

AHMEDEL-SOHEMY, PhD

Professor & Associate Chair
Department of Nutritional Sciences
Faculty of Medicine
University of Toronto

Founder & Chief Science Officer
NUTRIGENOMI 

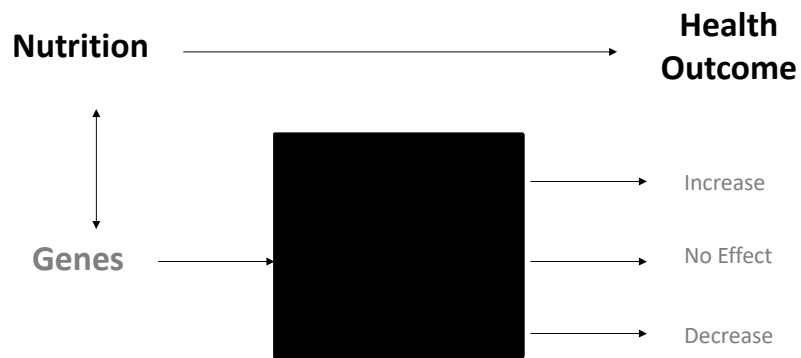
Precision Nutrition and Premenstrual Symptoms

Disclosures

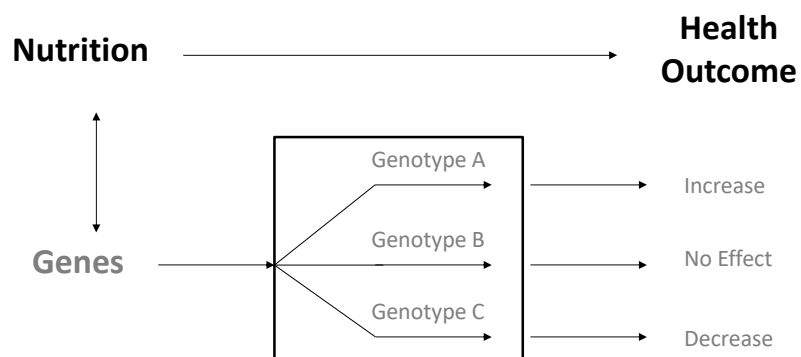
A.E-S. is the Founder and holds shares in Nutrigenomix Inc.

NUTRIGENOMI 

Precision Nutrition



Precision Nutrition



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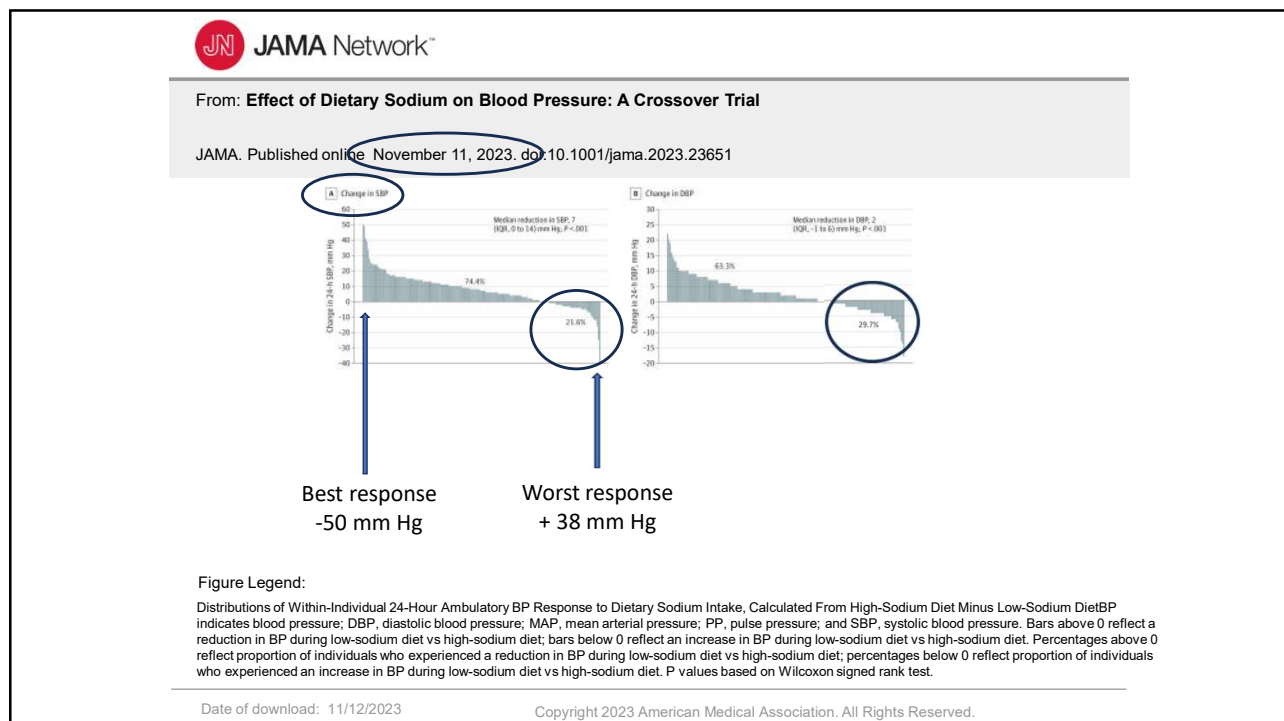
[Newsroom / Search News Releases / Reducing sodium intake significantly lowered blood pressure in as little as one week](#)

