrients: An open-label reversal design study. *Journal of Child and Adolescent Psychopharmacology*, *25*(10), 783–798. https://doi.org/10.1089/cap.2015.0105

Hambly, J. L., Francis, K., Khan, S., Gibbons, K. S., Walsh, W. J., Lambert, B., Testa, C., & Haywood, A. (2017). Micronutrient therapy for violent and aggressive male youth: An open-label trial. *Journal of Child and Adolescent Psychopharmacology*, *27*(9), 823–832. https://doi.org/10.1089/cap.2016.0199

Heilskov Rytter, M. J., Andersen, L. B., Houmann, T., Bilenberg, N., Hvolby, A., Molgaard, C., Michaelsen, K. F., & Lauritzen, L. (2015). Diet in the treatment of ADHD in children - a systematic review of the literature. *Nordic Journal of Psychiatry*, *69*(1), 1–18. https://doi.org/10.3109/08039488.2014.921933

Hennig, B., Ormsbee, L., McClain, C. J., Watkins, B. A., Blumberg, B., Bachas, L. G., Sanderson, W., Thompson, C., & Suk, W. A. (2012). Nutrition can modulate the toxicity of environmental pollutants: Implications in risk assessment and human health. *Environmental Health Perspectives*, *120*(6), 771–774. https://doi.org/10.1289/ehp.1104712

Hoare, E., Hockey, M., Ruusunen, A., & Jacka, F. N. (2018). Does fruit and vegetable consumption during adolescence predict adult depression? A longitudinal study of US adolescents [Original Research]. *Frontiers in Psychiatry*, *9*(581), 581. https://doi.org/10.3389/fpsyt.2018.00581

Hogy, P., Wieser, H., Kohler, P., Schwadorf, K., Breuer, J., Franzaring, J., Muntifering, R., & Fangmeier, A. (2009). Effects of elevated CO2 on grain yield and quality of wheat: Results from a 3-year free-air CO2 enrichment experiment. *Plant Biology (Stuttgart, Germany)*, *11 Suppl 1*, 60–69. https://doi.org/10.1111/j.1438-8677.2009.00230.x

Hsiao, E. Y., McBride, S. W., Hsien, S., Sharon, G., Hyde, E. R., McCue, T., Codelli, J. A., Chow, J., Reisman, S. E., Petrosino, J. F., Patterson, P. H., & Mazmanian, S. K. (2013). Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell*, *155*(7), 1451–1463. https://doi.org/10.1016/j.cell.2013.11.024

Huffman, S. L., Harika, R. K., Eilander, A., & Osendarp, S. J. M. (2011). Essential fats: How do they affect growth and development of infants and young children in developing countries? A literature review. *Maternal & Child Nutrition*, *7*(s3), 44–65. https://doi.org/10.1111/j.1740-8709.2011.00356.x

Jacka, F. N., Kremer, P. J., Berk, M., de Silva-sanigorski, A. M., Moodie, M., Leslie, E. R., Pasco, J. A., & Swinburn, B. A. (2011). A prospective study of diet quality and mental health in adolescents. *PloS One*, *6*(9), e24805. https://doi.org/10.1371/journal.pone.0024805

Jacka, F. N., O'Neil, A., Opie, R., Itsiopoulos, C., Cotton, S., Mohebbi, M., Castle, D., Dash, S., Mihalopoulos, C., Chatterton, M. L., Brazionis, L., Dean, O. M., Hodge, A. M., & Berk, M. (2017). A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial) [journal article]. *BMC Medicine*, *15*(1), 23. https://doi.org/10.1186/s12916-017-0791-y

Jacka, F. N., Ystrom, E., Brantsaeter, A. L., Karevold, E., Roth, C., Haugen, M., Meltzer, H. M., Schjolberg, S., & Berk, M. (2013). Maternal and early postnatal nutrition and mental health of offspring by age 5 years: A prospective cohort study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(10), 1038–1047. https://doi.org/10.1016/j.jaac.2013.07.002

Jacobson, M. F., & Schardt, M. S. (1999). *Diet, ADHD and behaviour: A quarter-century review*. Centre for Science in the Public Interest.

