

Intestinal microbiota in anxiety and depression

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Received: 20 Mar 2022,

Received in revised form: 12 Apr 2022,

Accepted: 18 Apr 2022,

Available online: 23 Apr 2022

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Keywords— Anxiety, Depression, Probiotics,
Intestinal microbiota.

Abstract— The overall purpose of this study is to review clinical studies involving probiotic supplementation and its effects on mental health in subjects with anxiety and depression. Probiotic supplementation is able to provide benefits on both qualitative and quantitative mental health parameters in anxiety and mood. Even with the limitation of studies regarding the use of probiotics in improving anxiety and depression in humans, most studies have identified positive results, in healthy or unhealthy people. One of the most commonly used probiotics is the genus *Bifidobacterium*. It has been shown to be efficient in inflammatory disorders, and it has been suggested that this probiotic may have antidepressant properties, since the balance between anti- and pro-inflammatory cytokines plays a relevant role in depression.

I. INTRODUCTION

Anxiety is considered a universal human experience and defined as a persistent feeling of impending doom, apprehension and fear, or restlessness and tension. It is considered pathological when the condition that triggers it is disproportionate, or when there is no specific object that

is directed, causing direct interference in the individual's quality of life.

Depression can affect individuals at any stage of life and, although recurrence is higher in middle ages, there has been a growth in adolescence and early adulthood. The disorders can vary according to severity, ranging from mild to very severe, occurring several times sporadically,

however, it can be chronic or recurrent, and women are more vulnerable to depressive states due to hormonal fluctuations that are especially exposed in the fertile period

Anxiety and depression are considered mental disorders with higher prevalence in several countries due to the consequences to human health, with the recommendation of interventional measures. A healthy diet and the consumption of probiotics can be a natural and practical option for the treatment of disorders.

Therefore, this study is justified by the fact that it searches for evidence in the scientific literature, suggesting that the use of probiotic bacteria helps in mental health, by modulating the diversity of the intestinal microbiota, the production of neurotransmitters and the balance of clinical biomarkers with association with the Central Nervous System (CNS).

The hypothesis is that consuming probiotics can improve the clinical parameters of both anxiety and depression in adult subjects. The general objective of this study is to review clinical studies involving probiotic

supplementation and its effects on the mental health of subjects with anxiety and depression. In addition, it has as specific objectives to understand the strains of microorganisms in relation to improving parameters related to anxiety and depression; and study what depression, anxiety and gut microbiota are.

II. INTESTINAL MICROBIAL

The word microbial refers to all microorganisms and the group of genetic variety of viruses, bacteria, protozoa and fungi distributed in various parts of the individual's body (HUMAN MICROBIOME PROJECT CONSORTIUM, 2012).

In 2001, the term microbiome was first used by physician Joshua Lederberg (URSELL et al., 2012) who defined it as “the ecological community of commensal, symbiotic and pathogenic microorganisms that literally share our space. body” (LEDERBERG; MCCRAY, 2001, p. 22).

