

## Need of Nutrigenomic Studies for the Prevention and Treatment of Mood and Neurodegenerative Disorders

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In the past decades, nutrition research has undergone an important shift in focus from epidemiology and physiology to molecular biology and genetics [1]. Interest in the use of nutraceuticals and functional foods has risen substantially, largely because of their safety, adequate efficacy as well as potency [2]. 'Nutrigenomics' is an emerging field that describes the role of nutrients in gene expression. While the nascent field of 'Nutritional Psychiatry' focuses on nutritional approaches to the prevention and treatment of mental disorders [3]. Considerable evidence suggests the role of nutrition in the genetics of many neuropsychiatric, neuro developmental, and neurodegenerative disorders [4]. Moreover, there is need of clinical studies on the efficacy of nutraceutical compounds for the treatment and prevention of mood and/or neurodegenerative disorders [5].

Optimal brain function results from highly complex interactions between numerous genetic and environmental factors including food intake, physical activity, age, and stress. The effects of nutrition on the brain are mediated by changes in gene expression. Epigenetic events suggest key mechanisms by which nutrition is involved in the pathogenesis of age-related cognitive decline: different nutrients, foods, and diets have both immediate and long-term effects on the epigenome, including energy status, that is, energy intake, physical activity, energy metabolism and related changes in body composition, and micronutrients involved in DNA methylation, for example, folate, vitamins B<sub>6</sub> and B<sub>12</sub>, choline, methionine. Nutrition-epigenetic interactions are implicated in the underlying mechanisms of many neurodegenerative disorders such as age-related cognitive decline and dementia. An understanding of the role of epigenetics in regulating gene expression throughout life is therefore central to understanding of the role of nutrition in age-related cognitive decline and dementia. Although epigenetic modifications can be stable and heritable, they can be reversible emphasizing critical roles for nutrition in both prevention and treatment of cognitive impairment. Therefore, in the study of neurodegenerative diseases, nutrigenomics augments the discovery of neuroprotective pathways using diet and through the use of new natural substances that may induce the expression of health-promoting genes and reduce the disease-promoting genes. Therefore, with the help of nutritional genomics prevention and treatment of diet-related mood and neurodegenerative diseases also possible [4,6,7].

A number of innovative studies are pointing to the exciting possibility that the effects of diet on mental health can be transmitted across generations. There is growing evidence of the specific nutrients and other food constituents that influence the epigenome. It is the nutrition that interacts with each individual's genetic makeup to modulate mental health throughout the life course. The interactions between nutrition and genetics are mediated by epigenetic marks and molecules, which have a central role in the causal pathways between diet, genotype, and phenotype (Figure1) [8].

Considerable evidence suggests that both maternal and infant nutrition have a critical role in brain function and cognitive performance later in life. Prenatally, there is a positive association between maternal intake of micronutrients such as folate, vitamin B<sub>12</sub>, omega-3 fatty acids and iron, and cognitive outcomes in children. Postnatally, breast milk is linked with enhanced neurodevelopment, and may exert its beneficial effects in part via long-chain poly unsaturated fatty acids and insulin-like growth factors (IGFs) [6]. Many studies have shown that omega-3 fatty acids-enriched diet is involved in neuroprotective and cognitive effects in humans and up regulating genes that are important for maintaining synaptic function and plasticity in rodents [9,10]. Prenatal maternal omega-3 fatty acid supplementation can normalize DNA methylation postnatally. Moreover, omega-3 fatty acids add to the effects of exercise on brain-derived neurotrophic factor (BDNF) gene expression. It is now also apparent that the beneficial effects of high-flavonoid intake on cognition are linked with changes in BDNF. Diet also affects non-coding RNAs (ncRNAs), and vitamin D supplements may have a beneficial effect on Alzheimer's disease (a chronic neurodegenerative disease), in part, via actions on microRNAs (miRNAs). Maternal vitamin D status affects DNA methylation in the young that may persist in multiple generations and