Johnstone, J., Hughes, A., Goldenberg, J. Z., Romijn, A. R., & Rucklidge, J. J. (2020). Multinutrients for the treatment of psychiatric symptoms in clinical samples: A systematic review and meta-analysis of randomized controlled trials. *Nutrients*, *12*(11), 3394. https://doi.org/10.3390/nu12113394

Johnstone, J., Leung, B., Gracious, B., Perez, L., Tost, G., Savoy, A., Hatsu, I., Hughes, A., Bruton, A., & Arnold, E. (2019). Rationale and design of an international randomized placebo-controlled trial of a 36-ingredient micronutrient supplement for children with ADHD and irritable mood: The micronutrients for ADHD in youth (MADDY) study. *Contemporary Clinical Trials Communications*, *16*, 100478. https://doi.org/10.1016/j.conctc.2019.100478

Kanissery, R., Gairhe, B., Kadyampakeni, D., Batuman, O., & Alferez, F. (2019). Glyphosate: Its environmental persistence and impact on crop health and nutrition. *Plants (Basel, Switzerland)*, *8*(11), 499. https://doi.org/10.3390/plants8110499

Kaplan, B. J., Crawford, S. G., Field, C. J., & Simpson, J. S. (2007). Vitamins, minerals, and mood. *Psychological Bulletin*, *133*(5), 747–760. https://doi.org/10.1037/0033-2909.133.5.747

Kaplan, B. J., Crawford, S. G., Gardner, B., & Farrelly, G. (2002). Treatment of mood lability and explosive rage with minerals and vitamins: Two case studies in children. *Journal of Child and Adolescent Psychopharmacology*, *12*(3), 205–219. https://doi.org/10.1089/104454602760386897

Kaplan, B. J., Fisher, J. E., Crawford, S. G., Field, C. J., & Kolb, B. (2004). Improved mood and behavior during treatment with a mineral-vitamin supplement: An open-label case series of children. *Journal of Child and Adolescent Psychopharmacology*, *14*(1), 115–122. https://doi.org/10.1089/104454604773840553

Kaplan, B. J., Hilbert, P., & Tsatsko, E. (2015). Micronutrient treatment for children with emotional and behavioral dysregulation: A case series. *Journal of Medical Case Reports*, *9*(1), 240. https://doi.org/10.1186/s13256-015-0735-0

Kaplan, B. J., Isaranuwatchai, W., & Hoch, J. S. (2017). Hospitalization cost of conventional psychiatric care compared to broad-spectrum micronutrient treatment: Literature review and case study of adult psychosis. *International Journal of Mental Health Systems*, *11*(1), 14. https://doi.org/10.1186/s13033-017-0122-x

Kaplan, B. J., & Leung, B. (2011). Multi-micronutrient supplementation for the treatment of psychiatric symptoms. *Integrative Medicine: A Clinician's Journal*, *10*(3).

Kaplan, B. J., Rucklidge, J., Romijn, A., & Dolph, M. (2015). A randomized trial of nutrient supplements to minimize psychological stress after a natural disaster. *Psychiatry Research*, *228*(3), 373–379. http://ac.els-cdn.com/S0165178115003935/1-s2.0-S0165178115003935-main.pdf?_tid=a6528ac4-b83a-11e6-8d2c-00000aab0f6c&acdnat=1480647452_07c0d1a05c43c6b64e66dd72b5633b7c

Kaplan, B. J., Rucklidge, J. J., Romijn, A., & McLeod, K. (2015). The emerging field of nutritional mental health: Inflammation, the microbiome, oxidative stress, and mitochondrial function. *Clinical Psychological Science*, *3*(6), 964–980. https://doi.org/10.1177/2167702614555413

Kaplan, B. J., & Shannon, S. (2007). Nutritional aspects of child and adolescent psychopharmacology. *Pediatric Annals*, *36*(9), 600–609. https://doi.org/10.3928/0090-4481-20070901-11

Kaplan, B. J., Simpson, J. S., Ferre, R. C., Gorman, C. P., McMullen, D. M., & Crawford, S. G. (2001). Effective mood stabilization with a chelated mineral supplement: An open-label trial in bipolar disorder. *Journal of Clinical Psychiatry*, *62*(12), 936–944. https://doi.org/10.4088/JCP.v62n1204

Karp, G. (2012). *Cell and molecular biology: Concepts and experiments*. John Wiley.

