Neuronutrition in the perspective of the prevention and treatment of depressive disorder

Neuronutrição na perspectiva da prevenção e tratamento da desordem depressiva

DOI:10.34119/bjhrv4n3-217

Recebimento dos originais: 08/05/2021
Aceitação para publicação: 08/06/2021

Maiana de Oliveira Guedes
Nutrição – Instituto Multidisciplinar em Saúde. Universidade Federal da Bahia-IMS/UFBA.
E-mail: maianahguedes@gmail.com

Amanda Gilvani Cordeiro Matias
Doutorado em Medicina e Saúde. Docente adjunto III no Instituto Multidisciplinar em Saúde. Universidade Federal da Bahia-IMS/UFBA.
E-mail: amathias.ufba@gmail.com

ABSTRACT
The father of medicine was a pioneer in suggesting the healing power of food nutrients, however it took a long time for science to recognize that food has functional properties and the ability to interfere with mood and brain health. Currently, neuroscience is showing research results, demonstrating the effectiveness of nutritional bioactive compounds with neuroprotective potential. Some metabolic changes are the basis of common neuropsychiatric diseases, such as depressive disorder, characterized by mood dysregulation, cognitive dysfunction, sleep disorders, appetite, fatigue and metabolic or inflammatory changes. Objective: to describe the potential of dietary and bioactive nutrients that interfere in the neurobiology of depressive disorder. Methodology: This is a systematic review, stratified in a time window of 2012-2021. As a search criterion for the articles, a guiding question was formulated: how does the relationship between food nutrition and its potential connections in the neurobiology of depression appear? DesCs-MESH indexes were pre-established in the English language: food nutrition, bioactive, neurobiology depressive disorders, in the vernacular: food nutrition, brain, bioactive, depressive disorder, allied to Boolean operators, to the StArt resource, to exclude duplicate manuscripts. Results: This short-review included 31 articles that met the criteria and demonstrated nutritional bioactivity involved in the neurobiological process of depressive disorder. Conclusion: the connection between diet and depression emerges with promising perspectives when demonstrating the potential of nutrients and bioactive with a neuroprotective effect. The clinical approach combined with the diet designed to produce antidepressant effects can work as an adjunct to the treatment and prevention of depressive symptoms.

Keywords: food nutrition, bioactive, neurobiology, depressive disorder
RESUMO
O pai da medicina foi pioneiro a sugerir o poder curativo dos nutrientes alimentares, todavia demorou muito tempo para que a ciência reconhecesse que os alimentos tem propriedades funcionais e, capacidade de interferir no estado de humor e na saúde do cérebro. Atualmente a neurociência desponta resultados de pesquisas, demonstrado a efetividade de compostos bioativos nutricionais com potencial neuroprotetor. Algumas alterações metabólicas estão na base de doenças neuropsiquiátricas comuns, como o transtorno depressivo, caracterizado pela desarregulação do humor, disfunção cognitiva, distúrbios do sono, do apetite, fadiga e alterações metabólicas ou inflamatórias. Objetivo: descrever sobre o potencial de nutrientes alimentares e bioativos que interferem na neurobiologia do transtorno depressivo. Metodologia: Trata-se de uma revisão sistematizada, estratificada numa janela temporal de 2012-2021. Como critérios de busca dos artigos, formulou-se uma pergunta norteadora: como se apresenta a relação da nutrição alimentar e suas conexões potenciais na neurobiologia da depressão? Foram pré-estabelecidos indexadores DesCs-MESH na língua inglesa: food nutrition, bioactive, neurobiology depressive disorders, na língua vernácula: nutrição alimentar, encéfalo, bioativos, transtorno depressivo, aliados aos operadores booleanos, recurso StArt, para excluir manuscritos em duplicidade. Resultados: Foram inclusos nesta short-review 31 artigos que atenderam aos critérios e, demonstraram bioatividade nutricional interveniente no processo neurobiológico do transtorno depressivo. Conclusão: a conexão entre dieta e depressão, desponta-se com perspectivas promissoras ao demonstrarem o potencial de nutrientes e bioativos com efeito neuroprotetor. A abordagem clínica aliada à dieta planejada para produzir efeitos antidepressivos podem funcionar como coadjuvante para o tratamento e prevenção de sintomas depressivos.