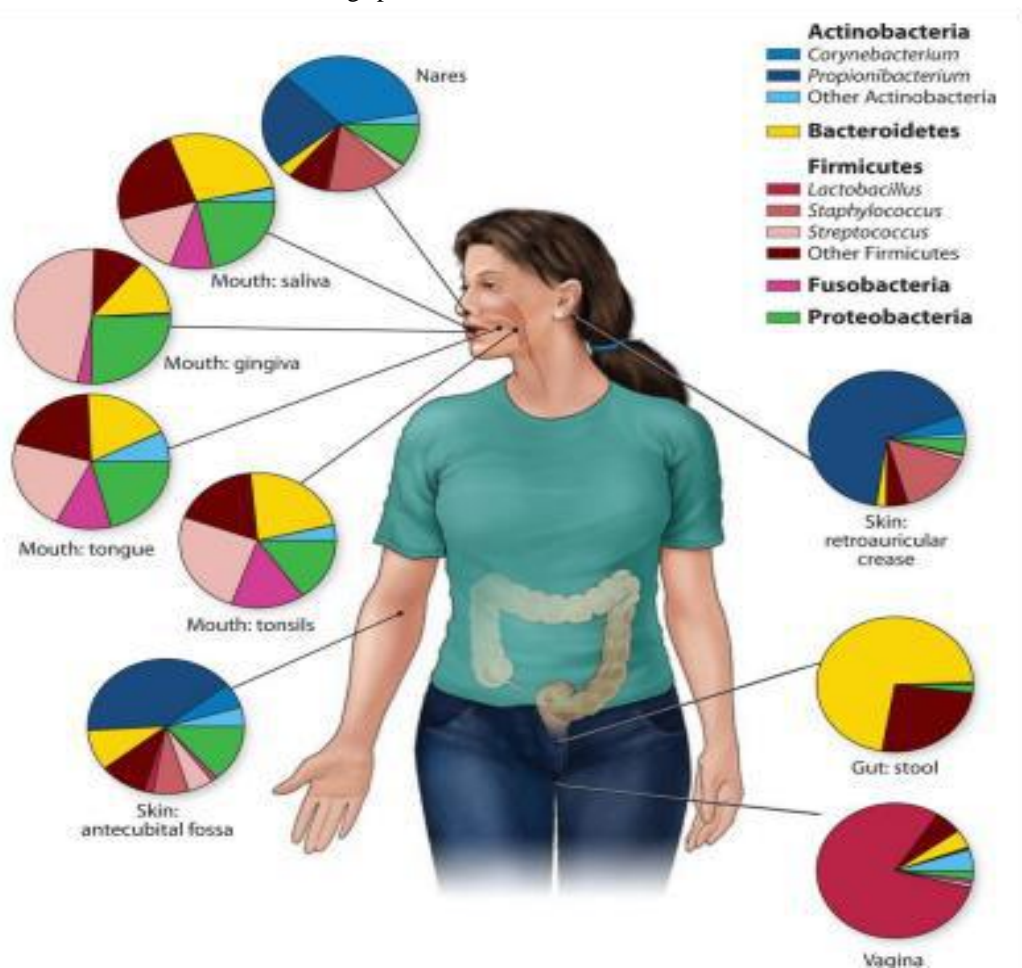


Fig.1: Microbioma humano e a sua diversidade na região corporal

Reference: Grice e Segre (2012)

The intestinal microbiota forms a set of microorganisms that are present in the human body (LEY; PETERSON; GORDON, 2006). A person's body harbors a large population of microorganisms, mainly bacteria, which are distributed in the nasal cavity, stomach, urogenital tract, mouth, skin, pharynx and intestine (TURNBAUGH et al., 2007). The diversity and wide variability of bacterial composition are different in each subject, and can be conceptualized by a genetic part (MORAES et al., 2014) and the other part by individual and environmental, such as

eating habits, age and birth (childbirth). cesarean or normal) (HUMAN MICROBIOME PROJECT CONSORTIUM, 2012; NELSON et al., 2015; PENDERS et al., 2006).

Organisms that inhabit the internal and external surface of the body are dependent on conditions such as pH, availability of nutrients, temperature and humidity to ensure their survival (RIBEIRO et al., 2014). Figure 2 shows the microbial variety and its abundance.