Lee-Kwan, S. H., Moore, L. V., Blanck, H. M., Harris, D. M., & Galuska, D. (2017). Disparities in state-specific adult fruit and vegetable consumption - United States, 2015. *MMWR: Morbidity and Mortality Weekly Report*, *66*(45), 1241–1247. https://doi.org/10.15585/mmwr.mm6645a1

Leonard, W. R., Robertson, M. L., Snodgrass, J. J., & Kuzawa, C. W. (2003). Metabolic correlates of hominid brain evolution. *Comparative Biochemistry and Physiology. Part A: Molecular and Integrative Physiology*, *136*(1), 5–15. https://doi.org/10.1016/s1095-6433(03)00132-6

Li, C., Miles, T., Shen, L., Shen, Y., Liu, T., Zhang, M., Li, S., & Huang, C. (2018). Early-life exposure to severe famine and subsequent risk of depressive symptoms in late adulthood: The China health and retirement longitudinal study. *British Journal of Psychiatry*, *213*(4), 579–586. https://doi.org/10.1192/bjp.2018.116

Li, Y., Lv, M. R., Wei, Y. J., Sun, L., Zhang, J. X., Zhang, H. G., & Li, B. (2017). Dietary patterns and depression risk: A meta-analysis. *Psychiatry Research*, *253*, 373–382. https://doi.org/10.1016/j.psychres.2017.04.020

Loewen, O. K., Maximova, K., Ekwaru, J. P., Asbridge, M., Ohinmaa, A., & Veugelers, P. J. (2020). Adherence to life-style recommendations and attention-deficit/hyperactivity disorder: A population-based study of children aged 10 to 11 years. *Psychosomatic Medicine*, *82*(3), 305–315. https://doi.org/10.1097/PSY.0000000000000787

Loewen, O. K., Maximova, K., Ekwaru, J. P., Faught, E. L., Asbridge, M., Ohinmaa, A., & Veugelers, P. J. (2019). Lifestyle behavior and mental health in early adolescence. *Pediatrics*, *143*(5), e20183307. https://doi.org/10.1542/peds.2018-3307

Ly, V., Bottelier, M., Hoekstra, P. J., Arias Vasquez, A., Buitelaar, J. K., & Rommelse, N. N. (2017). Elimination diets' efficacy and mechanisms in attention deficit hyperactivity disorder and autism spectrum disorder. *European Child and Adolescent Psychiatry*, *26*(9), 1067–1079. https://doi.org/10.1007/s00787-017-0959-1

Mao, W., Schuler, M. A., & Berenbaum, M. R. (2015). A dietary phytochemical alters caste-associated gene expression in honey bees. *Science Advances*, *1*(7), e1500795. https://doi.org/10.1126/sciadv.1500795

Marles, R. J. (2017). Mineral nutrient composition of vegetables, fruits and grains: The context of reports of apparent historical declines. *Journal of Food Composition and Analysis*, *56*, 93–103. https://doi.org/10.1016/j.jfca.2016.11.012

Martinez, A., & Al-Ahmad, A. J. (2019). Effects of glyphosate and aminomethylphosphonic acid on an isogeneic model of the human blood-brain barrier. *Toxicology Letters*, *304*, 39–49. https://doi.org/10.1016/j.toxlet.2018.12.013

Masi, G., Fantozzi, P., Muratori, P., Bertolucci, G., Tacchi, A., Villafranca, A., Pfanner, C., & Cortese, S. (2020). Emotional dysregulation and callous unemotional traits as possible predictors of short-term response to methylphenidate monotherapy in drug-naive youth with ADHD. *Comprehensive Psychiatry*, *100*, 152178. https://doi.org/10.1016/j.comppsych.2020.152178