Palavras-chave: nutrição alimentar, bioativos, neurobiologia, transtorno depressivo.

1 INTRODUCTION
The benefits of nutrition for human health have been appreciated since time immemorial. Hippocrates, the father of medicine, around 400 B.C., described: that food be your medicine and medicine be your food. Being corroborated by the prominent philosopher and physician Maimonides Moisés who wrote in the sec. XII: any disease that can be treated through diet, must be treated by no other means. Currently, there are researchers in the field of human health that reverberate results of studies on neuronutrition, such as functional foods and antioxidants, bioactive compounds capable of acting in the prevention and treatment of neurological diseases, brain and mental health (POPA & LADEA, 2012; ROSS, 2018; TSAI & HUANG, 2016).

For the same authors, food nutrition plays an important role in the structural and functional development of the brain. In addition to the metabolic programming that induces nutrition from the fetal age and other stages of human life, aiming at the healthy development of the body, brain and mind. However, nutritional deficiency at any age works as a risk factor for diseases that include neuropsychiatric diseases. Studies have shown the importance of
adequate nutrition for neurodevelopment processes during pregnancy and childhood, as a special phase of neuron proliferation and myelination, especially to avoid permanent cognitive deficits (ADAN et al., 2019; SARRIS, 2019).

Among psychiatric diseases, depressive disorder (DD), has received notable attention from researchers, regarding the connection of neurobiological and nutritional factors. In the field of neuropsychiatry, especially in recent decades, there has been an increase in the number of investigations on the role of food, which, in addition to the crucial role for physical nutrition, plays an extraordinary role in the mental health of individuals. Bearing in mind that, DD, for example, is a neuropsychiatric condition that has a close relationship with the nutritional quality of the diet (ADAN et al., 2019; SARRIS, 2019).

Major depressive disorder (MDD) is one of the most common psychiatric illnesses in the world and highly disabling. It affects people of all ages and is predominant in women and individuals aged 50-74 years. Epidemiological evidence has accumulated in recent decades on the impact of DD on structural, functional and mental processes. Although there are classes of antidepressant chemical drugs, side effects are associated, delay in remission of symptoms, even lack of response. The primordial theories justify that depression is caused by chemical imbalance in the brain, reverberating in the complex conjecture of neural networks and plasticity, whose therapeutic approach must be equally complex (MATIAS et al., 2016; MANOSSO et al., 2015).

The expansion of the concepts of depressive disease, allowed a better understanding of the neurobiological mechanisms, therapeutic and preventive interventions to mitigate the effects of this multifactorial disease. Like recent neuronutrition studies, which aim to understand the potential of chemical, bioactive compounds and food nutrients, with the capacity to preserve, prevent and recover brain health and optimize quality of life, especially in neuropsychiatric conditions (ADAN et al., 2019; MATIAS et al., 2016).

The growing evidence suggests that ensuring a quality diet in the face of nutritional deficiencies has a differential in the treatment of neuropsychiatric disorders. Allopathic therapy is important, but the challenges of costly and complicated drug interactions, adverse effects and the possibility of adaptations to the drug and addiction still persist. Thus, researchers in the field of public health are alert to bioactive nutritional viability, as an adjunct alternative for the prevention and treatment of neurobiological disorders (POPA & LADEA, 2012; ADAN et al., 2019).
The functioning, structural and functional composition of the brain depends on the availability of adequate nutrients, such as lipids, amino acids, vitamins and minerals, in a balanced way (LEPINAY et al., 2015). Therefore, the intake of bioactive foods of nutritional quality, have an impact on the functioning of the brain, this makes the diet a target for maintaining balance, being a modifiable variable to achieve mental health and good neurocognitive performance (SANDHU et al., 2017; SARRIS, 2019).

The absence of a mechanistic understanding of eating disorders and their neurobiological connections has frustrated efforts to develop more effective and evidence-based interventions on neurobiology, depressive neuropsychiatric disorders and the potential of diet. Changes in the brain circuit linked to reward and inhibition, in particular, appear to be involved in maladaptive eating behavior and neuropsychological endocrine disorders.