Categories: [Scientific Conferences & Meetings](#), [Heart News](#), [Stroke News & Brain Health](#) | Published: November 11, 2023

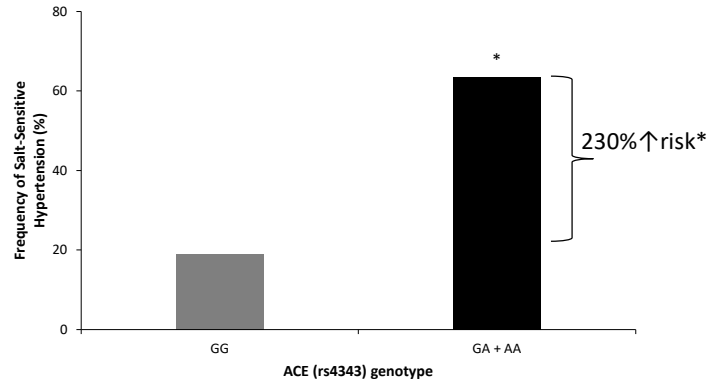
Reducing sodium intake significantly lowered blood pressure in as little as one week

American Heart Association Scientific Sessions 2023, Late-Breaking Science Abstract in LBS.04

Salt
Pile of salt.
copyright American Heart Association



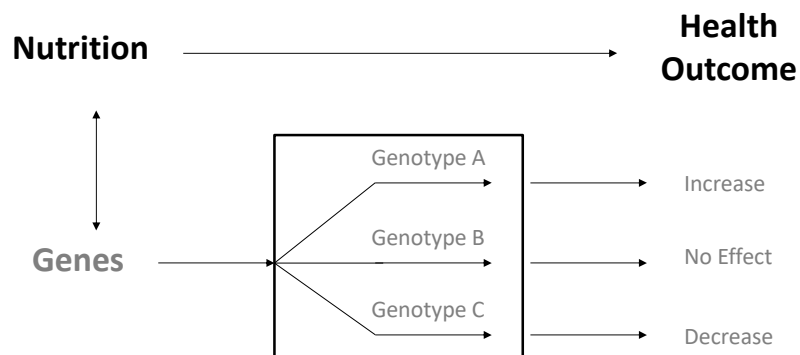
Prevalence of salt-sensitive hypertension by *ACE* genotype



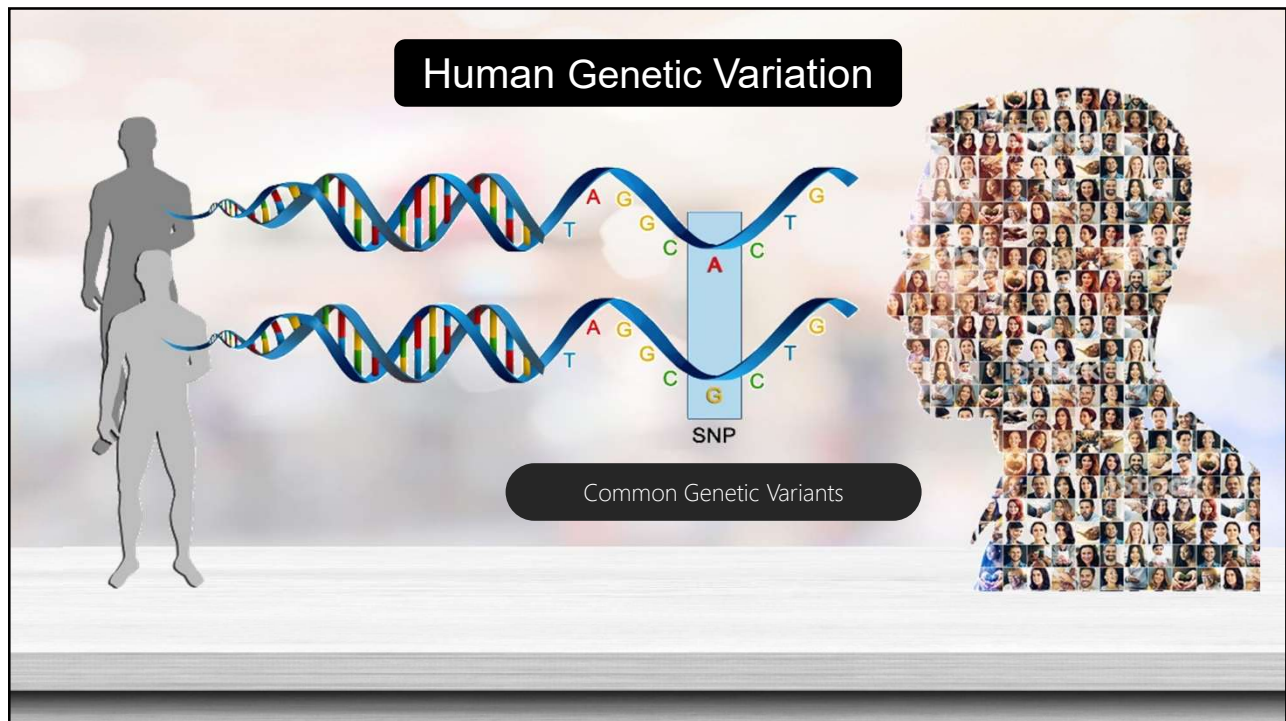
* Relative risk of salt-sensitive hypertension with the GA or AA genotype compared to the GG genotype.