Mathee, K., Cickovski, T., Deoraj, A., Stollstorff, M., & Narasimhan, G. (2020). The gut microbiome and neuropsychiatric disorders: Implications for attention deficit hyperactivity disorder (ADHD). *Journal of Medical Microbiology*, *69*(1), 14–24. https://doi.org/10.1099/jmm.0.001112

McCann, J. C., & Ames, B. N. (2009). Vitamin K, an example of triage theory: Is micronutrient inadequacy linked to diseases of aging? *American Journal of Clinical Nutrition*, *90*(4), 889–907.

McNamara, R. K., & Carlson, S. E. (2006). Role of omega-3 fatty acids in brain development and function: Potential implications for the pathogenesis and prevention of psychopathology. *Prostaglandins, Leukotrienes and*

Essential Fatty Acids, *75*(4–5), 329–349. https://doi.org/10.1016/j.plefa.2006.07.010

McVey Neufeld, K. A., Luczynski, P., Seira Oriach, C., Dinan, T. G., & Cryan, J. F. (2016). What's bugging your teen?-The microbiota and adolescent mental health. *Neuroscience and Biobehavioral Reviews*, *70*, 300–312. https://doi.org/10.1016/j.neubiorev.2016.06.005

Mehl-Madrona, L., Leung, B., Kennedy, C., Paul, S., & Kaplan, B. J. (2010). Micronutrients versus standard medication management in autism: A naturalistic case-control study. *Journal of Child and Adolescent Psychopharmacology*, *20*(2), 95–103. https://doi.org/10.1089/cap.2009.0011

Mehl-Madrona, L., & Mainguy, B. (2017). Adjunctive treatment of psychotic disorders with micronutrients. *Journal of Alternative and Complementary Medicine*, *23*(7), 526–533. https://doi.org/10.1089/acm.2016.0215

Mohn, E. S., Kern, H. J., Saltzman, E., Mitmesser, S. H., & McKay, D. L. (2018). Evidence of drug-nutrient interactions with chronic use of commonly prescribed medications: An update. *Pharmaceutics*, *10*(1), 36. https://doi.org/10.3390/pharmaceutics10010036

Moubarac, J. C., Batal, M., Louzada, M. L., Martinez Steele, E., & Monteiro, C. A. (2017). Consumption of ultra-processed foods predicts diet quality in Canada. *Appetite*, *108*, 512–520. https://doi.org/10.1016/j.appet.2016.11.006

Nanri, A., Mizoue, T., Poudel-Tandukar, K., Noda, M., Kato, M., Kurotani, K., Goto, A., Oba, S., Inoue, M., & Tsugane, S., & Japan Public Health Center-based Prospective Study, G. (2013). Dietary patterns and suicide in Japanese adults: The Japan public health center-based prospective study. *British Journal of Psychiatry*, *203*(6), 422–427.

Nigg, J. T., Lewis, K., Edinger, T., & Falk, M. (2012). Meta-analysis of attention-deficit/hyperactivity disorder or attention-deficit/hyperactivity disorder symptoms, restriction diet, and synthetic food color additives [doi:10.1016/j.jaac.2011.10.015]. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(1), 86–97 e88. https://doi.org/10.1016/j.jaac.2011.10.015

O'Neil, A., Quirk, S. E., Housden, S., Brennan, S. L., Williams, L. J., Pasco, J. A., Berk, M., & Jacka, F. N. (2014). Relationship between diet and mental health in children and adolescents: A systematic review. *American Journal of Public Health*, *104*(10), e31–42. https://doi.org/10.2105/AJPH.2014.302110

Opie, R. S., O'Neil, A., Itsiopoulos, C., & Jacka, F. N. (2015). The impact of whole-of-diet interventions on depression and anxiety: A systematic review of randomised controlled trials. *Public Health Nutrition*, *18*(11), 2074–2093. https://doi.org/10.1017/S1368980014002614

