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Effects of Nutrition on Neurology

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Abstract

Increasing attention has been paid to the importance of nutrition early in life, including the foetal milieu. The relationship between diet, brain function and the risk of mental disorders has been the subject of intense research in recent years. Nutritional guidelines around the globe use very similar methods in presenting their concepts of the ideal dietary pattern, and give consumers a selection of recommended food groups. Despite the impact of fermented foods and beverages on gastro-intestinal wellbeing and diseases, their many health benefits or recommended consumption has not been widely translated to global inclusion in world food guidelines. Nutrition research in cognitive development, mental health/well-being, with normal or fermented food or beverage, reveals a direct influence of gut microbiota. This is achieved by boosting the antioxidant and anti-inflammatory activity or directly in gut-to-brain connections. The gut-microbiota-brain axis controls bowel functionalities and influences the communication between the immune and nervous systems and vice versa. Alterations in the intestine microbiota composition in humans have been linked to a variety of neuropsychiatric conditions. Mushroom biomass and fermented foods and beverages have long been a part of the human diet, and with further supplementation with probiotics, in some cases, they offer nutritional and health attributes worthy of recommendation of regular consumption namely on mental disorders.

Keywords: Nutrition; Fermented Foods; Mushroom Biomass; Neurology

Abbreviations: CNS: Central Nervous System; CJD: Creutzfeldt-Jacob Disease; SOD: Superoxide Dismutase; AD: Alzheimer´s Disease; EBV: Epstein-Barr Virus; CMV: cytomegalovirus ; HHV-6: Human Herpesvirus-6.

Introduction

Human nutrition begins with milk. Fermented milk products have been recognized as healthy foods since

ancient times. Fermentation processes and products are believed to have been developed around 10 000 years BC in order to preserve food for times of deficiency, improve flavour, and reduce poisonous effects [1]. Recommendations for the consumption of certain nutritious foods date back to the Hippocratic Corpus of Ancient Greece [2].

Increasing attention has been paid to the importance of nutrition early in life, including the foetal milieu. Thousands of different fermented foods and beverages are still unknown outside the native area in which they have been produced for centuries, many going back even before recorded history [3].

Our previous review examined different nutritional guidelines, some case studies, providing insights and discrepancies, in the regulatory framework of Food Safety Management of some of the world's economies [4].

Nutritional guidelines around the globe use very similar methods in presenting their concepts of the ideal dietary pattern, and give consumers a selection of recommended food groups. Fermented foods and beverages have long been a part of the human diet, and with further supplementation of probiotic microbes, in some cases, they offer nutritional and health attributes worthy of recommendation of regular consumption [5]. However, not all forms of fermentation or fermented foods are beneficial. Some fungi associated with pickled foods may enhance the production of N-nitroso compounds, formed endogenously from intake of nitrite and nitrate, a potent group of carcinogens [6].

Nutrition and Progressive Neurodegenerative Disorders

The relationship between diet, brain function and the risk of mental disorders has been the subject of intense research in recent years. Neurodegenerative diseases (e.g. Parkinson's, Alzheimer's, and Huntington's) are incurable and debilitating conditions that result in progressive degeneration and/or death of nerve cells. This causes problems with movement (ataxias), or mental functioning (dementias).

Energy homeostasis is kept through a complex interplay of nutritional, neuronal and hormonal inputs that are integrated at the level of the central nervous system (CNS). A disruption of this regulation gives rise to several life-threatening conditions. The CNS regulates nutrient intake by innate transmitting processes, which becomes disturbed in CNS lesions. On the other hand, brain degenerative disorders may steadily affect nutritional status. Adequate nutritional support is considered relevant adjuvant therapy in retarding or inhibiting chronic neurological diseases, malnutrition being a risk factor [7].

The gut microbiota provides essential capacities for the fermentation of non-digestible substrates like dietary fibres and endogenous intestinal mucus. It is well known since the 60's that feeding a ruminant (e.g. cattle, sheep, goats) is feeding the vast microflora requirements in two compartments, the rumen and the large intestine, which by microbial fermentation produces short chain volatile fatty acids, gases and microbial protein that subsequently may cover the animal requirements in energy, protein and other nutrients [8,9].

