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Review Article

Do Genes Dictate Our Nutrient Needs?

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Abstract

The greatest wealth that one can ever earn is good health! In the recent years, one of the best aspects of health care reform is that it has started to emphasize on prevention, especially through lifestyle interventions. Gene-nutrient interactions epitomize the synergy of genetics and lifestyle in deciding health outcomes. 'One size fits all' approach to lifestyle recommendations leaves a gap which stands miles away from best desirable results for an individual. Hence, the need of the hour is a personalized health care approach focusing on gene-based lifestyle modifications. Personalized healthcare approach innovatively defines disease prevention through the indulgence of nutrigenetics. Nutrigenetics, a field of Life Science identifies an individual's genetic susceptibility to diseases and emphasizes the vital role of genetic variation in affecting nutrient intake. The effect of dietary factors on health status has been recognized since antiquity. Food and its components directly or indirectly influence gene expression. Genetic predispositions in turn dictate unique dietary needs and requirements. A small genetic change, or variation, that occurs within the DNA sequence can have an impact on nutrient metabolism. Genetic information in relation to a nutrient metabolism has relevance to health conditions [1-8].

Keywords: Nutrigenetics; Genetic Predisposition; Gene-Nutrient Interaction; Genetic Make-Up; Genetic Expression

Introduction

Genetic make-up and lifestyle occupy equal shares in any health outcome. Hence, recommendations for health betterment should be tailor-made suiting the person's tolerance/acceptance to dietary components based on his genes. Right Food and right exercises are subjective to your genetic make-up! Let's understand this better with the following examples.

Discussion on examples signifying gene-nutrient interactions in health outcome

Weighty concerns can be effectively addressed through gene-nutrient interactions

Genetic risks may be offset by favorable changes in lifestyle. For instance, your meal pattern, meal timings and even the type of snacks can be recommended to suit you the best if you understand the pattern of genes like FTO, LEP, LEPR and CCK which influence appetite, meal quantity, satiety response and the urge to snack. Individuals carrying a variation in such genes tend to have a difficulty in following proper meal timings and meal quantities and thereby they are likely to overeat [9]. Generally, a balanced diet with adequate dietary fiber, and healthy snacks timed appropriately is proven beneficial in weight control. Further on to this, an insight into nutrigenetics will personalize weight control remedies for people carrying genetic variations in weight-regulating genes. For instance, genetic variations in leptin or leptin receptor genes demand gene-specific nutrients like omega-3 fatty acids and zinc [10]. Another good example is PPARG gene, which is a vital regulator of carbohydrate and fat metabolism. Variations

in this gene may influence the type of macronutrient that has to be restricted by an individual for his weight management.

Coffee cups and timings are gene-dependent!

Coffee is the most popular social drink, owing to its refreshing aroma and tiredness-averting qualities. Caffeine, the component responsible for giving us alertness or briskness on consuming coffee/tea is a non-nutrient. And hence an enzyme present in our liver, CYP1A2 (cytochrome enzyme P-450 1A2) takes up the responsibility of eliminating caffeine from our body. Based on the efficiency of this enzyme, caffeine gets eliminated at varying timelines (say 3 to 6 hours) in each of us, making us fast or slow metabolizers. This inter-individual difference is caused by variations in the CYP1A2 gene which encodes the caffeine-metabolizing enzyme. Low CYP1A2 activity due to an unfavorable genetic change has been associated with higher caffeine toxicity (caffeine gets retained for an unusually longer time), increasing the risk for caffeine-associated health disturbances like sleep deprivation, anxiety, high blood pressure, palpitation, and heart ailments [11,12]. For instance, extra two cups of coffee could potentially increase the systolic and diastolic BP by around 8 mmHg and 6 mmHg in a slow metabolizer [13]. An insight on our genetic make-up, can help us prevent caffeine-related health disturbances by alternating that extra cup of coffee with another refreshing beverage. A cup of coffee contains approximately 96 mg of caffeine. Generally, healthy adults can tolerate up to 400 mg of caffeine in a day which equates to 2-3 cups of coffee/tea [14]. But in slow metabolizers of caffeine, recommendations are revised to below 100 milligrams of caffeine in a day amounting to 1 cup of coffee/2 cups of tea [15]. Additionally nutrigenetic recommendations insist on the avoidance of vegetables like carrot, celery, parsley and parsnip for at least an hour after caffeine intake as they can slow down caffeine metabolism [16]. On the contrary, cruciferous vegetables increase the rate of caffeine metabolism; consuming 500g of broccoli can increase caffeine elimination from our body by upto 1.2 times, thus minimizing its ill effects [17,18].