In this context, the objective of this short review is to describe the potential of dietary and bioactive nutrients that interfere in the neurobiology of depressive disorder.

2 METHODOLOGY

This research is characterized by a systematic review, using pre-established search criteria to identify original articles in the SciELO, Science Direct and PubMed/NCBI databases, considering the article filter, in 2012-2021, time window, whose search took place from February to April 2021.

The inclusion criteria were: articles should have results from experimental research in vivo or in vitro, randomized clinical trials (RCTs), cohort study and meta-analyses, on the neurobiology of depressive disorder, its connection with neuronutrition or food or supplemental bioactives.

The search strategy for the articles was based on specific descriptors in the English language, with the terms: food nutrition, brain, neurobiology, neuro-nutritions, depressive disease and, in the vernacular language: food nutrition, neurobiology, phytochemicals, neurotransmitters, linking operators boolean “and/or” to minimize excess results. In addition, the State of the Art through Systematic Review (StArt) specificity system was used to identify duplicate manuscripts.

Then, the limitations of the articles and possible inconsistencies of the results (heterogeneity), mode of intervention and comparison, inaccuracies and publication biases were evaluated. The pre-established criteria were previously submitted to the guiding
question of the study: What is neurobiology, its connection and responses to the phytochemical compounds of food nutrients, in neuropsychiatric conditions?

During the search and reading stages, in parallel, the analysis of the titles was carried out, removal of duplicates by StArt, of abstracts, of the methodology, then the full articles to be included in the review were selected, in view of the prerogative of the question, guiding principle and pre-established criteria.

3 RESULTS

From the selected manuscripts, thirty-one published scientific documents were identified, which met the pre-established inclusion criteria. The next steps were the evaluation of the title and abstracts, which resulted in the selection of only 58 articles related to research on neuronutrition and depressive disorder in this step, after which the methodology and results of the manuscripts were read and evaluated, with 12 articles being excluded due to duplication, or didn't meet the criteria of this study. Finally, there are a total of 31 articles selected to support and contextualize this research, according to the flowchart below.

Figure 1 - Flowchart of the main articles that respond to the methodology and the pre-established criteria, researched in March and April 2021.

Source: Flowchart of the search phases of the manuscripts (prepared by the authors).

Some of the main manuscripts selected in the databases, SiELO, ScienceDirect and National Center for Biotechnology Information NCBI / PUBMED, were highlighted, which met the eligibility criteria and which directly answer the guiding question, which are correlated in Table 1, summarizing the drawing methodology of the articles, outcome and potential.
Chart 1: main selected manuscripts that present potential results of neuroprotective nutrients and bioactive and modulators.