Adapted from Poch et al. Hypertension. 2001;38:1204-1209.

Precision Nutrition



One size does not fit all



Coffee, CYP1A2 Genotype, and Risk of Myocardial Infarction

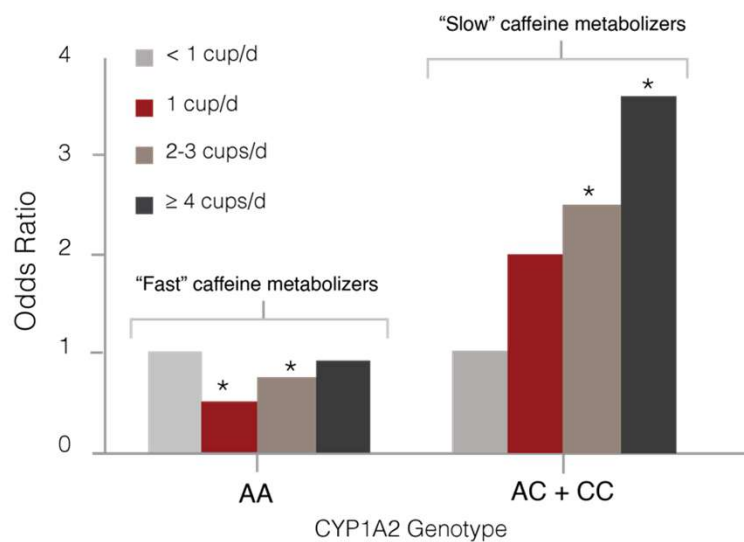
Marilyn C. Cornelis, BSc; Ahmed EL-Soheemy, PhD; Edmond K. Kabagambe, PhD; [et al](#)

Article Information

JAMA. 2006;295(10):1135-1141. doi:10.1001/jama.295.10.1135

JAMA
The Journal of the American Medical Association

Coffee Intake, CYP1A2 & Risk of Myocardial Infarction

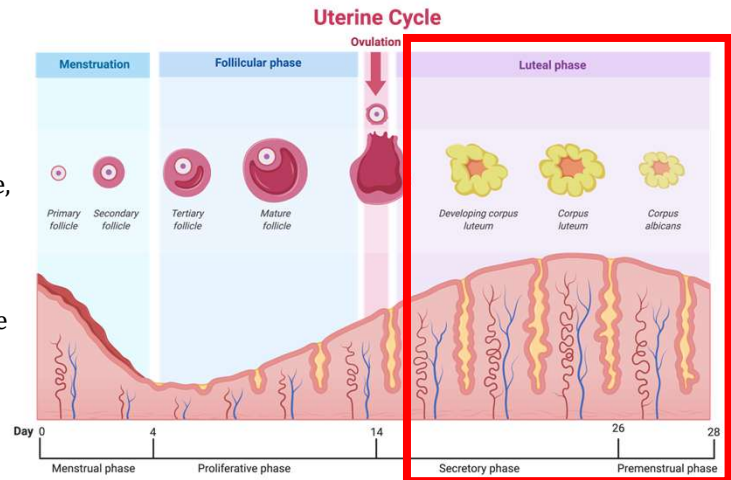


Cornelis et al. JAMA. 2006;295:1135-41.