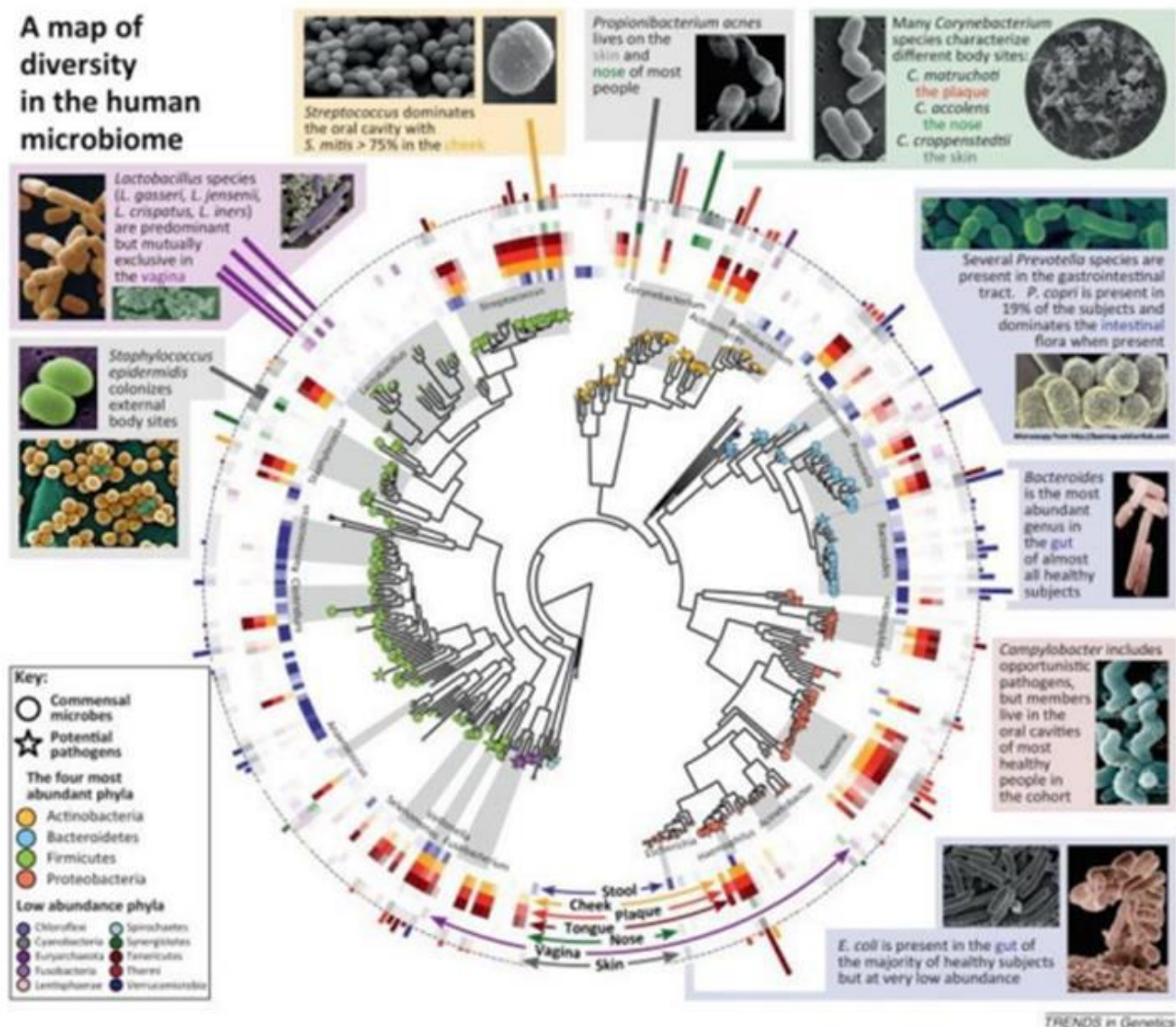


Fig.2: Mapa da diversidade microbiana. Na parte central é representada pela árvore filogenética dos micro-organismos mais abundantes no microbioma humano. As barras laterais, exteriores ao círculo, são proporcionais à taxa de abundância na região corporal predominante.

Reference: KHODOR; SHATAT, 2016

The gastrointestinal tract (GIT), preferably in the intestine, is a place rich in microorganisms, with around

1014 bacteria, that is, ten times higher than the number of human cells (EVRENSEL; CEYLAN, 2015; TURNBAUGH). et al., 2007).

A higher bacterial concentration is presented by the large intestine, most of which are resident in the distal colon with 10¹¹ -10¹² cells/g of intestine (LEY; PETERSON; GORDON, 2006; WHITMAN; COLEMAN; WIEBE, 1998).

What is known is that the intestinal microbiome provides about 150 times more genes than the human genome itself (QIN et al., 2010), bringing the elucidation of how relevant it is to characterize the microbiome, bringing potentiation to the knowledge of the human organism.

The TGI is extremely dynamic and it contains allochthonous or autochthonous bacteria. The autochthonous microorganisms colonize the host, carrying out the formation of populations with a significant size in a certain region of the intestine, without producing diseases under normal circumstances. Allochthonous, on the other hand, can be acquired through food ingestion, remaining for a limited time in the ecosystem (LEY; PETERSON; GORDON, 2006; WALTER, 2008). However, it is often difficult to differentiate whether the micro-organism is autochthonous even to the host (BERG, 1996).