<table>
<thead>
<tr>
<th>Author/Date</th>
<th>Study Design</th>
<th>Results and Potentials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imran et al., 2021</td>
<td>Experimental with models</td>
<td>There was a reduction in anxiolytic behavior in the central area of the brain (p&lt;0.05) and antidepressant activity (p&lt;0.05). Significant increase in SOD and GPx levels (p&lt;0.05), reduction in AChE and MDA (p&lt;0.05). Effects of G.asiatica on the improvement of neurological disorders.</td>
</tr>
<tr>
<td>Ghaleiha et al., 2016</td>
<td>RCT, controlled, double-blind</td>
<td>There were significant and positive results in the thiamine test group, capable of relieving (DS) quickly, free of adverse effects, compared to the control. Thiamine showed antidepressant and time-neutralizing potential.</td>
</tr>
<tr>
<td>Grosso et al., 2015</td>
<td>Meta-analysis of RCTs</td>
<td>Significant clinical efficacy was obtained with the use of omega-3, as an adjunct to treatment. Omega-3 PUFA has been shown to be effective in decreasing DS. Anti-inflammatory compounds, omega-3 polyunsaturated fatty acids in a combined diet, can work as antidepressants.</td>
</tr>
<tr>
<td>Kaner et al., 2015</td>
<td>RCT, controlled, 59 people</td>
<td>Individuals with depression had low serum levels of vitamin B, B12 and folic acid and measures of abdominal obesity.</td>
</tr>
<tr>
<td>Horikawa et al., 2018</td>
<td>Cohort follow-up, 2335 people</td>
<td>Intakes of EPA (243mg/day) and DHA (469mg/day) were effective in reducing DS in adults and the elderly. High fish consumption may be associated with low risk of DD.</td>
</tr>
<tr>
<td>Jacka et al., 2017</td>
<td>RCT, controlled, double-blind 166 people</td>
<td>Diet rich in grains, vegetables, fruits, nuts, eggs, fish, chicken, free of sugars, showed significant improvement in depressive symptoms, in relation to the control (t(60.7)=4.38, p&lt;0.001, T.Cohen:1.16.</td>
</tr>
<tr>
<td>Knippenberg et al., 2014</td>
<td>RCT prospective 2-3 anos</td>
<td>Sun exposure was inversely associated with depression scores (β-0.26 (95% CI-0.40-0.12), p≤ 0.001). High levels of sun exposure, instead of 25 (OH) D levels, were effective in reducing DS.</td>
</tr>
<tr>
<td>Manosso et al., 2015</td>
<td>Controlled experiment. Animal model</td>
<td>Spinach extract was able to reduce depressive behavior and serum corticosterone levels in mice. Increased levels of glutamate and glutamine in the prefrontal cortex, antidepressant effect.</td>
</tr>
<tr>
<td>Son et al., 2018</td>
<td>Controlled experiment. Animal model</td>
<td>Regular consumption of sugary drinks is associated with depression among women (OR1.27; 95% CI: 1.10-1.48). While the sugar-restricted diet has beneficial potential in cases of depression.</td>
</tr>
<tr>
<td>Sousa et al., 2020</td>
<td>Cross-sectional cohort 46.785 people</td>
<td>Serum SOD and CAT activities in patients with depression were significantly higher than the control group, low serum levels of PCC (protein oxidation marker) were lower. There was an increase in SOD and CAT as indicators of acute depressive episodes.</td>
</tr>
<tr>
<td>Tsai &amp; Huang, 2016</td>
<td>RCT, controlled</td>
<td>Depressed patients had lower levels of vitamins A, C and. After dietary supplementation of these vitamins, there was a significant reduction in D, increase in serum levels of antioxidants (p&lt;0.05) except for vitamin E.</td>
</tr>
<tr>
<td>Yary et al., 2016</td>
<td>Cohort follow-up, 20-year</td>
<td>There was a significant reduction in anxiety p&lt;0.014 and depression p&lt;0.001. Diets with olive oil (ω-3) was able to reduce anxiety and DS in obese adults. Recommend integrated clinical approach to neuronutrition.</td>
</tr>
</tbody>
</table>

**ACHe**: Acetylcholinesterase; **Akt**: protein kinase; **BDNF**: Neurotrophic factor derived from the **CAT**: Catalase enzyme, **CaMKII**: Calcium-Calmodulin kinase II; **DHA**: docosahexaenoic acid; **RCT**: EPA randomized clinical trial; **Eicosapentaenoic acid; **ERK**: Protein kinases regulated by extracellular stimuli; **GBS-3B**: Glycogen synthase kinase 3 beta; **GPx**: Glutathione peroxidase; **MDA**: Malondialdehyde; **PI3K**: PI3B; **S**: Akt; **SOD**: Superoxide dismutase; **TST**: Total sleep time; **WBC**: White blood cells.
DISCUSSION

From the researched literature, it was possible to verify that there is evidence, with results of RCTs in vivo and in vitro, and meta-analyses, which substantiate the benefits of planned neuronutrition, for the treatment of neuropsychiatric disorders such as depression. Some nutrients can serve as preventive and palliative aids in cases of mental illness, mainly due to their antidepressant potential. They are alternatives that can be integrated into clinical treatment protocols for anxiety and depressive symptoms.