Opie, R. S., O'Neil, A., Jacka, F., Pizzinga, J., & Itsiopoulos, C. (2018). A modified Mediterranean dietary intervention for adults with major depression: Dietary protocol and feasibility data from the SMILES trial. *Nutritional Neuroscience*, *21*(7), 487–501. https://doi.org/10.1080/1028415X.2017.1312841

Opie, R. S., Segal, L., Jacka, F. N., Nicholls, L., Dash, S., & Pizzinga, J. (2015). Assessing healthy diet affordability in a cohort with major depressive disorder. *Journal of Public Health Epidemiology*, *7*. https://doi.org/10.5897/jphe2014.0668

Parletta, N., Zarnowiecki, D., Cho, J., Wilson, A., Bogomolova, S., Villani, A., Itsiopoulos, C., Niyonsenga, T., Blunden, S., Meyer, B., Segal, L., Baune, B. T., & O'Dea, K. (2019). A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). *Nutritional Neuroscience*, *22*(7), 474–487. https://doi.org/10.1080/1028415X.2017.1411320

Pauling, L. (1968). Orthomolecular psychiatry. *Science*, *160* (3825), 265–271. https://doi.org/10.1126/science.160.3825.265

Paxton, A. E., Strycker, L. A., Toobert, D. J., Ammerman, A. S., & Glasgow, R. E. (2011). Starting the conversation performance of a brief dietary assessment and intervention tool for health professionals. *American Journal of Preventive Medicine*, *40*(1), 67–71. https://doi.org/10.1016/j.amepre.2010.10.009

Phillips, J. G. P. (1910). The treatment of melancholia by the lactic acid bacillus. *British Journal of Psychiatry*, *56*(234), 422-NP.

Popper, C. (2001). Do vitamins or minerals (apart from lithium) have mood-stabilising effects? *Journal of Clinical Psychiatry*, *62*(12), 933–935. http://www.psychiatrist.com/JCP/article/_layouts/ppp.psych.controls/BinaryViewer.ashx?Article=/jcp/article/pages/2001/v62n12/v62n1203.aspx&Type=Article

Popper, C., Kaplan, B. J., & Rucklidge, J. J. (2017). Single and broad-spectrum micronutrient treatments in psychiatry practice. In P. L. Gerbarg, P. R. Muskin, & R. P. Brown (Eds.), *Complementary and integrative treatments in psychiatric practice* (pp. 75–104). American Psychiatric Association Publishing.

Rios-Hernandez, A., Alda, J. A., Farran-Codina, A., Ferreira-Garcia, E., & Izquierdo-Pulido, M. (2017). The Mediterranean diet and ADHD in children and adolescents. *Pediatrics*, *139*(2), e20162027. https://doi.org/10.1542/peds.2016-2027

Robertson, R. C., Seira Oriach, C., Murphy, K., Moloney, G. M., Cryan, J. F., Dinan, T. G., Paul Ross, R., & Stanton, C. (2017). Omega-3 polyunsaturated fatty acids critically regulate behaviour and gut microbiota development in adolescence and adulthood. *Brain, Behavior, and Immunity*, *59*, 21–37. https://doi.org/10.1016/j.bbi.2016.07.145

Rodway, M., Vance, A., Watters, A., Lee, H., Bos, E., & Kaplan, B. J. (2012). Efficacy and cost of micronutrient treatment of childhood psychosis. *BMJ Case Reports*, 10.1136/bcr-2012-007213. https://doi.org/10.1136/bcr-2012-007213

Rucklidge, J. J. (2019). 20.1 micronutrients for emotional dysregulation in children. *Journal of the American Academy of Child and Adolescent Psychiatry*, *58*(10), S329. https://doi.org/10.1016/j.jaac.2019.07.773

Rucklidge, J. J., Andridge, R., Gorman, B., Blampied, N., Gordon, H., & Boggis, A. (2012). Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses. *Human Psychopharmacology*, *27*(5), 440–454. https://doi.org/10.1002/hup.2246

