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MINIREVIEW

Heart and Brain: A neutro-genomic link

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Abstract

The philosophy of heart and brain are very ancient in our literature where the things good for the heart are not suggested good for the brain and vice-versa. Modern medicine is characterized by a high degree of specialization and the heart-brain connection that could be targeted to treat these complex cardiovascular/brain disorders. The idea that adverse diet/genome interactions can cause disease is not new. In the recent era the science of nutritional genomics have increased our understanding of diet-health-gene interactions and have provided a number of benefits for individuals, groups and societies. Since dietary chemicals are regularly ingested and participate indirectly and directly in regulating gene expression, it follows that a subset of genes regulated by diet must be involved in disease initiation, progression, and severity. In this regards Liver X Receptor (LXR)-α, a key transcription factors, associated with the several chronic pathological situation including coronary heart disease and neurodegenerative diseases have recently been found to be regulated by the dietary components. The crucial findings at molecular biology unit, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, INDIA have not only forced us to explore nutritional genomics as a holistic systems approach to understand the relationship between diet and health, but also to look into the disease preventing and health promoting foods that match our lifestyles, cultures and genetics. After all, we are what we eat.

Key words: Heart; Brain; Nutrition; Gene interaction; Liver X Receptor

Core tip: The progression from a healthy phenotype to a chronic disease phenotype comes into existence by abnormal regulation of gene expression, influenced by the dietary components and gene environment interaction. Liver X Receptor-α is one of the key transcription factor which is modulated by the dietary components such as oxycholesterol, withaferin A, vitamin C, vitamin D and statins. Thus the molecule attracts its role in the field of neutro-genomics.

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INTRODUCTION

The philosophy of heart and brain are very ancient in our literature where the things good for the heart are not suggested good for the brain and vice-versa. Modern medicine is characterized by a high degree of specialization and the heart-brain connection that could be targeted to treat these complex cardiovascular/brain disorders[1]. In the recent era the science of nutritional genomics have increased our understanding of diet-health-gene interactions and have provided a number of benefits for individuals, groups and societies[2].

Here, I would like to share my experience at Dr. Kaul's molecular biology unit, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, INDIA, where I have become the witness of some crucial findings which correlates the heart and brain at neutro-genomic level.

LIVER X RECEPTOR-α: NEUTRO-GENOMIC LINKER BETWEEN HEART AND BRAIN

Under the light of the existing literature in the field of cardiovascular as well as neurodegenerative diseases, ligand activated nuclear receptor Liver X Receptor-α (LXR-α) have caught imagination of researcher for its ability to regulate an array of genes involved in lipid metabolism, inflammation, glucose homeostasis and innate immunity[3]. LXR-α is highly expressed in the normolipidemic and hyperlipidemic coronary heart disease subjects which shows a nature's protective role against the disease[4] but due to presence of inherent genetic aberration in such subjects this molecule is not been able to protect the disease[5]. Interestingly reports from Molecular Biology Unit, PGIMER, Chandigarh, INDIA show that vitamin C and statins increases the expression of LXR[6], whereas vitamin D3 can serve as an alternative ligand for the aberrant form of LXR-α and thus can restore its functional abnormality[7]. Further statins which are the best drug of choice to treat cardiovascular patients, also increases the serum vitamin D3 level and thus they serves to increases the expression as well as provides the functional ligands for aberrant LXR-α[7]. The observation also supports to the fact that low level of vitamin D3 is associated with higher risk of coronary heart disease[8]. Withaferin A which is a dietary component isolated from Withania somnifera also act as a ligand for LXR-α[5]. Thus by altering the dietary components, which may facilitate LXR-α activation can lead to regression in the development of cardiovascular diseases.

Withania somnifera is classified in Ayurveda (ancient Hindu system of medicine) as a *rasayana*, a group of plant-derived drugs reputed to promote physical and mental health, augment resistance of the body against disease and diverse environmental factors, revitalizes the body in debilitated conditions and increases longevity[9,10]. Interesting reports from molecular biology unit at PGIMER, Chandigarh, INDIA shows that exposure of neuroblastoma cells with LXR agonist like Withaferin A and 24(S) hydroxycholesterol connects LXR-α activation with the genes recognised to be involved in the regulation of aberrant beta amyloid production leading to the generation of toxic and inflammatory mediators responsible for neuronal death, a hallmark of Alzheimer disease[11]. This fact is correlated by the observation that cerebrospinal fluid of Alzheimer's patient possesses increases 24(S)-hydroxycholesterol compared to healthy controls[12].

CONCLUSION

Thus the findings have not only forced us to explore nutritional genomics as a holistic systems approach to understand the relationship between diet and health, but also to look into the disease preventing and health promoting foods that match our lifestyles, cultures and genetics. After all, we are what we eat.

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