Sleep is the best and easiest meditation and we all love it. Its importance in health is so pronounced that we should act promptly even if we miss a bit of it. Sleep inadequacy can have its root cause in caffeine metabolism. Caffeine being a brain-stimulant, we use it after waking up in the morning or to remain alert during the day. Caffeine makes us feel alert by blocking certain sleep-inducing chemicals in the brain. Adenosine is one such sleep-inducing chemical that our brain produces and keeps accumulating during our waking hours. The more it builds up, the sleepier we become towards the end of the day. When caffeine blocks this process, we remain alert and vigilant. Adenosine build-up also relates with our circadian rhythm or sleep-wake cycle, wherein the darkness of night and adenosine build-up induce sleep. Caffeine can impact the onset of sleep and reduce the sleep quality. Caffeine-interrupted sleep can lead to sleep deprivation the following day, which will show up as fatigue and problems with learning, memory and problem-solving. The Adenosine receptor gene, ADORA2A, regulates the adenosine levels in brain which makes us aware of the sleep timings. Unfavorable changes in this gene can impact sleep, especially in slow caffeine metabolizers. And hence caffeine intake should be managed accordingly. Favorable genetic expression reduces the probability of caffeine-induced sleep disturbances and hence avoidance of caffeine-containing foods and beverages nearly 6 hours prior to sleep is sufficient. While individuals who are predisposed to caffeine-induced sleep disturbances due to unfavorable genetic changes are recommended to avoid the consumption of caffeine-containing foods and beverages for at least 8 hours prior to their sleep [19-21].

Fitness can be enhanced through nutrigenetics!

Nutritional recommendations based on genetic insights have also carved a niche in the area of fitness. Gene-based nutritional recommendations can elevate the ease with which you perform your activities, alongside improving your exercise response in terms of health benefits. For instance, while exercising if you feel breathless or if your muscles get fatigued very soon, then, there may be genetic reasons [22]. For instance, Peroxisome proliferator-activated receptor α (PPARA) gene regulates body's adaptive response to exercise by facilitating more energy fuel provision to the target organ and improves energy utilisation by muscles during exercise. A variation in this gene relates to sub-optimal energy utilization in muscles and hence makes its carrier more prone to fatigue and tiredness while doing exercise [23,24]. Similarly, Adenosine-mono-phosphate-deaminase 1(AMPD1) encodes the AMPD1 enzyme which actively participates in the catabolism of adenine nucleotide. When muscles use up energy during physical activity, the energy molecule AMP (Adenosine monophosphate)

needs to be converted to IMP (Inosine monophosphate). The accumulation of AMP in muscle causes muscle pain and weakness, a sign of fatigue. AMPD1 gene supports AMP degradation to IMP thus diminishing muscle fatigue. A variation in this gene is associated with sub-optimal activity of AMPD1 enzyme, thus posing a risk for AMP accumulation in exercising muscle and consequently spasms, tiredness and muscle pain after training sessions [25].

To cope with such genetic variations, a start slow and steady approach along with adequate rest periods prove remedial. Additionally, gene-specific nutrients like Coenzyme Q10 or CoQ10 and magnesium can improve your oxygen utilization capacity thereby averting breathlessness. CoQ10 is a cofactor for mitochondrial uncoupling proteins and serves as an integral component of the mitochondrial oxidative phosphorylation system. Its primary dietary sources include oily fish (such as salmon and tuna), organ meats (such as liver), and whole grains [26-35]. Magnesium is critical for basic mitochondrial functions, including the production of ATP, and confers a protective role to skeletal muscle mitochondria. Magnesium increases glucose availability in muscle tissue and favours lactate clearance from muscle [36-42].