Premenstrual symptoms (PMSx)

- A collection of somatic and behavioral symptoms that affect women late in their luteal phase
- Common symptoms:
 - Somatic: bloating, headache, fatigue, and muscle cramps
 - Behavioral: anxiety, mood swings, change in appetite, and depression
- ~80% of women experience at least one PMSx



Braverman. *J Pediatr Adolesc Gynecol*, 12(1):3-12. (2007)
Halbreich. *Gynecol Endocrinol*, 19(6):320-334. (2004)

Premenstrual symptoms (PMSx)

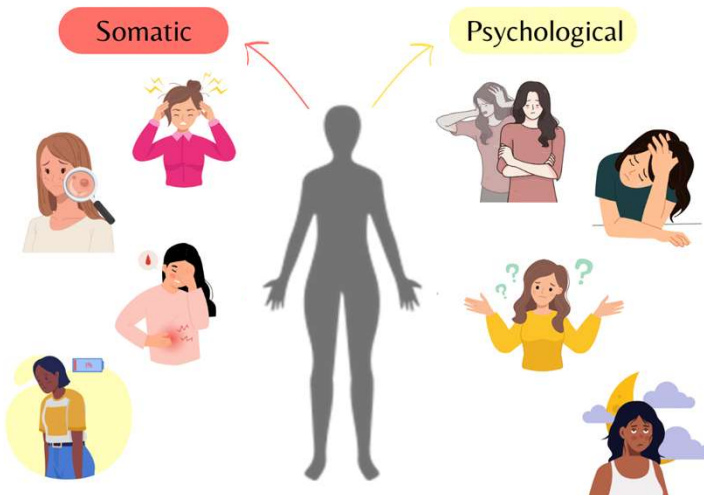


Table 1. Symptoms Associated with Premenstrual Syndrome and Premenstrual Dysphoric Disorder

Physical	Psychological and Behavioral
Abdominal bloating	Anger, irritability
Body aches	Anxiety
Breast tenderness and/or fullness	Changes in appetite (overeating or food cravings)
Cramps, abdominal pain	Changes in libido
Fatigue	Decreased concentration
Headaches	Depressed mood
Nausea	Feeling out of control
Swelling of extremities	Mood swings
Weight gain	Poor sleep or increased need for sleep
	Tension
	Withdrawal from usual activities

Biggs et al. (2011). *American Family Physician*, 84(8), 918-924.

Premenstrual Disorders

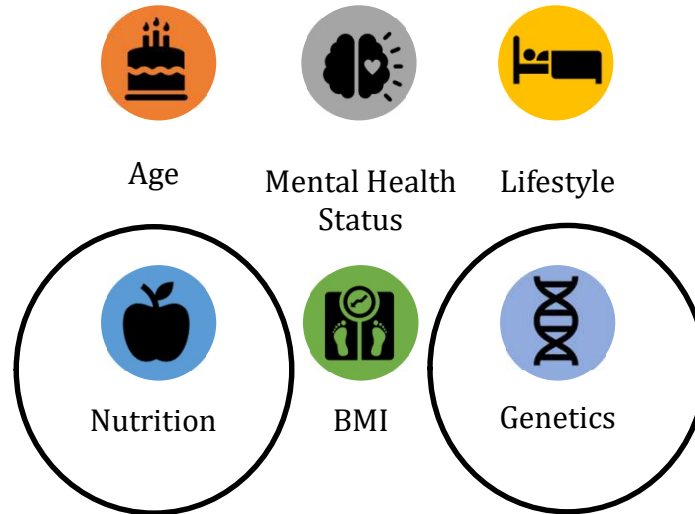
Premenstrual Syndrome (PMS)	Premenstrual Dysphoric Disorder (PMDD)
≥ 1 moderate/severe somatic symptom ≥ 1 moderate/severe affective symptom	A) ≥ 1 moderate/severe symptom: - Depression - Mood swings - Anxiety - Irritability B) ≥ 1 moderate/severe symptom: - Difficulty concentrating - Fatigue - Appetite changes - Insomnia/hyper insomnia - Physical symptoms (bloating, cramps) A + B = ≥ 5 symptoms
- Symptoms identified prospectively for a minimum of 2 menstrual cycles - Disturbance not an exacerbation of symptoms of another disorder	
20-30% of women experience PMS	3-8% of women experience PMDD

ACOG. Premenstrual Syndrome. *ACOG Practice Bulletin*. (2000) DSM. 5th ed. American Psychiatric Association; Arlington, VA. (2013)