Under healthy circumstances, there is a balance between the host and the microorganisms. Its presence can benefit the health of the host by collaborating with the digestion of food, the production of molecules that can decrease inflammation, the production of short-chain grazoa acids and the development of the immune system (MOOS et al., 2016). An example is that, in the digestion of dietary fiber, bacterial strains are needed in which some carry out the production of vitamin K (BROWN et al., 2012) and others produce some B vitamins, such as vitamin B6, B12 and folic acid (BIESALSKI, 2016). It still affects the physiological properties of the individual, such as, for example, controlling intestinal epithelial proliferation, protecting against pathogens and cellular differentiation (BACKHED, 2005).

The lack of balance in the microbiota with pathogenic bacteria is defined as dysbiosis, and has been associated with the compromise of the host's health, since it is associated with several diseases, such as neurological disorders, inflammatory bowel disease, cancer, malnutrition and obesity (CLARKE et al., 2012).

2.1. ANXIETY

Anxiety is considered a vague and unpleasant feeling of apprehension, fear, whose characterization is given by the tension or discomfort that derives from something strange or unknown, from the anticipation of fear

(ALLEN; LEONARD; SWEDO, 1995; SWEDO et al., 1994).).

According to DSM-5, anxiety disorders encompass related behavioral disorders and disorders that share characteristics of anxiety and excessive fear. These disorders have included selective mutism, separation anxiety disorder, specific phobia, panic disorder, social anxiety disorder (SAD), agoraphobia, medication/substance-induced anxiety disorder, generalized anxiety disorder (GAD), and anxiety disorder. as a result of a medical condition. Anxiety and fear overlap, however, have differentiation, since fear is considered the response to a perceived or real threat, while anxiety is seen as the anticipation of a future threat (APA, 2013).

According to Metzler, Mahoney and Freedy (2016) highlight that the main physical symptoms of anxiety are chest tightness or pain, muscle tension, gastrointestinal disorders and headache. They still show an increase in the levels of use of medical services, a reduction in productivity and a lower quality of life.

In addition to psychosocial implications, there are also physiological factors of the disease. The neural pathways that process visceral pain signals also regulate the response to gastrointestinal function, mood, anxiety and stress (GRUNDY et al., 2006).

In the Central Nervous System, the main mediators of the symptoms of anxiety disorders seem to be serotonin, γ -aminobutyric acid (GABA), neropinephrine and dopamine (FREITAS-FERRARI et al., 2010).

There may also be involvement of the neurotransmitter corticotropin-releasing hormone (CHR) (ROY-BYRNE et al., 2008), resulting in excessive sympathetic activation, disruption of the HPA axis and modification of the inflammatory response, leaving patients predisposed to increased risks. for the development of the disease (DONG et al., 2015).

Not much is known about the relationship between eating and anxiety (YANNAKOULIA et al., 2008). However, anxiety is related to chronic stress (COHEN, 2000) and, as a result, exposure to stressful conditions can lead to the development of eating disorders (TORRES; NOWSON, 2007).

An example is the excessive workload, test stress and exposure to chronic stressors, which cause the induction of an increase in the consumption of caloric foods (CHAPUT; TREMBLAY, 2007).

2.2. DEPRESSION

Depression is also known as depressive disorder and is considered a frequent condition associated with lack of functional capacity and impairment of the

person's physical health (CUNHA; BASTOS; DUCA, 2012). This disorder is characterized by the set of disorders associated with social, family, psychological and genetic factors (STOPA et al., 2015).

According to the World Health Organization (WHO, 2016), at least 350 million individuals are affected by depression. Symptoms of depression are negative thoughts about oneself and others, changes in appetite, feelings of deep sadness, lack of interest in social activities, lack and/or loss of confidence and even suicide (CUNHA; BASTOS; DUCA, 2012).

Dejection and sadness are considered emotional symptoms most commonly presented in cases of depression. The person feels sad, being torn apart, often bursts into tears, and may contemplate suicide. A lack of satisfaction with life still occurs frequently. The gestures that once generated satisfaction seem insignificant and sad. Most patients with depression say they no longer enjoy previous activities, and many say they lose affection and interest in people (ATKINSIN et al., 2002).

Atkinson et al. (2002) state that cognitive symptoms have involved low self-esteem, negative thoughts and feelings of guilt for failures. People doubt your ability to do anything to improve your life.

With regard to physical symptoms, sleep disturbances, loss of energy, change in appetite and fatigue are presented. The person is focused on the interior and not on external events, may worry about health and exaggerate discomfort and minor pain (ATKINSON et al., 2002).