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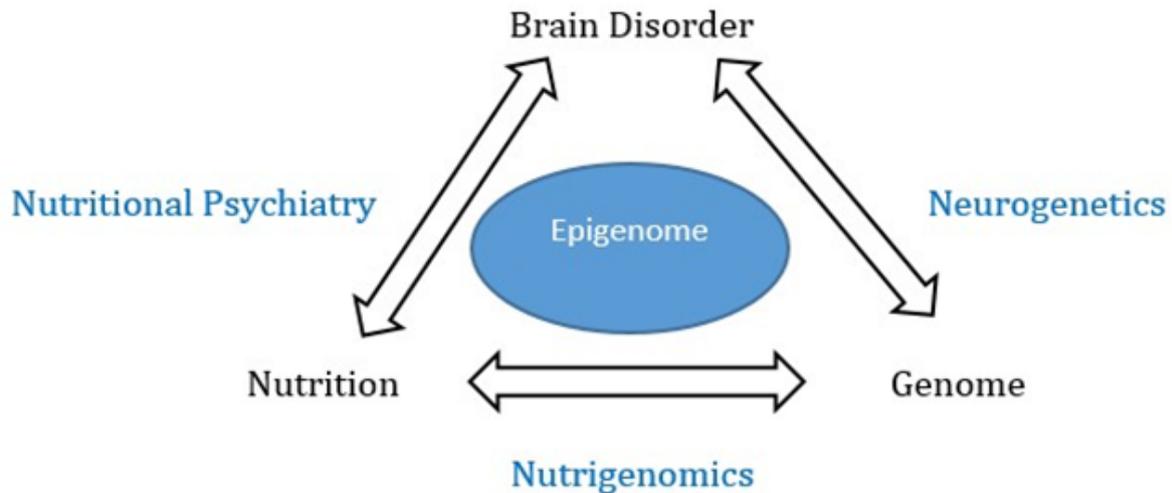
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**Figure 1:** Epigenomic triangle: The epigenome is central to interactions between diet and the genome in determining brain disorder

have an impact on brain function and Alzheimer's disease [7].

Nutrition affects the brain throughout life, with profound implications for cognitive decline and dementia. Deficiency of vitamin A during pregnancy has been shown to cause malformation of the fetal brain. It was reported that maternal vitamin A restriction caused altered brain development in offspring in terms of tissue weight, DNA, RNA, and protein levels, and biosynthesis of DNA and proteins. It has also been reported that dietary supplementation with *Nigella sativa* (Black cumin) during lactation and in the neonatal and juvenile periods enhanced learning and memory in rats [11]. Long term oral administration of Black cumin has also shown nootropic effects in adult rats [2]. Previously, it has been reported that supplementation of nanoemulsion of thymoquinone (TQ), an active component of Black cumin, could ameliorate memory deficit, lipid peroxidation and soluble  $\beta$ -amyloid ( $A\beta$ ) levels as well as improving the total antioxidant status and antioxidant genes expression levels in adult rats. Thus TQ, possibly through its antioxidant properties was able to protect against the earlier destructive damage towards Alzheimer's disease pathology. These investigations may support the notion that Black cumin or its active components may influence epigenetic events in cells [12,13].

The effects of diet are mediated by changes in expression of multiple genes, and responses to nutrition may in turn affected by individual genetic variability. Therefore, to be able to recommend "personalized food or nutrition" to individuals it may be necessary to define typical pattern of genes, environmental influences, and individual behavior that describe, how food molecules can be metabolized differently in individual bodies that match one of those patterns. It appears that DHA-rich (docosahexaenoic acid) nutrition is associated with increased risk of Alzheimer's disease for carriers of the apolipoprotein E  $\epsilon$ 4 (APOE4)-gene [14,15]. While it is contrary to the other studies which indicate that dietary intake of omega-3 fatty acids and weekly consumption of fish may reduce the risk of incident Alzheimer's disease [16]. That's why personalized dietary advice sometimes conflicts with general public health recommendations. Therefore, any individualized nutritional advice should start with testing the client for such genetic markers which are known today as being of relevance to the metabolism of nutritional molecules. However, this concept needs some further clarifications and systematic analyses based on the present evidence in science.

In conclusion, understanding how multiple inputs from nutrition, other epigenetic regulators, and genetic variability affect the brain should help in the development of novel preventive and therapeutic

approaches to various mood and neurodegenerative disorders such as cognitive decline, dementia, Alzheimer's disease, etc. There is growing evidence of the nutraceuticals that influence the epigenome of many brain disorders but, to date, the underlying molecular pathways through which nutritional exposures and status are transduced (received and recorded) remain to be elucidated. Future studies linking nutrition with advances in neuroscience, genomics and epigenomics should provide novel approaches to the prevention of various mood and neurodegenerative disorders.

**Conflict of Interest:** There are no conflicts of interest.

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