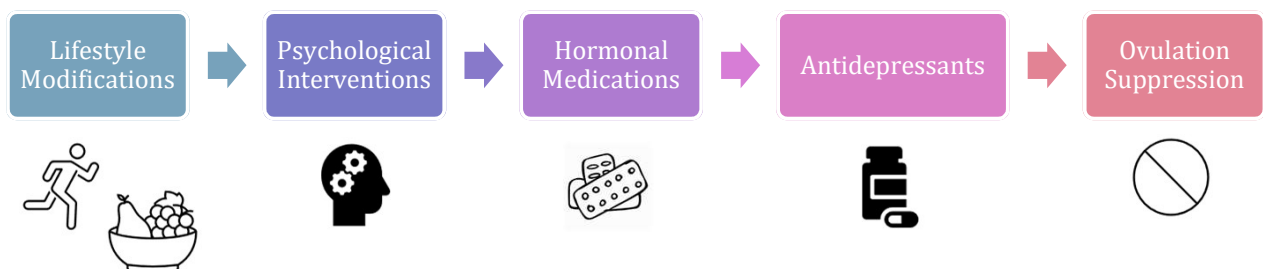
PMS vs. PMSx

- PMS $\neq$ PMSx
- Mechanism of each symptom (ie PMSx) could be unique
- Etiology of one symptom $\neq$ etiology of another

Risk Factors for PMSx



Current Treatment Methods



Micronutrients and PMSx

The American Journal of CLINICAL NUTRITION

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Am J Clin Nutr. 2011 May; 93(5): 1080–1086. PMID: PMC3076657
Published online 2011 Feb 23. doi: [10.3945/ajcn.110.009530](https://doi.org/10.3945/ajcn.110.009530) PMID: 21346091

Dietary B vitamin intake and incident premenstrual syndrome^{1,2,3}

Patricia O Chocano-Bedoya, JoAnn E Manson, Susan E Hankinson, Walter C Willett, Susan R Johnson, Lisa Chasan-Taber, Alayne G Ronnenberg, Carol Bigelow, and Elizabeth R Bertone-Johnson²⁰

Original Article

Obstet Gynecol Sci 2017;60(1):100-105
<https://doi.org/10.5468/ogs.2017.60.1.100>
pISSN 2287-8572 eISSN 2287-8580

Obstetrics & Gynecology Science

Effect of calcium on premenstrual syndrome: A double-blind randomized clinical trial

Fatemeh Shobeiri¹, Fahimeh Ezzati Araste¹, Reihaneh Ebrahimi¹, Ensiyeh Jenabi², Mansour Nazari³

JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION
2019, VOL. 38, NO. 7, 648-656
<https://doi.org/10.1093/ajcn.119.5.648>

REVIEW

The Association Between Vitamin D and Premenstrual Syndrome: A Systematic Review and Meta-Analysis of Current Literature

Arman Arab^a, Sahar Golpour-Hamedani^b, and Nahid Rafie^b

^aDepartment of Community Nutrition, School of Nutrition and Food Science, Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran; ^bDepartment of Clinical Nutrition, School of Nutrition and Food Science, Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

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Toronto Nutrigenomics and Health Study

Study Design

- Cross sectional study of 1,600 individuals launched in 2004
- 915 female participants, 20-29 years old
- Multiethnic population

General Health and Lifestyle Questionnaire

- Medical conditions and medication usage
- Hormonal contraceptive usage patterns (type, how long)
- Physical activity
- PMSx severities

Dietary Assessment

- Toronto-modified 196-item Harvard food frequency questionnaire

PMSx Severity Questionnaire

Symptoms	None	Mild	Moderate	Severe
Acne, skin blemish				
Bloating, swelling, breast tenderness				
Cramping				
Mood swings, crying easily, irritability, angry outbursts				
Increased appetite, food cravings				
Fatigue				
Headaches				
Anxiety, tension, nervousness				
Clumsiness				
Confusion, difficulty concentrating, forgetfulness				
Sexual desire/activity change				
Insomnia				
Nausea				
Depression				
Desire to be alone				
Other (specify) _____				