2.3. PROBIOTICS

The Food and Agriculture Organization of the United Nations (FAO) together with the World Health Organization, in 2001, define the definition of probiotics as live microorganisms that, when administered at appropriate levels, provide benefits to the host health (FAO; WHO, 2001). This concept excludes metabolic and microbial components (ISHIBASHI; YAMAZAKI, 2001).

The main determinants of the definition have included the fact that the probiotic bacteria need to be administered live and undergo a controlled evaluation to document the benefits to the host where they are not necessarily human beings (SANDERS, 2009).

Most probiotics are sold as drugs (sachets or capsules) or food, and it is essential to consider their safety (Ishibashi & Yamazaki, 2017). The safety factors for use in humans are:

strains should preferably be of human origin; need to be isolated from the human TGI; have a history of non-pathogenic or

associated GI disease; not cause deconjugation of bile salts and must not carry transmissible antibiotic resistance genes (DIAS, 2017, p. 24).

Knowledge about the intestinal microbiota and interactions enabled the increase of new strategies for the stimulation and maintenance of resident bacteria (FOOKS; FULLER; GIBSON, 1999).

Healthy people suffer damage due to environmental and physiological factors, in which they achieve normal intestinal functioning and the balance of the intestinal microbiota (PARVEZ et al., 2006).

Therefore, the introduction of probiotics through food is recommended as a beneficial agent capable of improving/balancing the microbiota, acting in the modulation of the intestinal mucosa immune system and protecting against inflammation in the intestine (O'BRIEN et al., 1999; SHI et al., 2016).

Dian et al. (2013) emphasize that "psychobiotics" are considered living organisms that, when ingested in sufficient quantities, are beneficial to the health of people with mental illness. According to Wang et al. (2016) it was reported that probiotics influence the Central Nervous System, modifying the composition of the intestinal microbiota, directly or not, increasing the number of studies in the last ten years.

Even though evidence is presented in the literature that the brain-gut axis can impair intestinal function, it is suggested that the intestine also brings changes in the Central Nervous System (DESBONNET et al., 2008).

Memory agility and psychiatric disorders are altered with the use of probiotics (WANG et al., 2016). Directly, probiotics can modify the biochemistry of the CNS, reaching concentrations of the neurotrophic factor that derives from the brain, dopamine, serotonin and GABA, influencing behavior (LIU, et al., 2016).

One of the most used probiotics is from the genus *Bifidobacterium*. It has been shown to be efficient in inflammatory disorders, such as Irritable Bowel Syndrome, where treatment with bifidobacteria is able to ament the existing balance between anti-inflammatory and pro-inflammatory cytokines. Thus, it is suggested that this probiotic may have antidepressant properties, since the balance between anti- and pro-inflammatory cytokines plays a relevant role in depression. (O'MAHONY et al., 2005).

Desbonnet et al. (2010) carried out a study in which a probiotic with *Bifidobacterium infantis* was administered to rats with maternal separation and observed a reduction in

the levels of norepinephrine in the brain, an increase in mRNA (messenger RNA) levels of HLC and peripheral pro-inflammatory secret. of IL-6. The probiotic performed the reversal of behavior problems, normalizing the levels of noradrenaline in the brain and in the immune system, which suggests the use of *Bifidobacterium infantis* as a therapeutic application in neural processes.

Another study also analyzed the ability of bacteria of the *Bifidobacterium* and *Lactobacillus* genera to produce GABA, given that its dysfunction generates symptoms of anxiety and depression. The result was that the production of GABA was more efficient with *Bifidobacterium dentium* and *Lactobacillus brevis* among the strains that were tested, although variation in the production of GABA in bifidobacteria was presented between the types (BARRETT et al., 2012).

Probiotic supplementation is able to provide benefits on both qualitative and quantitative parameters of mental health, anxiety and mood. Even with the limitation of studies regarding the use of probiotics to improve anxiety and depression in humans, most studies identified positive results, in healthy or not (DIAS, 2017).

The microorganisms most used in the composition of the probiotic were *Bifidobacterium longum*, *Lactobacillus acidophilus* and *Lactobacillus casei*, in sachet or capsule, together with other strains. *Lactobacillus* and *Bifidobacterium* are seen as beneficial bacteria and demonstrate improvement in gut immune barrier, reduction in pro-inflammatory cytokine production and promotion of balanced microbiota (INOUE; SHIMOJO, 2015).