Rucklidge, J. J., Eggleston, M. J. F., Boggis, A., Darling, K., Gorman, B., & Frampton, C. M. (2019). Do changes in blood nutrient levels mediate treatment response in children and adults with ADHD consuming a vitamin-mineral supplement? *Journal of Attention Disorders*, 1087054719886363. https://doi.org/10.1177/1087054719886363

Rucklidge, J. J., Eggleston, M. J. F., Darling, K. A., Stevens, A. J., Kennedy, M. A., & Frampton, C. M. (2019). Can we predict treatment response in children with ADHD to a vitamin-mineral supplement? An investigation into pre-treatment nutrient serum levels, MTHFR status, clinical correlates and demographic variables. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *89*, 181–192. https://doi.org/10.1016/j.pnpbp.2018.09.007

Rucklidge, J. J., Eggleston, M. J. F., Ealam, B., Beaglehole, B., & Mulder, R. T. (2019). An observational preliminary study on the safety of long-term consumption of micronutrients for the treatment of psychiatric symptoms. *Journal of Alternative and Complementary Medicine*, *25*(6), 613–622. https://doi.org/10.1089/acm.2018.0352

Rucklidge, J. J., Eggleston, M. J. F., Johnstone, J. M., Darling, K., & Frampton, C. M. (2018). Vitamin-mineral treatment improves aggression and emotional regulation in children with ADHD : A fully blinded, randomized, placebo-controlled trial. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *59*(3), 232–246. https://doi.org/10.1111/jcpp.12817

Rucklidge, J. J., Frampton, C. M., Gorman, B., & Boggis, A. (2014). Vitamin-mineral treatment of attention-deficit hyperactivity disorder in adults: Double-blind randomised placebo-controlled trial. *British Journal of Psychiatry*, *204*(4), 306–315. https://doi.org/10.1192/bjp.bp.113.132126

Rucklidge, J. J., Frampton, C. M., Gorman, B., & Boggis, A. (2017). Vitamin-mineral treatment of ADHD in adults: A 1-year naturalistic follow-up of a randomized controlled trial. *Journal of Attention Disorders*, *21*(6), 522–532. https://doi.org/10.1177/1087054714530557

Rucklidge, J. J., Gately, D., & Kaplan, B. J. (2010). Database analysis of children and adolescents with bipolar disorder consuming a micronutrient formula. *BMC Psychiatry*, *10*(1), 74. https://doi.org/10.1186/1471-244X-10-74

Rucklidge, J. J., Harris, A., & Shaw, I. (2014). Are the amounts of vitamins in commercially available dietary supplement formulations relevant for the management of psychiatric disorders in children? *New Zealand Medical Journal*, *127*(1392), 73–85. https://www.ncbi.nlm.nih.gov/pubmed/24806250

Rucklidge, J. J., Johnstone, J., Gorman, B., Boggis, A., & Frampton, C. M. (2014). Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *50*, 163–171. https://doi.org/10.1016/j.pnpbp.2013.12.014

Rucklidge, J. J., Johnstone, J., & Kaplan, B. J. (2009). Nutrient supplementation approaches in the treatment of ADHD. *Expert Review of Neurotherapeutics*, *9*(4), 461–476. https://doi.org/10.1586/ern.09.7

Rucklidge, J. J., Taylor, M., & Whitehead, K. (2011). Effect of micronutrients on behavior and mood in adults with ADHD: Evidence from an 8-week open label trial with natural extension. *Journal of Attention Disorders*, *15*(1), 79–91. https://doi.org/10.1177/1087054709356173

Sanchez-Villegas, A., Delgado-Rodriguez, M., Alonso, A., Schlatter, J., Lahortiga, F., Serra Majem, L., & Martinez-Gonzalez, M. A. (2009). Association of the Mediterranean dietary pattern with the incidence of depression: The Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. *Archives of General Psychiatry*, *66*(10), 1090–1098. https://doi.org/10.1001/archgenpsychiatry.2009.129

Sarris, J., Mischoulon, D., & Schweitzer, I. (2011). Adjunctive nutraceuticals with standard pharmacotherapies in bipolar disorder: A systematic review of clinical trials. *Bipolar Disord*, *13*(5–6), 454–465. https://doi.org/10.1111/j.1399-5618.2011.00945.x