Absent
Present

Mendelian Randomization



Review

Using Mendelian Randomization to Study the Role of Iron in Health and Disease

Tara Zeitoun and Ahmed El-Sohehy *

Int. J. Mol. Sci. 2023, 24, 13458

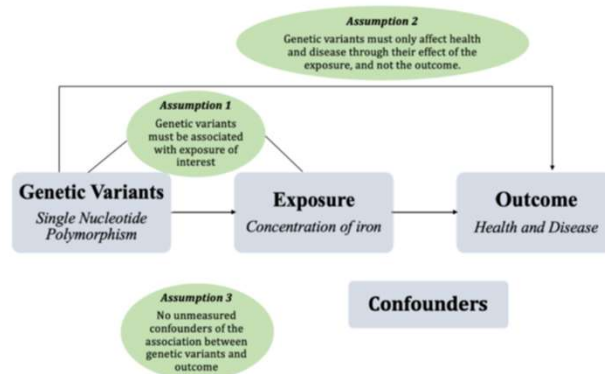
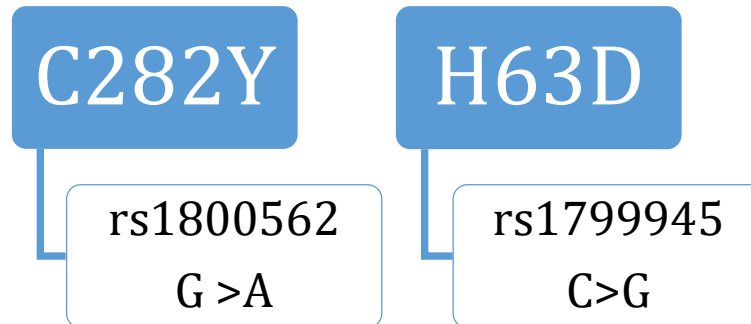


Figure 2. Depiction of mendelian randomization analysis when assessing the role of iron in health and disease.

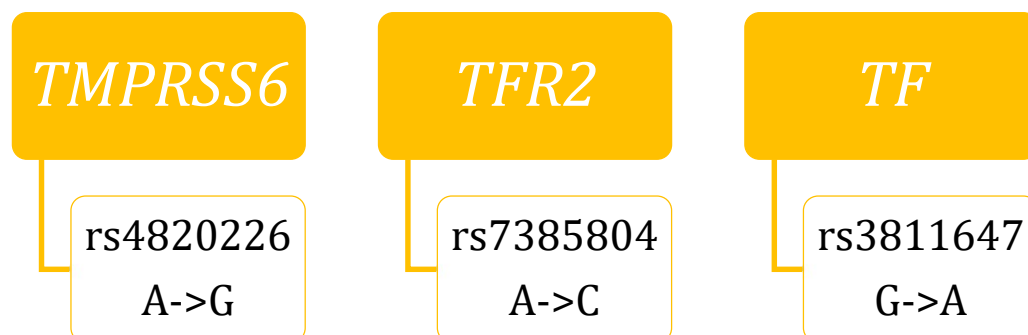
Iron and PMS

SNPs affecting Iron Overload (*HFE* gene)



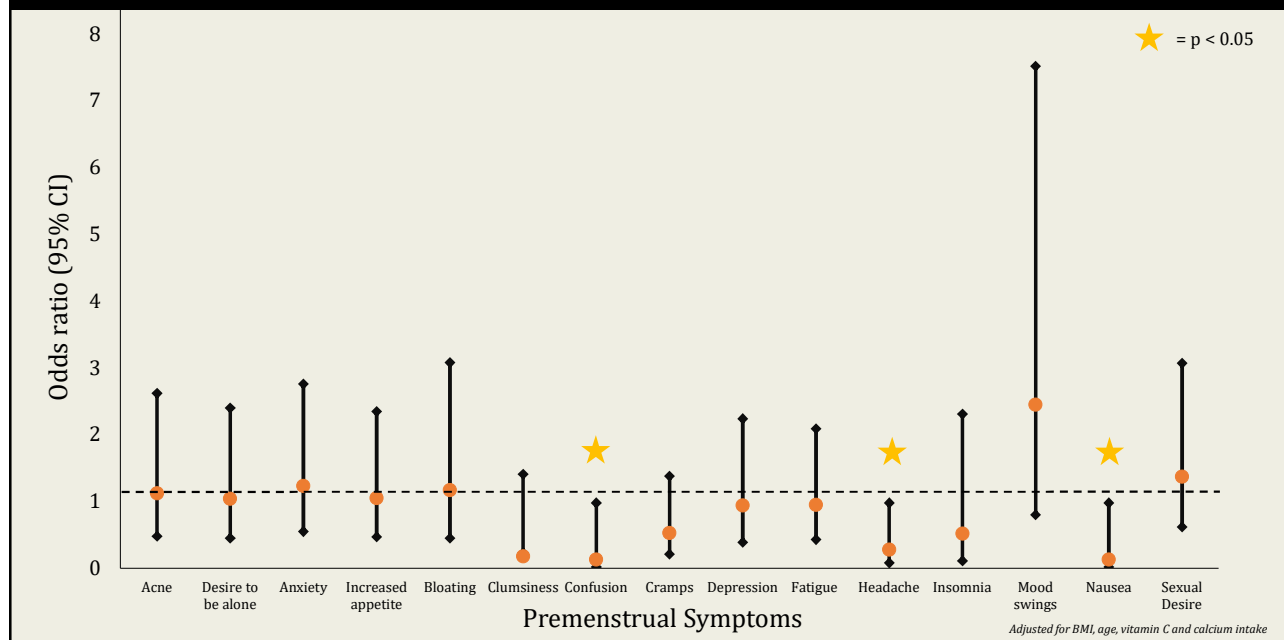
Ganesh, et al. *Not Genet*, 41(11): p.1191-8. (2009)
Merryweather-Clarke, AT., et al. *Genet Test*, 4(2): 183-98. (2000)