We recall the outbreak of BSE (mad cow disease, bovine spongiform encephalopathy) in 1986 an interesting disease from a medical standpoint because of the causative agent, prions, which are infectious proteins, not a virus, caused by intake of animal protein. This CNS disease, with links to Creutzfeldt-Jacob Disease (CJD), clearly reveals the connection of food and brain injury, characterised by spongiform changes associated with neuronal loss, and a failure to induce inflammatory response.

Nutrition is a target of research in cognitive and mental well-being and health, now known as nutritional psychiatry. Patients with neurological diseases are at increased risk of micronutrient deficiency and dehydration. On the other hand, nutritional factors may be involved in the pathogenesis of neurological diseases [10].

Microbiome is the collective genomes of the microorganisms in a particular environment while microbiota is the community of microorganisms themselves. The gut resident microbes affect many aspects of human physiology and are linked to mental health (e.g. anxiety and depression) [11].

There is a tremendous complexity of the human gut microbiota, established during infancy, in both health and disease states and a healthy microbiota consists of an inter-dependent network of microbes rather than a particular bacterial genera. Intestinal bacteria produce numerous neurotoxic metabolites (e.g. lactic acid and ammonia) with potential encephalo toxicity. Probiotics and prebiotics may limit production of lactic acid in the gut. The direct effects of probiotics in the gut are well documented and include up-regulation of

immunoglobulins such as IgA, down-regulation of inflammatory cytokines, and enhancement of gut barrier function [12].

The application of fermentation is an ancient art and fermented food or beverage directly influences our own microbiota via magnified antioxidant and anti-inflammatory activity or directly in gut-to-brain communication via a beneficial shift in the intestinal microbiota [13]. Depression and other mental health disorders are characterized by chronic, low-grade inflammation and oxidative stress. High-fat or high-sugar and low nutrient-value foods are commonly consumed by those with depression, anxiety, and high levels of chronic distress [14].

The long-term gut-brain communication may exist and may clarify the relationship between potentially beneficial food-derived microorganisms and brain health although still unknown how to enhance the microbiome [15].

Fermented Foods

The shift away from traditional lifestyles has been linked to increased rates of depression and other mental health disorders [16]. The purposeful application of fermentation in food and beverage preparation, as a means to provide palatability, nutritional value, preservative, and medicinal properties, is an ancient practice. Fermented foods and beverages continue to make a significant contribution to the overall patterns of traditional dietary practices [17].

As our knowledge of the human microbiome increases, including its connection to mental health (e.g. anxiety and depression), it is becoming increasingly clear that there are untold connections between our resident microbes and many aspects of physiology [18].

The consumption of mushrooms and fermented foods may be particularly relevant to the emerging research linking traditional dietary practices and positive mental health. The extent to which traditional dietary items may mitigate inflammation and oxidative stress may be controlled, at least to some degree, by microbiota. A properly controlled fermentation may often increase the activity and bioavailability of a specific nutrient and phytochemical content of foods, the ultimate value of which may be associated with mental health; furthermore, the microbese.g.*Lactobacillus* and *Bifidobacteria* species associated with fermented foods may also influence brain health via direct and indirect pathways [19,20].

Fermentation and Reduced Inflammation

There are thousands of fermented foods and beverages, and they are still absent as a category indifferent national food guides. For understanding the inconsistencies in claims concerning fermented foods among various regulatory systems, each legal system should be considered unique.

The purposeful application of fermentation for food preservation, palatability, and other reasons is an ancient art. The connection between fermented dairy products and the growth of beneficial intestinal microbes has been well described. However, the findings that (non-dairy) fermented foods, mushrooms and herbs can have a positive influence on the intestinal microbiota and influence long-term gut-brain communication [21].

Depression and other mental health disorders are characterised by chronic, low-grade inflammation and oxidative stress. Conversely, a traditional diet rich in antioxidant, anti-inflammatory foods may confer some level of protection against depression [22].

An intestinal ‘inflammatory microbiome’ appears to exist, one that may contribute to altered mood via intestinal permeability, systemic and local lipopolysaccharide (LPS) burden, and even direct-to-brain microbe communication [23].

Thought to be a result of changes in diet and lifestyle patterns, high density diets in energy (sugar and fat) and low nutrient-value foods are commonly consumed by those with depression, anxiety, and high levels of chronic distress, thus contributing to the likelihood of an inflammatory microbiome [24].