Administration of these probiotics is able to decrease gastrointestinal symptoms in people with IBS (Whorwell et al. 2006). However, there is still a need to carry out additional studies to evaluate the strains individually to identify which ones generate benefits for mental health (WALLACE; MILEV, 2017).

In general, the studies showed that the use of probiotic supplements with *Bifidobacterium* and *Lactobacillus* is efficient in mental health, causing balance of neurochemical and metabolic biomarkers. Ingestion of probiotics for 4 or 8 weeks appears to be sufficient to generate satisfactory results, even though the optimal intervention time to observe specific effects is still unknown (WALLACE; MILEV, 2017).

III. CONCLUSION

With the exploration and recognition of the human intestinal microbiome, new treatments to modify the intestinal bacterial concentration beneficial to the health of the individual have been carried out with the use of

probiotic supplements, changing symptoms of anxiety and depression.

Most of the research regarding the communication between the brain and the gut and the existing benefits of probiotics in modifying the chemical imbalance in the brain and in behavior is done in animals. However, human studies have confirmed the benefits of probiotic supplementation in people with mental illness.

REFERENCES

- [1] ATKINSON, L. R.; et al. **Introdução à Psicologia de Hilgard**. Tradução Bueno, D.; 13. Ed. Porto Alegre: Artmed, 2002. p. 562-563.
- [2] ALLEN, A. J.; LEONARD, H.; SWEDO, S. E. Current Knowledge of Medications for the Treatment of Childhood Anxiety Disorders. **Journal Of The American Academy Of Child & Adolescent Psychiatry**, [s.l.], v. 34, n. 8, p.976-986, 1995.
- [3] APA. Diagnostic and Statistical Manual of Mental Disorders: fifth edition. **American Psychiatric Association**, England, 2013.
- [4] BÄCKHED, F. et al. **Host-Bacterial Mutualism in the Human Intestine**. *Science*, [s.l.], v. 307, n. 5717, p.1915-1920, 25 mar. 2005.
- [5] BARRETT, E. et al. γ -Aminobutyric acid production by culturable bacteria from the human intestine. **Journal of Applied Microbiology**, [s.l.], v. 113, n. 2, p.1384-1386, 15 jun. 2012.
- [6] BERG, R. D. **The indigenous gastrointestinal microflora**. *Trends In Microbiology*, [s.l.], v. 4, n. 11, p.430-435, nov. 1996
- [7] BIESALSKI, H. K. Nutrition meets the microbiome: micronutrients and the microbiota. **Annals Of The New York Academy Of Sciences**, [s.l.], v. 1372, n. 1, p.53-64, maio 2016.
- [8] BROWN, K. et al. **Diet-Induced Dysbiosis of the Intestinal Microbiota and the Effects on Immunity and Disease**. *Nutrients*, [s.l.], v. 4, n. 8, p.1095-1119, 21 ago. 2012.
- [9] CHAPUT, J. P.; TREMBLAY, A. Acute effects of knowledge-based work on feeding behavior and energy intake. **Physiology & Behavior**, [s.l.], v. 90, n. 1, p.66-72, jan. 2007.
- [10] CLARKE, S. F. et al. The gut microbiota and its relationship to diet and obesity: new insights. **Gut Microbes**, [s.l.], v. 3, n. 3, p.186-202, maio 2012.
- [11] COHEN, J. I. Stress and mental health: a biobehavioral perspective. **Issues Ment Health Nurs**, [s.i.], v. 21, n. 2, p.185-202, mar. 2000.
- [12] CUNHA, R. V.; BASTOS, G. A. N.; DUCA, G. F. Prevalência de depressão e fatores associados em comunidade de baixa renda de Porto Alegre, Rio Grande do Sul. **Revista Brasileira de Epidemiologia**, São Paulo, v. 15, n. 2, p.346-54, jun. 2012.
- [13] DESBONNET, L. et al. Effects of the probiotic *Bifidobacterium infantis* in the maternal separation model of

