

Prenatal Vitamins, One-carbon Metabolism Gene Variants, and Risk for Autism

Epidemiology

July 2011 Volume 22, pp. 476–485

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BACKGROUND FROM DAN MURPHY (super simple):

[mainly from The H Factor Solution by James Braly, MD, 2003, and my memory]

A methyl group is a carbon atom with 3 hydrogen atoms: -CH₃

Methylation denotes the addition of a methyl group to a molecule.

Embryonically, proper methylation of the genome is critical for gene expression and to knockout genetic mutations.

Methylation is critically important in the genetic development of the brain.

Approximately a third of DNA mutations that cause disease are attributed to problems in methylation.

Homocysteine is an amino acid, but it is not involved in creating protein.

Homocysteine was discovered in 1962.

Elevated levels of homocysteine are very bad for us.

High homocysteine levels means your genes are more vulnerable to damage and they are poorly repaired once damaged.

High homocysteine levels are a marker for premature aging, all cause mortality, and oxidative stress (free radical damage), and about 100 diagnosed diseases.

The KEY is methylation. Methylation is a process that is absolutely vital for the brain.

We get rid of homocysteine by adding a methyl group to it.

Adding a methyl group to homocysteine requires optimum levels of vitamins B6, B12, folic acid, and the mineral zinc.

Methylation of homocysteine does 2 important things for us:

- 1) It gets rid of a very bad molecule for human physiology and health.**
- 2) It initiates the process of converting homocysteine into very good molecules for human physiology and health, including glutathione, serotonin, melatonin, dopamine, and others.**

Glutathione is the key to our health. It functions as our most powerful detoxifying molecule and as our master endogenous antioxidant.

[Glutathione, The Key to Our Health, Jimmy Gutman, MD, 2008]

We have seen several studies linking low levels of glutathione to autism.

FROM ABSTRACT:

Background: Causes of autism are unknown. Associations with maternal nutritional factors and their interactions with gene variants have not been reported.

Methods: Northern California families were enrolled from 2003 to 2009 in the CHARGE (CHildhood Autism Risks from Genetics and Environment) population-based case-control study. Children aged 24–60 months were evaluated and confirmed to have autism (n 288), autism spectrum disorder (n 141), or typical development (n 278) at the University of California–Davis Medical Investigation of Neurodevelopmental Disorders Institute using standardized clinical assessments.

We calculated adjusted odds ratios (ORs) for associations between autism and retrospectively collected data on maternal vitamin intake before and during pregnancy.

We explored interaction effects with functional genetic variants involved in one-carbon metabolism as carried by the mother or child. [7 specific genes]

Results: Mothers of children with autism were less likely than those of typically developing children to report having taken prenatal vitamins during the 3 months before pregnancy or the first month of pregnancy (38% less).

Conclusions: Periconceptional use of prenatal vitamins may reduce the risk of having children with autism, especially for genetically susceptible mothers and children.

KEY POINTS FROM THIS ARTICLE

- 1) “Autism is a neurodevelopmental disorder defined by the presence of impaired social reciprocity, abnormal communication, and restricted interests or repetitive behavior, with symptoms apparent by 3 years of age.”
- 2) Autism affects about 1 in 110 children in the US and its incidence is rising.
- 3) The rise in autism cannot be wholly genetically explained and therefore there must be interactions between susceptibility genes and environmental factors.
- 4) Short intervals between pregnancies has been linked to autism, which “suggests that nutritional factors could play a role.”
- 5) Folic acid and other B vitamins are critical for neurodevelopment. Disruption of folic acid metabolism can induce autism, and this neuropathology may originate early in pregnancy (specifically, the first trimester).

- 6) "Some children with autism have altered B vitamin metabolism and reduced methylation capacity." Studies have linked autism with functional gene variants that alter folic acid metabolism and methylation (a function requiring folic acid).
- 7) "Mothers of children with autism were less likely to report having consumed prenatal vitamins than mothers of typically developing children during all months examined, especially during the 3 months before and the first month of pregnancy."
- 8) Prenatal vitamin use during the 3 months before and the first month of pregnancy was associated with lower risk for autism by 38%. "No associations were observed for intake during months 2 through 9 of pregnancy."
- 9) Increased frequency of prenatal vitamin intake during the periconceptional period was associated with reductions in autism risk.
- 10) Women who are not planning a pregnancy are unlikely to take prenatal supplements before conceiving.
[Creating an increased risk of that pregnancy leading to an autistic child].
- 11) A report of no periconceptional prenatal vitamin intake was associated with significantly greater risk for autism in the child.
- 12) "No association was observed for reported multivitamin intake during the same period." "Prenatal vitamins typically contain more iron, vitamins B6 and B12 and twice as much folic acid (800 mcg) as multivitamins (400 mcg), to ensure levels adequate to protect against neural tube defects." "Our findings could therefore reflect the higher concentrations of certain nutrients in prenatal vitamins, which might be needed to substantially reduce risk" of autism. **[Important]**
- 13) Mothers who took folic acid-containing supplements before/during the first trimester have children with fewer behavioral problems, improved verbal scores, social competence, and attention measures, and reduced hyperactivity and peer problems.
- 14) "Iron or B vitamins other than folic acid are also essential for neurodevelopment, and are present at higher levels in prenatal vitamins as compared with multivitamins."
- 15) "Folate and other dietary methyl donors (betaine, choline, vitamin B12, and methionine) are vital for methylation of DNA, proteins, phospholipids, and neurotransmitters."
- 16) "Supplementing the periconceptional maternal diet with methyl donors alters epigenetic regulation of gene expression in their offspring in a manner that affects their long-term health."

17) "Maternal periconceptual folic acid increases methylation in specific gene regions of the child."

18) Children with autism and their mothers have impaired methylation capacity that could contribute to the etiology of autism.

19) "Periconceptual folic acid and other B vitamins may protect against neural tube defects, and possibly autism, through methylation mechanisms."

20) "All maternal gene variants that were associated with greater autism risk in the child in the absence of periconceptual prenatal vitamin supplementation are known to confer less efficient one-carbon metabolism and higher homocysteine levels."

21) "In summary our data suggest that supplementation with prenatal vitamins before pregnancy and during the first month of pregnancy might protect against autism, particularly in genetically susceptible individuals."

COMMENTS FROM DAN MURPHY:

Homocysteine is bad.

Adding a methyl group (methylation) to homocysteine is good.

Aspects of homocysteine methylation are genetically controlled and others are environmentally controlled (primarily through the availability of optimum levels of vitamins B6, B12, folic acid, and the mineral zinc).

Improved periconceptual methylation of homocysteine reduces autism risk.

[Improved methylation of homocysteine elevates glutathione].

[Elevated glutathione reduces autism risk].

Periconceptual supplementation with vitamins B6, B12, folic acid, and zinc improve the methylation of homocysteine, elevates glutathione, and reduces autism risk.

The most beneficial time to supplement with vitamins B6, B12, folic acid, and zinc is prior to conception and during the first trimester.

Multiple vitamin/mineral supplements do not have optimum levels of vitamins B6, B12, folic acid, and zinc and therefore are generally inferior to specific prenatal supplements in reducing the risk of autism.