SNPs affecting Low Iron Status



Benyamin, B., et al. *Amer J Hum Genet*, 84: p60-65. (2009a)
Pichler, I., et al. *Hum Mol Genet*, 20(6): 1232-40. (2011)

Risk of PMSx with Elevated risk of Iron Overload



> J Nutr. 2021; Jul 1;151(7):1747-1754. doi: 10.1093/jn/nxab048.

Genetics of Iron Metabolism and Premenstrual Symptoms: A Mendelian Randomization Study

Tara Zeitoun ¹, Negar Dehghan Noudeh ¹, Bibiana Garcia-Bailo ¹, Ahmed El-Sohemy ¹

Affiliations + expand

PMID: 33758941 DOI: 10.1093/jn/nxab048

What about other micronutrients?

Vitamin A and PMSx

Nutrients, 2021



nutrients



Article

Plasma carotenoids and premenstrual symptoms in a multiethnic population of young women

Sophia Kerzner ¹, Tara Zeitoun ¹, Alicia Jarosz ¹, Bibiana Garcia-Bailo ¹ and Ahmed El-Sohemy ^{1, *}

- Beta-cryptoxanthin associated with moderate/severe premenstrual increased appetite
- No observed associations between other plasma carotenoids and other PMSx

JOURNAL OF THE AMERICAN NUTRITION ASSOCIATION
<https://doi.org/10.1080/27697061.2023.2186963>

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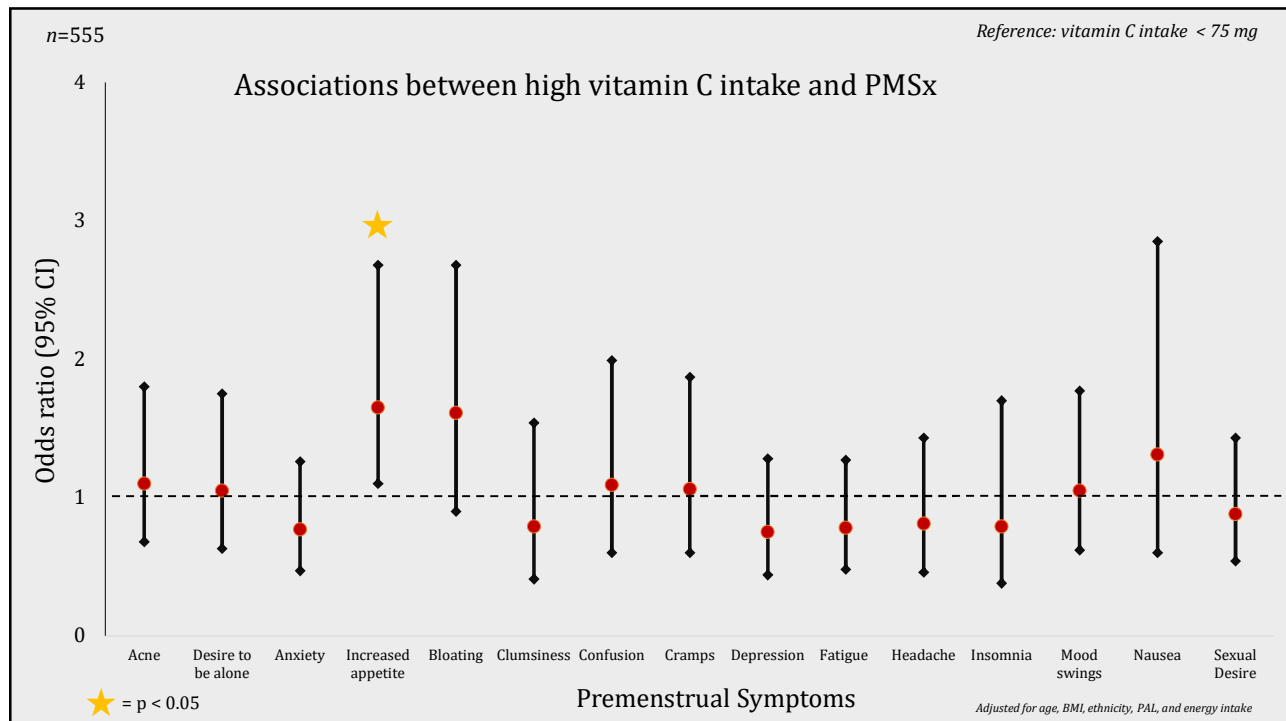
Check for updates