Traditional fermentation techniques of conventional diets (e.g. breads, soy germ, wheat germ, rice bran) rich in dietary fibre consisting of non-starch polysaccharides and other plant components such as cellulose, resistant starch, resistant dextrins, inulin, lignins, chitins, pectins, β-glucans, and oligosaccharides, have been shown to produce novel bioactive compounds capable of producing beneficial immune, glycemic, and anti-inflammatory activities [25]. The action of fermenting cultures is determinant for the different degradation of the cell wall, disrupting the protein-carbohydrate integration, thus reducing the solubility of dietary fibre [26].

There are only a few medical problems that evolution has not "resolved" and inflammation is one of them. Recent evidence suggests that the health-promoting target of bioflavonoids, secondary metabolites from plant and fungus (although functional foods such as mushrooms do not contain flavonoids), is directed toward the human gut bacterial pool of genes or metagenomes, and that these benefits have an evolutionary origin and benefit [27].

Researchers have examined the *in vivo* properties of an herbal blend typically used in traditional medicine to treat inflammatory disorders, comparing its effects in the unfermented and fermented form. Markers of systemic inflammation were lower with fermented foods [28].

It can therefore be said that fermented foods and beverages act through positive influence on nutritional status, via magnified antioxidant and anti-inflammatory activity, reduction of intestinal permeability, depletion of the detrimental effects of the endoxin lipopolysaccharide, and improved glycaemic control [29].

Neuroprotective Effects of Mushrooms

Chronic brain inflammation sustains the progression of Alzheimer´s disease, so the objective is to find molecules that can reduce brain inflammation; thereby providing a disease-modifying therapy for dementia.

In the past ten years, the clinical development of mushroom nutrition has determined that *Coriolus versicolor* biomass has viral protective properties, while *Hericium erinaceus* biomass is extremely high in super-oxid dismutase (SOD) content which is important given that with herpes simplex virus infection, apoE4 intensifies virus latency and is associated with the increased oxidative damage to the central nervous system. In addition there is some evidence that herpes simplex virus infection in combination with the apoE4 genotype may be associated with increased risk of Alzheimer´s disease (AD) [30].

Consistent with this notion *Coriolus versicolor* biomass has a clinically verified use in the reduction of viral load of Epstein-Barr virus (EBV), cytomegalovirus (CMV) and human herpesvirus-6 (HHV-6) [31].

Alterations in the gut microbiota composition in humans have also been linked to a variety of neuropsychiatric conditions, including depression, autism and Parkinson's disease and the microbiota may be a modifiable factor modulating the development or pathogenesis of neuropsychiatric disorders [32].

Mushrooms are particularly rich in leucine and lysine, deficient in many grains, proteins, such as lectins, fungal immunomodulatory proteins, ribosome inactivating proteins, ribonucleases, laccases and other enzymes have interesting biological activities including anti-convulsant activity [33-36].

We have studied the role of feeding mushroom (*Coriolus versicolor*) biomass on Alzheimer's Disease [37]. Abnormal redox homeostasis and oxidative stress have been proposed to play a role in the aetiology of several neuropsychiatric disorders and emerging interest has recently focused on markers of oxidative stress and neuroinflammation in neurodegenerative disorders as well as in different forms of chronic mental illness. Mushroom products, extracts or biomass, known for their potent antioxidant property, have attracted interest due to their potential in neuroprotection, antioxidant, and anti-inflammatory effects, in mitochondrial dysfunctions associated disorders [38].

This nutritional approach is not a cure, but a stop-gap approach until a pharmaceutical alternative can be discovered and confirmed.

Conclusions

As we are entering an era where we can increasingly modify health through food and measure the effects through our microbes or metabolites, modern research is emphasising the likely value of inherited dietary practices on mental health, and on resiliency against depression in particular.

At the same time, there has been progress toward better understanding of the role played by the low-grade inflammation and the intestinal microbiome in human health and mental well-being.

The present global regulatory framework for fermented foods and beverages is confusing and limiting. Foods prepared by fermentation will increase in amount and use as they contribute to the diversity of gut microbiota and indirectly impact on mental health and other disorders.

Future studies must account for possible microbiota-targeted intervention strategies that could improve health status and prevent psychiatric disorders. Hopefully, further research will illuminate the ways in which

fermentation might be connected to the emerging discipline of nutritional psychiatry. Many challenges still remain regarding the establishment of dietary guidelines integrating education, agriculture, health, environment and industry.

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