

A trip to the nutrigenetics of Hyperhomocysteinemia

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Introduction

Nutritional genomics is a science studying the interactions existing between genes and diet to prevent diseases through nutrition. It includes nutrigenomics and nutrigenetics, which have become a powerful tool of preventive medicine. For its part, nutrigenetics focuses on studying how individual differences in genome cause different responses compared to food, and it analyzes how, these genetic variants confer a susceptibility to certain diseases, trying to prevent them through personalized nutrition.

From the perspective of the nutrigenetics, the study of Hiperhomocysteinemia (HHcy) becomes interesting because it is an independent risk factor for cardiovascular diseases (CVD), which are the leading cause of death in Spain. Genetic defects in MTHFR and CBS genes, among others, and deficiencies in certain vitamins, such as vitamin B6, B9 and B12 can cause HHcy since they are involved in homocysteine (Hcy) metabolism as enzyme cofactors.

Key words: CBS; hiperhomocysteinemia (HHcy); homocysteine (Hcy); nutrigenetics; MTHFR; Vitamin B₆; Vitamin B₉; Vitamin B₁₂

Hcy metabolism¹

Hcy is produced in all cells as an intermediate of the methionine cycle. Once formed, Hcy is catabolized via two metabolic pathways: remethylation, to form methionine and transsulfuration, resulting in cysteine (Fig. 1).

Under normal conditions, among 40-50% of Hcy is remethylated, between 40-50% is converted into cysteine, and a small amount is exported. When there is an increase in the production of Hcy or a decrease in its catabolism, it results in an excess of Hcy export to the extracellular space, leading to HHcy.

Nutrigenetics of HHcy

Genetic factors determining of HHcy³

- CBS deficiency*
- MS deficiency*
- MSR deficiency*
- MTHFR deficiency*
- MTHFR 677TT genotype
- MTHFR 129CC genotype

*Involved in homocystinuria pathogenesis.

Nutritional factors

Deficiencies in three B-group vitamins have been reported to cause HHcy^{4,5}:

- Deficiencies in vitamin B6 (PLP) and methionine supplementation functioned synergistically to cause an accumulation of tHcy because Hcy formation overcome its metabolism.
- Deficiencies in vitamins B9 (folate) and B12 (cobalamin) also cause increase of tHcy levels. Vitamin B12 deficiency is the main cause of HHcy in vegan people.

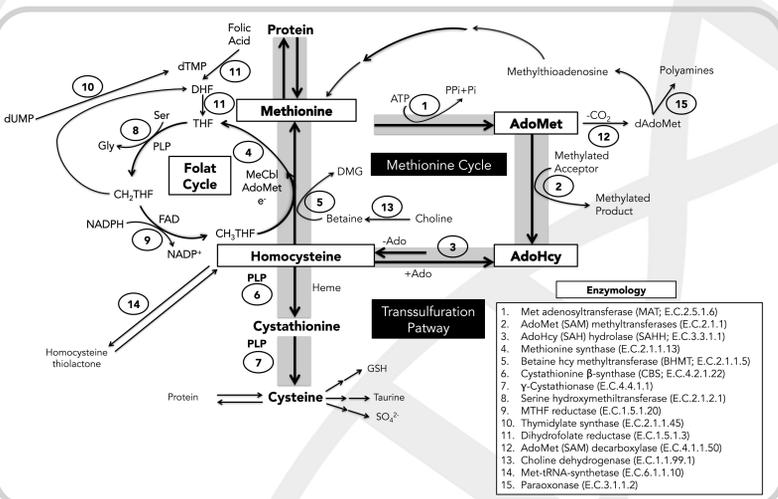
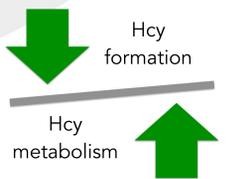


Fig.1. Homocysteine metabolism in liver and kidney¹.

MTHFR 677TT genotype

Most common genetic defect associated with moderate HHcy

CBS 844ins68 genotype

Protective effect of 844ins68 in heterozygous individuals

Pathophysiology of HHcy

High levels of Hcy cause adverse effects on cells due to⁵:

- Inducing oxidative stress by generating Reactive Oxygen Species (ROS);
- Altering gene expression;
- Increasing stress in the endoplasmic reticulum;
- Activating the biosynthesis of cholesterol.

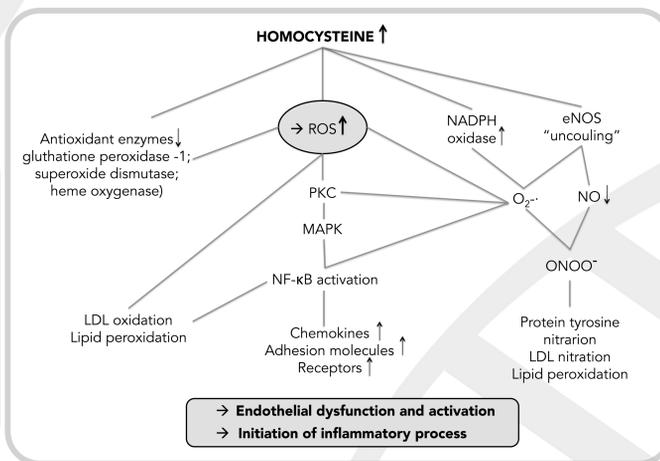


Fig. 2. HHcy leads to induce endothelial dysfunction and initiate inflammatory processes².

Elaboration of genetic profile

Obtaining a DNA sample

Genotyping DNA chip

Evaluation of genetic variants

There is an increasing number of centers and laboratories that perform nutritional genomics studies:

- A search of the most convenient choice according to our needs has to be performed.
- The scientific reliability of the center should be always be reviewed.

Elaboration of personalized diet

Materials & Methods

Creation of a blog

- Publications
- "La genètica, una ciència desconeeguda?"
 - "La genòmica nutricional, un pilar base de la medicina preventiva"
 - "La hiperhomocisteinèmia i la seva nutrigenètica"
 - "On puc realitzar-me un estudi nutrigenètic?"



Expected Results

After the creation of the information campaign aimed to both the general population and populations at risk of CVD, it is expected to:

- Have an overview of the importance of advances in genomics.
- Recognize nutrigenetics as a key tool in preventive medicine.
- Know the main aspects of HHcy and their relationship with CVD.
- Acquire the ability to evaluate nutrigenetic services currently offered.

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