- depression. **Neuroscience**, [s.l.], v. 170, n. 4, p.1179-1188, nov. 2010.
- [14] DIAS, P.D.C. **Efeito da suplementação de probióticos na depressão e ansiedade**: Uma revisão sistemática. Trabalho de Conclusão de Curso (Bacharelado em Nutrição). Universidade Federal do Rio Grande do Sul. Porto Alegre, 2017.
- [15] DINAN, T.G., et al. Psychobiotics: A novel class of psychotropic. **Biological Psychiatry**, v. 74, n. 10, p. 720–726, 2013
- [16] DONG, Y. et al. Managing Anxiety in the Medically Ill. **Psychiatric Times**, [s.l.], p.1-6, jan. 2015.
- [17] EVRENSEL, A.; CEYLAN, M. E. The Gut-Brain Axis: The Missing Link in Depression. **Clinical Psychopharmacology And Neuroscience**, [s.l.], v. 13, n. 3, p.239-244, 31 dez. 2015.
- [18] FAO; WHO. **Health and Nutrition Properties of Probiotics in food including Powder Milk with Live Lactic Acid Bacteria**. p. 1–4, 2001.]
- [19] FOOKS, L. J.; FULLER, R.; GIBSON, G. R. Prebiotics, probiotics and human gut microbiology. **International Dairy Journal**, [s.l.], v. 9, n. 1, p.53-61, jan. 1999.
- [20] FREITAS-FERRARI, M. C. et al. Neuroimaging in social anxiety disorder: a systematic review of the literature. **Progress In Neuropsychology And Biological Psychiatryopharma**, [s.l.], v. 34, n. 4, p.565-580, maio 2010.
- [21] GRICE, E. A.; SEGRE, J. A. The Human Microbiome: Our Second Genome. **Annual Review Of Genomics And Human Genetics**, [s.l.], v. 13, p.151-170, 2012
- [22] GRUNDY, D. et al. **Fundamentals of Neurogastroenterology**: Basic Science. **Gastroenterology**, [s.l.], v. 130, n. 5, p.1391-1411, abr. 2006.
- [23] HUMAN MICROBIOME PROJECT CONSORTIUM. **Structure, Function and Diversity of the Healthy Human Microbiome**. **Nature**, v. 486, n. 7402, p. 207–214, 2012.
- [24] Inoue, Y., Shimojo, N. Microbiome/microbiota and allergies. **Seminars in Immunopathology**, 37(1): 57–64, 2015
- [25] ISHIBASHI, N.; YAMAZAKI, S. Probiotics and safety. **American Journal Of Clinical Nutrition**, [s.l.], v. 73, p.465-470, jul. 2001.
- [26] KHODOR, S. A.; SHATAT, I. F. Gut microbiome and kidney disease: a bidirectional relationship. **Pediatric Nephrology**, [s.l.], v. 32, n. 6, p.921-931, 29 abr. 2016.
- [27] LEDERBERG, J.; MCCRAY A. T. 'Ome sweet 'omics - a genealogical treasury of words. **Scientist**, v. 15, 2001.
- [28] LEY, R. E.; PETERSON, D. A.; GORDON, J. I. **Ecological and Evolutionary Forces Shaping Microbial Diversity in the Human Intestine**. **Cell**, [s.l.], v. 124, n. 4, p.837-848, fev. 2006.
- [29] LIU, Y. W. et al. Psychotropic effects of *Lactobacillus plantarum* PS128 in early lifestressed and naïve adult mice. **Brain Research**, [s.l.], v. 1631, p.1-12, jan. 2016.
- [30] METZLER, D. H.; MAHONEY, D.; FREEDY, J. R. Anxiety Disorders in Primary Care. **Primary Care: Clinics in Office Practice**, [s.l.], v. 43, n. 2, p.245-261, jun. 2016.
- [31] MOOS, W. H. et al. **Microbiota and Neurological Disorders**: A Gut Feeling. **Bioresearch Open Access**, [s.l.], v. 5, n. 1, p.137-145, 2016.
- [32] MORAES, A. C. F. et al. Microbiota intestinal e risco cardiometabólico: mecanismos e modulação dietética. **Arquivos Brasileiros de Endocrinologia & Metabologia**, [s.l.], v. 58, n. 4, p.317-327, jun. 2014.
- [33] NELSON, M. H. et al. Harnessing the Microbiome to Enhance Cancer Immunotherapy. **Journal Of Immunology Research**, [s.l.], v. 2015, p.1-12, 2015.
- [34] O'BRIEN, J. et al. **Safety evaluation of probiotics**. **Trends In Food Science & Technology**, [s.l.], v. 10, n. 12, p.418-424, 1999.