Schab, D. W., & Trinh, N. H. (2004). Do artificial food colors promote hyperactivity in children with hyperactive syndromes? A meta-analysis of double-blind placebo-controlled trials. *Journal of Developmental and Behavioral Pediatrics*, *25*(6), 423–434. http://ovidsp.tx.ovid.com/ovftpdfs/FPDDNCDCJECMCN00/fs047/ovft/live/gv031/00004703/00004703-200412000-00007.pdf

Schoenthaler, S., Amos, S., Doraz, W., Kelly, M.-A., Muedeking, G., Wakefield, J., Amos, S., Doraz, W., Kelly, M.-A., Muedeking, G., Wakefield, J., Doraz, W., Kelly, M.-A., Muedeking, G., Wakefield, J., Kelly, M.-A., Muedeking, G., Wakefield, J., Muedeking, G., Wakefield, J., & Wakefield, J. (1997). The effect of randomized vitamin-mineral supplementation on violent and non-violent antisocial behavior among incarcerated juveniles. *Journal of Nutritional and Environmental Medicine*, *7*(4), 343–352. https://doi.org/10.1080/13590849762475

Schoenthaler, S., & Bier, I. (2000). The effect of vitamin-mineral supplementation on juvenile delinquency among American schoolchildren: A randomized, double-blind placebo-controlled trial. *Journal of Alternative and Complementary Medicine*, *6*(1), 7–17. https://www.liebertpub.com/doi/abs/10.1089/acm.2000.6.7

Simpson, S., Crawford, S., Goldstein, E., Field, C., Burgess, E., & Kaplan, B. (2011). Systematic review of safety and tolerability of a complex micronutrient formula used in mental health. *BMC Psychiatry*, *11*(1), 62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3094286/pdf/1471-244X-11-62.pdf

Steenweg-de Graaff, J., Tiemeier, H., Steegers-Theunissen, R. P., Hofman, A., Jaddoe, V. W., Verhulst, F. C., & Roza, S. J. (2014). Maternal dietary patterns during pregnancy and child internalising and externalising problems.

The generation R study. *Clinical Nutrition*, *33*(1), 115–121. https://doi.org/10.1016/j.clnu.2013.03.002

Stevens, A. J., Purcell, R. V., Darling, K. A., Eggleston, M. J. F., Kennedy, M. A., & Rucklidge, J. J. (2019). Human gut microbiome changes during a 10 week Randomised Control Trial for micronutrient supplementation in children with attention deficit hyperactivity disorder. *Scientific Reports*, *9*(1), 10128. https://doi.org/10.1038/s41598-019-46146-3

Stevens, A. J., Rucklidge, J. J., Darling, K. A., Eggleston, M. J., Pearson, J. F., & Kennedy, M. A. (2018). Methylomic changes in response to micronutrient supplementation and MTHFR genotype. *Epigenomics*, *10*(9), 1201–1214. https://doi.org/10.2217/epi-2018-0029

Szopinska-Tokov, J., Dam, S., Naaijen, J., Konstanti, P., Rommelse, N., Belzer, C., Buitelaar, J., Franke, B., Aarts, E., & Arias Vasquez, A. (2020). Investigating the gut microbiota composition of individuals with attention-deficit/hyperactivity disorder and association with symptoms. *Microorganisms*, *8*(3), 406. https://doi.org/10.3390/microorganisms8030406

Tammam, J. D., Steinsaltz, D., Bester, D. W., Semb-Andenaes, T., & Stein, J. F. (2016). A randomised double-blind placebo-controlled trial investigating the behavioural effects of vitamin, mineral and n-3 fatty acid supplementation in typically developing adolescent schoolchildren. *British Journal of Nutrition*, *115*(2), 361–373. https://doi.org/10.1017/S0007114515004390