Similarly, if post-exercise muscle pain disturbs your regularity of physical activity then it might be related to a genetic reason as well. Genes like COL5A1 (encoding type 5 collagen), COL1A1 (encoding type 1 collagen) and GDF5 (encoding growth differentiation factor 5) have a crucial role in maintaining ligaments and tendons in proper health [25,43]. As ligaments and tendons are natural lubricants that are essential for flexibility, genetic variations in such genes may cause exercise-induced muscle injury or tendinopathy [44]. This genetic variation can be managed and your exercise can be regularized with collagen-strengthening dietary components like anthocyanins, glutathione, vitamin C and certain amino acids like Methionine, Cysteine and Taurine. Flexibility-improving fitness recommendations such as proper pre and post exercise stretching, and random exercising of different muscle groups can also prove beneficial [45-47].

The degree of flexibility helps in determining how well an individual can adapt to his workout based on his propensity for developing swelling and inflammation in joints after exercise [48,49]. Sometimes the delay that you witness in recovering from exercise-induced stress and strain may affect your exercise regimen. This again has an association with genes like TNFα, IL6, CRP, amongst others [50]. Variations in these genes can disrupt the balance between pro and anti-inflammatory markers, prolonging exercise-induced inflammation for undesirably longer. Nutrigenetic recommendations focus on dietary components like omega-3 fatty acids and probiotics which have anti-inflammatory benefits and thus can hasten recovery [45-47]. Longer rest periods in between exercises are also helpful along with intake of Branched chain amino acids (BCAA) including leucine, isoleucine and valine. In athletic community, BCAA gained particular interest since they can stimulate protein synthesis in the muscle [51,52].

The gene-nutrient interplay in autism

Autism is a complex developmental disability characterized by abnormalities in spoken language, socialization and repetitive behaviours. Autism has a link with Advanced Glycation End (AGE) Products, which are intrinsic stressors to the cell causing cell damage. They should be metabolized and degraded by the enzyme Glyoxalase 1(GLO1) which is encoded by the GLO1 gene. High levels of GLO1 expression is seen in Purkinjie, hippocampal pyramidal, and dentate gyrus cells to keep our brain in prime health. Unfavorable variations in GLO1 gene reduce the enzyme activity causing an accumulation of AGE products in the brain of individuals with autism. Glyoxalase 1 is a zinc metalloenzyme; hence this gene-specific nutrient (zinc) provided through dietary sources improves the activity of GLO1 in individuals who carry a variation in this gene. For instance, the 'A' allele of rs2736654 and rs1130534 in GLO1 gene results in reduced enzyme (GLO1) activity implying an increased cell damage due to Glycation [53,54].

The glyoxalase pathway functions to detoxify reactive dicarbonyl compounds, most importantly methylglyoxal. Methylyglyoxal (MG) is partly responsible for harmful protein alterations in living cells, notably in neurons, leading to their dysfunction, and recent studies have shown a negative correlation between GLO1 expression and tissue damage. The glyoxalase pathway is an antioxidant defense mechanism that is essential for neuroprotection. Excessive concentrations of methylglyoxal have deleterious effects on cells, leading to increased levels of inflammation and oxidative stress. Neurodegenerative diseases – including Alzheimer's, Parkinson's, Aging and Autism Spectrum Disorder – are often induced or exacerbated by accumulation of methylglyoxal. Antioxidant compounds possess several distinct mechanisms that enhance the glyoxalase pathway and function as neuroprotectants. Flavonoids

are well-researched secondary plant metabolites (commonly found in fruits and vegetables) that appear to be effective in reducing levels of oxidative stress and inflammation in neural cells. Glutathione is a major constituent of the glyoxalase pathway, and one of the most important endogenous antioxidants for neutralization of dicarbonyl compounds and maintaining redox balance in cells [55].

Conclusion

Our Genes and Nutrients are age-old friends! So let's value individualized nutrient needs based on genetic make-up, and ensure right food choices are just right for you. Individuals cannot change their genetics, but they can eat the right foods to support genetic predispositions.

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