- [35] O'MAHONY, L. et al. **Lactobacillus and bifidobacterium in irritable bowel syndrome**: Symptom responses and relationship to cytokine profiles. **Gastroenterology**, [s.l.], v. 128, n. 3, p.541-551, mar. 2005.
- [36] PARVEZ, S. et al. Probiotics and their fermented food products are beneficial for health. **Journal Of Applied Microbiology**, [s.l.], v. 100, n. 6, p.1171-1185, jun. 2006.
- [37] PENDERS, J. et al. **Factors Influencing the Composition of the Intestinal Microbiota in Early Infancy**. **Pediatrics**, [s.l.], v. 118, n. 2, p.511-521, ago. 2006.
- [38] QIN, J. et al. **A human gut microbial gene catalogue established by metagenomic sequencing**. **Nature**, [s.l.], v. 464, n. 7285, p.59-65, mar. 2010.
- [39] RIBEIRO, A. A. et al. **Microbioma Humano: Uma Interação Predominantemente Positiva?**. **Uningá Review**, [s.l.], v. 19, n. 1, p.38-43, 2014
- [40] ROY-BYRNE, P. P. et al. **Anxiety disorders and comorbid medical illness**. **General Hospital Psychiatry**, [s.l.], v. 30, n. 3, p.208-225, maio 2008
- [41] SANDERS, M. E. **How Do We Know When Something Called "Probiotic" Is Really a Probiotic?** A Guideline for Consumers and Health Care Professionals. **Functional Food Reviews**, [s.l.], v. 1, n. 1, p. 3–12, 2009.
- [42] SHI, L. H. et al. **Beneficial Properties of Probiotics**. **Tropical Life Sciences Research**, [s.l.], v. 27, n. 2, p.73-90, 2016.
- [43] STOPA, S. R. et al. Prevalência do autorrelato de depressão no Brasil: resultados da Pesquisa Nacional de Saúde, 2013. **Epidemiologia e Serviços de Saúde**, [s.l.], v. 18, n. 2, p. 170-180, jun. 2015.
- [44] SWEDO, S. E. et al. New developments in childhood affective and anxiety disorders. **Current Problems In Pediatrics**, [s.l.], v. 24, n. 1, p.12-38, jan. 1994.
- [45] TORRES, S. J.; NOWSON, C. A. **Relationship between stress, eating behavior, and obesity**. **Nutrition**, [s.l.], v. 23, n. 11-12, p.887-894, nov. 2007.
- [46] TURNBAUGH, P. J. et al. **The Human Microbiome Project**: exploring the microbial part of ourselves in a changing world. **Nature**, [s.l.], v. 449, n. 7164, p.804-810, out. 2007.
- [47] URSELL, L. K. et al. **Defining the human microbiome**. **Nutrition Reviews**, [s.l.], v. 7, n. 1, p.38-44, ago. 2012.
- [48] WALLACE, C. J. K.; MILEV, R. The effects of probiotics on depressive symptoms in humans: a systematic review. **Annals of General Psychiatry**, 16: 2–10, 2017.
- [49] WALTER, J. Ecological Role of *Lactobacilli* in the Gastrointestinal Tract: Implications for Fundamental and

- Biomedical Research. **Applied And Environmental Microbiology**, [s.l.], v. 74, n. 16, p.4985-4996, jun. 2008.
- [50] WANG, H. et al. Effect of Probiotics on Central Nervous System Functions in Animals and Humans: A Systematic Review. **Journal Of Neurogastroenterology and Motility**, [s.l.], v. 22, n. 4, p.589-605, out. 2016
- [51] WHITMAN, W. B.; COLEMAN, D. C.; WIEBE, W. J. Prokaryotes: the unseen majority. **Proceedings of the National Academy of Sciences**, [s.l.] v. 95, n. 12, p. 6578–6583, 1998.
- [52] WHO. **Depression** [Internet]. n. 369, 2016. Disponível em: <http://www.who.int/mediacentre/factsheets/fs369/en/>. Acesso em: 19 abr. 2022.
- [53] YANNAKOULIA, M. et al. **Eating habits in relations to anxiety symptoms among apparently healthy adults**. A pattern analysis from the ATTICA Study. **Appetite**, [s.l.], v. 51, n. 3, p.519-525, nov. 2008.