Neuronutrition refers to the nourishment necessary to achieve a healthy brain and good neurocognitive function, with dietary manipulations being a viable strategy to increase cognitive skills and protect the brain from damage. Lately, the study and use of nutrients in order to optimize health, prevent and treat some psychiatric disorders, has been recognized as neuronutrition, which aims to highlight potentials of bioactive food and how they affect brain functions (POPA & LADEA, 2012; ROSS, 2018).

Although the integrative neuronutritional approach is an emerging paradigm in neuropsychiatry and mental health, current evidence recognizes the concentric interface of nutrition, neurochemistry, brain functions and behavior. They corroborate that poor eating habits, nutrition and unbalanced metabolic mechanisms, are permeated by inflammation, microbiota imbalance, oxidative stress and impaired mitochondrial function, which plague brain function and, ultimately, mood and behavior (SOUSA et al., 2020; SANDHU et al., 2017).

The same authors explain that unhealthy eating habits are largely driven by substantial changes in the global food system, which somehow contribute to chronic non-communicable diseases and also function as risk factors for mental disorders, such as depression and dementia. Especially in recent decades, studies have demonstrated the association of diet and lifestyle with diseases such as cancer, cardiovascular and neuropsychiatric diseases that includes depressive disorder (DD).

The pathophysiology of depression and its interface with the diet have multifactorial influences, whether genetic, immunological, biochemical and neurodegenerative. The diet has a nutritive and modulating function for each of the factors, resulting in the impact of the processes and their development. Diet rich in vegetables, fruits, vegetables, grains, fish, olive oil and low-fat dairy products, is correlated with low levels of inflammatory markers, in
contrast to a diet rich in refined carbohydrates, sugars, which are associated with higher levels of C-reactive protein (ZAINUDDIN 2012; JACKA et al., 2017; SOUSA et al., 2020).

Primary metabolites such as vitamins, minerals, fatty acids and amino acids have well-established nutritional properties in the metabolic pathways. The proper combination of these nutrients has several palliative benefits for the treatment of neurological disorders. For example, fatty acids and their compounds, which improve the functioning of the brain and assist in the reduction of cholesterol present in the arteries, helping with lipid-lowering effects, say Souza et al., (2019); Zainuddin (2012); Lepinay et al. (2015). They corroborate that foods such as fatty acids (omega-3), flavonoids, red fruit antioxidants and resveratrol stimulate neurogenesis, are neuroprotective, reduce oxidative activity and regulate the pro-inflammatory process (IMRAN et al., 2021).

The challenge for nutritional psychiatry is to substantiate comprehensive, cohesive and scientifically rigorous evidence that defines the functioning of dietary nutrients in various aspects of mental health. Especially, the link between the body’s exposure to specific micro and macronutrients, food or supplement, (dependent on intake, bioavailability, metabolic function and tangled organic systems) and a wide range of mental health problems, such as stress and DD, involved in the mechanisms modulators of neuronal function and synaptic plasticity (ADAN et al., 2019; JACKA et al., 2017).

Some mechanisms of depression are already well recognized in the literature, about their association with defective antioxidant defenses, high levels of serum SOD, serum malondialdehyde (MDA), and reduced levels of plasma ascorbic acid and vitamin E. In this sense, the recognition of the role of nutrition for the treatment of people with DS, especially antioxidants, such as PUFA-omega-3, folic acid, vitamins B12, D, polyphenols, which are cofactors for enzymes, act in the inhibition of free radicals and minimize neurodegeneration processes (TSAI & HUANG 2016; JACKA et al., 2017).

It is worth mentioning a controlled RCT, which investigated patients with DD, anxiety and the difference in serum levels of antioxidants (vitamins A-β-carotene, C and). Comparing the control and test group, it was found that supplementation of adequate doses of vitamins was able to produce a reduction in DS. Antioxidant supplementation is useful for reducing stress-induced psychiatric disorders, with positive and significant results (p<0.05). As a recommended supporting therapeutic strategy, the authors state Gautam et al., (2012).