Tengeler, A. C., Dam, S. A., Wiesmann, M., Naaijen, J., van Bodegom, M., Belzer, C., Dederen, P. J., Verweij, V., Franke, B., Kozicz, T., Arias Vasquez, A., & Kiliaan, A. J. (2020). Gut microbiota from persons with attention-deficit/hyperactivity disorder affects the brain in mice. *Microbiome*, *8*(1), 44. https://doi.org/10.1186/s40168-020-00816-x

Tenore, G. C., Daglia, M., Orlando, V., D'Urso, E., Saadat, S. H., Novellino, E., Nabavi, S. F., & Nabavi, S. M. (2015). Coffee and Depression: A Short Review of Literature. *Current Pharmaceutical Design*, *21*(34), 5034–5040. https://doi.org/10.2174/1381612821666150825145112

Thys-Jacobs, S., Starkey, P., Bernstein, D., & Tian, J. (1998). Calcium carbonate and the premenstrual syndrome: Effects on premenstrual and menstrual symptoms. Premenstrual syndrome study group. *American Journal of Obstetrics and Gynecology*, *179*(2), 444–452. https://doi.org/10.1016/S0002-9378(98)70377-1

Valles-Colomer, M., Falony, G., Darzi, Y., Tigchelaar, E. F., Wang, J., Tito, R. Y., Schiweck, C., Kurilshikov, A., Joossens, M., Wijmenga, C., Claes, S., Van Oudenhove, L., Zhernakova, A., Vieira-Silva, S., & Raes, J. (2019). The neuroactive potential of the human gut microbiota in quality of life and depression. *Nature Microbiology*, *4*(4), 623–632. https://doi.org/10.1038/s41564-018-0337-x

Valzelli, L. (1984). Reflections on experimental and human pathology of aggression. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *8*(3), 311–325. https://www.ncbi.nlm.nih.gov/pubmed/6385139

van der Burg, K., Cribb, L., Firth, J., Karmacoska, D., & Sarris, J. (2019). Nutrient and genetic biomarkers of nutraceutical treatment response in mood and psychotic disorders: A systematic review. *Nutritional Neuroscience*, 1–17. https://doi.org/10.1080/1028415X.2019.1625222

Walsh, R. (2011). Lifestyle and mental health. *American Psychologist*, *66*(7), 579–592. https://doi.org/10.1037/a0021769

West, A. E., Celio, C. I., Henry, D. B., & Pavuluri, M. N. (2011). Child mania rating scale-parent version: A valid measure of symptom change due to pharmacotherapy. *Journal of Affective Disorders*, *128*(1–2), 112–119. https://doi.org/10.1016/j.jad.2010.06.013

Young, L., Pipingas, A., White, D., Gauci, S., & Scholey, A. (2019). A systematic review and meta-analysis of B vitamin supplementation on depressive symptoms, anxiety, and stress: Effects on healthy and 'At-Risk' individuals. *Nutrients*, *11*(9), 2232. https://www.mdpi.com/2072-6643/11/9/2232

Zaalberg, A., Nijman, H., Bulten, E., Stroosma, L., & van der Staak, C. (2010). Effects of nutritional supplements on aggression, rule-breaking, and psychopathology among young adult prisoners. *Aggressive Behavior*, *36*(2), 117–126. https://doi.org/10.1002/ab.20335

Zhu, C., Kobayashi, K., Loladze, I., Zhu, J., Jiang, Q., Xu, X., Liu, G., Seneweera, S., Ebi, K. L., Drewnowski, A., Fukagawa, N. K., & Ziska, L. H. (2018). Carbon dioxide (CO2) levels this century will alter the protein, micronutrients, and vitamin content of rice grains with potential health consequences for the poorest rice-dependent countries. *Science Advances*, *4*(5), eaaq1012. https://doi.org/10.1126/sciadv.aaq1012

Zobiole, L. H., Oliveira, R. S., Visentainer, J. V., Kremer, R. J., Bellaloui, N., & Yamada, T. (2010). Glyphosate affects seed composition in glyphosate-resistant soybean. *Journal of Agricultural and Food Chemistry*, *58*(7), 4517–4522. https://doi.org/10.1021/jf904342t