A growing base of evidence suggests that eating patterns may play an important tactic in the treatment and prevention of neuropsychiatric disorders. Nutritional guidelines for
preventing depression indicate that brain health and mental illness are affected by nutritional quality and its mechanisms. Nutrients such as long-chain omega-3 fatty acids, zinc, magnesium, promote the expression of the Brain Derived Neurotropic Factor (BDNF) and neuroplasticity. Nutrients are modifiable determinants of systemic inflammation, demonstrated by the neuroinflammatory hypothesis of DD (COWEN, 2016; LIU et al., 2017; BERK et al., 2020).

Depressive disorders are complex neurobiological conditions, associated with physiological and cognitive abnormalities. The large number of pathological features, identified lately, has stimulated the development of new theories, in an attempt to explain the triggering of clinical symptoms and dysfunctions. One of these most influential neurobiological perspectives is related to dysfunctions of monoaminergic neurotransmitters (serotonin, norepinephrine and dopamine), elucidating the need to enhance the activity of these monoamines (COWEN, 2016; KAVIANI et al., 2020).

The proinflammatory condition in individuals with DD exhibits elevated levels of circulating proinflammatory cytokines (IL-1 IT-6 interleukins, tumor necrosis factor alpha (TNF-a) and some soluble interleukin receptors (stimulate the hypothalamic-axis). pituitary-adrenal-HPA), participate in the innate immune response and inflammation, have important metabolic effects, neurotransmitters, neuroendocrine function and neural plasticity, such as the administration of IL-6, which induces depressive behaviors and neutralizes fluoxetine's antidepressant effect in animals experimental (LIU et al., 2017; BERK et al., 2020).

The compression of the interface between inflammation and depression has led to new questions and immunological investigations in depressed patients, requiring the development of more effective anti-inflammatory treatments (COWEN, 2016; LIU et al., 2017). The abnormalities of HPA continue to be a focus of interest, in the context of neuropsychiatric comorbidities that complicate chronic depression, perpetuated by pro-inflammatory dietary patterns, as explained by Firth et al., Berk et al.,

Recently, new compressions of depressive neurobiology embody the theory of neuroplasticity and stress, reinforced by environmental and dietary issues as etiopathogenic factors. Antidepressant drug therapy raises the hypothesis that inhibiting the reuptake of neurotransmitters is not, in itself, sufficient to establish desirable changes. The increasing prevalence of DD can involve complex conditions, such as the contemporary lifestyle, permeated by stress, physical inactivity, sleep deprivation, adoption of unhealthy dietary habits, which requires more elaborate therapies (LIU et al., 2017; SOUSA et al., 2020).
Depressive symptoms appear as depressed or irritable mood, decreased interest or pleasure, sleep and appetite disorders, agitation or psychomotor retardation, fatigue, loss of energy, feelings of worthlessness, guilt, decreased ability to concentrate, recurring thoughts of death, suicidal ideation, which lasted more than a week, according to the Statistical Diagnostic Manual of Mental Disorders (DSM-5). They also receive the International Classification of Mental and Behavioral Disorders (ICD-10), as a disease with psychic manifestation associated with neurobiological disorders and reduced brain health (MATIAS et al., 2016; BERK et al., 2020).

Neurobiological processes are responsible for metabolizing nutrients that protect brain cells, are necessary for the formation and maintenance of neurotransmitters, in turn, stimulate emotions, mood and concentration. The healthy brain works as a line of defense against anxiety, depression, energy and mood disorders. When deficiency of essential nutrients occurs, the brain's potential is affected, for example, niacin deficiency conditions dermatitis, diarrhea, dementia, depression, apathy, memory loss and other changes (KANER et al., 2015; FIRTH et al., 2019).

The decrease in the neurotransmitter called serotonin, has been associated with the presence of depressive symptoms, with premenstrual dysphoric disorder, aggressive behaviors and, correlated to the deficiency of B vitamins, minerals such as magnesium, the prohormone vitamin D. Another neurotransmitter that participates in emotional processes is norepinephrine, linked to anxiety, depression, sadness and, with the emotion of fear (YARY et al., 2016).

The interface between nutrients, supplementation and DS are supported by prospective and epidemiological research. Kaner et al., (2015), explain that the benefits of eating fish and olive oil, work as adjuvants in the treatment and prevention of DS. The diet rich in fish, nuts, vegetables and cereals were associated with the lowest disease severity score. In addition, it was found that the Mediterranean diet with these foods, moderate alcohol intake, low meat and dairy intake, had a protective effect against DS. However, the consumption of sweets, high consumption of fast food and processed cakes, was associated with greater risks for worsening symptoms (CANHETA et al., 2020; JACKA et.al., 2017; SOUSA et al., 2020).

A meta-analysis conducted by Grosso et al., 2015, found results from fourteen studies, comparing brain health and levels of omega-3 long-chain polyunsaturated fatty acids (PUFA), were recognized as essential in the diet to safeguard mental health. This sparked
the interest of researchers on the omega-3-6 series, fish oil, which contains high levels of EPA, as essential and beneficial nutrients in depressed patients.

Depressive disorder is a common and complex mental illness. There are several nutritional deficiencies that can interfere with brain health and trigger DS. The lack of iron and zinc minerals are the target of investigation, their bioactive play a fundamental role in neurodegenerative inflammatory pathways in depression. Low serum iron concentrations have been associated with cognitive decline (dementia, depression, memory loss), worsening nutritional status and increased risk for comorbidities (SHAFI et al., 2018; HORIKAWA et al., 2018).

Vitamin D deficiency, although common, is extremely important for the condition of the individual with TD. This pre-hormone has a relevant neurobiological protection and whose deficiency in plasma levels can impair the synthesis of dopamine and serotonin. According to the researchers, supplementation for eight weeks, dose: 50,000IU, is capable of significantly increasing serum concentrations of 25(OH) and reducing depressive symptoms (YOSAEE et al., 2020; KAVIANI et al., 2020).

An ECR analogue, assessed the level of anxiety in a group, which received a capsule with supplementation composed of L-tryptophan, omega 3, magnesium and B vitamins, showed a reduction in anxiety and DS. Magnesium stands out for the diversity of functions it performs in metabolic and enzymatic pathways of neurotransmitters that regulate mood. They concluded that supplementation has effective benefits and leads to a significant decrease in symptoms of depression and anxiety (YARY et al., 2016).

An experimental study with animal models, found that spinach extract was able to reduce the levels of corticosterone in the blood of mice and the induced depressive behavior, there was an increase in the levels of glutamate and glutamine in the prefrontal cortex compared to the control. They concluded that the spinach extract has antidepressant properties and is even considered a “superfood” containing compounds such minerals, vitamins A, B, C, D, E K, folate, lecithin, secretin; saponins, flavonoids (SON et al., 2019).

Mental disorders result from failures in the communication of neurotransmitters with the Nervous System. These neuronal chemicals act in psychomotor activities, appetite, sleep and mood. Neurotransmitters associated with DD, such as serotonin, whose precursor is tryptophan, act in the control of different body functions, in the brain, in appetite, body temperature, libido, mood and others. Some nutrients rich in serotonin and tryptophan
include oats, oysters, snails, octopus, squid, bananas, pineapples, plums, which are widely recommended and researched due to their nutritional content (FIRTH et al., 2019).

Scientific evidence shows that diet is just as important for psychiatry as it is for other areas of human medicine. This theme has attracted investments from several countries to investigate the association between intestinal microbiome, neurobiological conditions, food and supplemental nutrition, as a key to the prevention or mitigation of neuropsychiatric diseases, especially depression (ALAM et al., 2017; LEPINAY et al., 2015).

Dietary interventions in neuropsychiatric patients, in the short and long term, cause changes in the structure, chemistry and physiology of the brain, leading to changes in behavior. These neurobiological aspects, which are very common among human and non-human animals, exhibit a reproducible pattern of what they eat, which may be under neurochemical and hormonal control by the organism itself. Food can be used unconsciously to regulate the mood of supposedly normal individuals, with abstinence from drugs, seasonal affective disorders and social withdrawal (ALAM et al., 2017).

The mechanisms by which dietary bioactive products can benefit mental health, still need clarification, however, nutrients contain properties that can act through several ways, involved in the body and brain. It includes the oxidative stress pathways, inflammation and mitochondrial dysfunction, which are usually interrupted in individuals with mental disorders. Dysbiosis is one of the intervening factors, due to the role of the microbiome in modulating the stress response, immune function, neurotransmission and neurogenesis (FIRTH et al., 2019; YARY et al., 2016; BERK et al., 2020).

These authors state that a healthy diet contains a wide variety of bioactive compounds that interact beneficially with these brain pathways. Vegetables and fruits, fibers, fatty acids (omega 3), minerals (zinc, magnesium) contain bioactive substances with a high concentration of polyphenols and probiotics, capable of modulating and reducing SD, the inflammatory action and inexorably contribute to mental health (FIRTH et al., 2019; YARY et al., 2016).

Ghaleiha et al., Support that thiamine, for example, has bioactive and energetic potential to neutralize the lapse of certain antidepressant effects, acts as an adjunct in reducing depressive symptoms and increasing well-being. After 6 weeks of the RCT, they concluded that the improvements in DS remained until the end of the study free of side effects. This can be explained, based on the monoaminergic proposition, which postulates
the pathophysiology of depression as a chemical and energetic imbalance of monoaminergic levels in the brain.

Another interesting research found that the fruit Grewia asiatica L., a berry consumed in the form of juices, is rich in antioxidants such as phenols, flavonoids, anthocyanins and vitamin C, has neuromodulator, anti-apoptotic and neuroprotective activities. The results of the study showed that there was a reduction in anxiolytic behavior (p<0.05) and antidepressant activity (p<0.05), in models. Biochemical studies of isolated mouse brains confirmed a significant increase in SOD and GPx levels (p<0.05) and a reduction in AChE and MDA levels (p<0.05). Indicating the berry's potential to reduce oxidative damage in the brain, modulate the cholinergic system and improve neurological disorders (IMRAN et al., 2021).

Malnutrition to some degree compromises the individual's biochemical, physiological and behavioral performance. The subliminal or expressive effects of neuropsychiatric diseases on the quality of life, consolidate the importance of research to understand the mechanisms and effects of malnutrition in the different stages of life. In this sense, neurobiology studies the cells of the nervous system and their organization within functional circuits and processes information mediated by behavior. The brain is selective and has a direct relationship with the diet. Selectivity includes fats, proteins, micronutrients (antioxidants, vitamers), and glucose, which require essential food nutrients for proper functioning (CANHETA et al., 2020; JACKA et.al., 2017; GAUTAM et al., 2012).

The same authors add that the amino acids of the ingested proteins structure the neurons, fats and fatty acids, maintaining the flexibility of the responsive neuronal membranes. Glucose provides the energy for synaptic transit, and even fibers favor the microbiome for the production of part of the neurotransmitters. Together, these nutritional elements contribute to neural plasticity and reduce inflammation in cases of DD. Thus, the relationship of diet, nutrition and mood intertwine in the reciprocal mechanism between organic subsystems of the brain.

The preventive and therapeutic approach to DD based on nutrients and supplements, is an emerging field, however promising. Even though, this new area of research has been well conducted through RCTs, notably, there is still a research gap on the potential for nutrients for brain health. Suggesting the need for further studies to broaden the understanding of the modulating mechanisms of the diet on the health of the mind and brain and neuropsychiatric disorders.
5 CONCLUSION

The main objective of this study is to deepen the understanding of the interaction between neuronutrition and the factors involved in neurobiology depression. Understanding this neuropsychiatric disease as multifactorial, the bidirectional relationship between inflammation and depression and the palliative viability, of prevention and treatment, through dietary nutrients and or supplementation, as adjuvants in the therapeutic approach of depressive disorder.

Recognize the modifiable risk factors in depression, such as the diet represents an alternative in clinical management, with planned nutritional interventions with antidepressant potential. Nutrition is a basic human need and a prerequisite for healthy living, while the specificity of neuronutrition refers to the supply of nutrients that affect brain functions. It monitors and controls all the uninterrupted energy metabolism in the body, with neuronutrition being a necessary strategy to achieve a healthy brain and good neurocognitive functionality.
REFERÊNCIAS