Associations Between Dietary Vitamin C, Serum Ascorbic Acid, and *GSTT1* Genotype and Premenstrual Symptoms

Tara Zeitoun and Ahmed El-Sohehy

Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

To cite this article: Tara Zeitoun & Ahmed El-Sohehy (2023): Associations Between Dietary Vitamin C, Serum Ascorbic Acid, and *GSTT1* Genotype and Premenstrual Symptoms, Journal of the American Nutrition Association, DOI: 10.1080/27697061.2023.2186963



2009

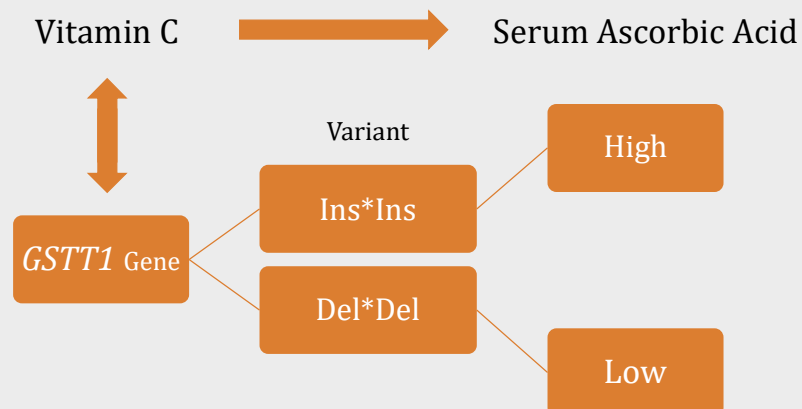
See corresponding editorial on page 1121.

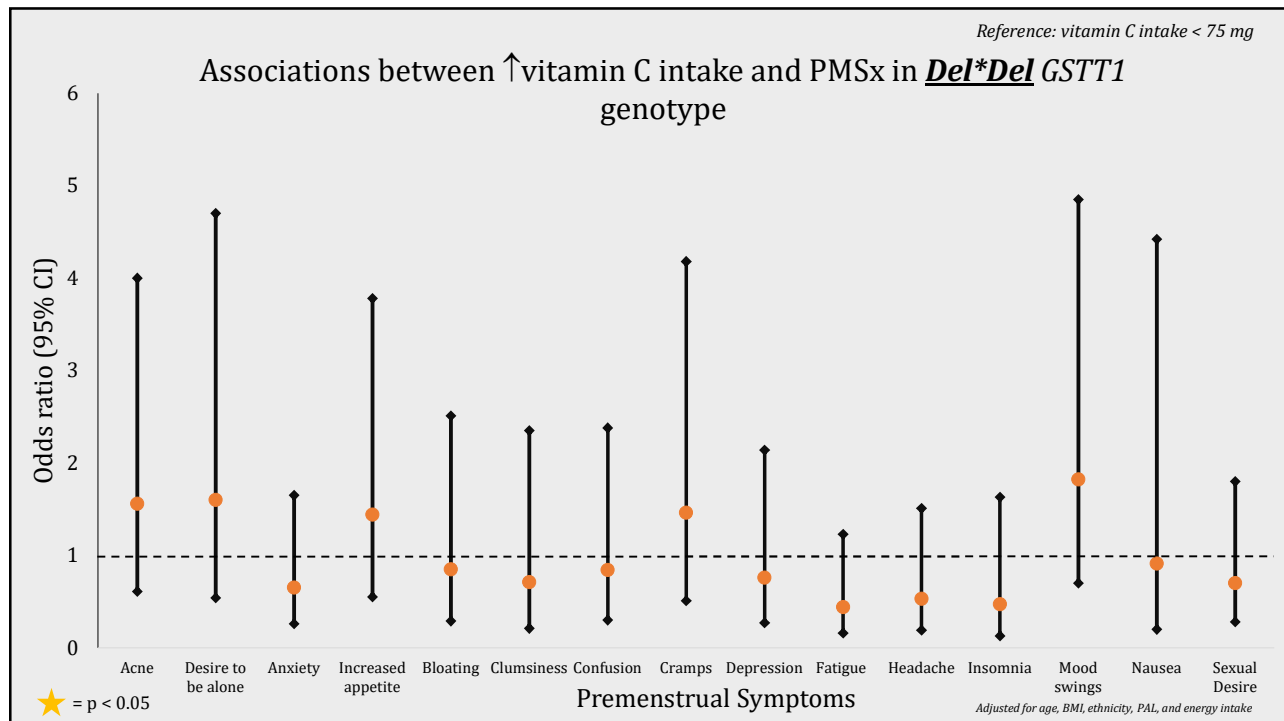
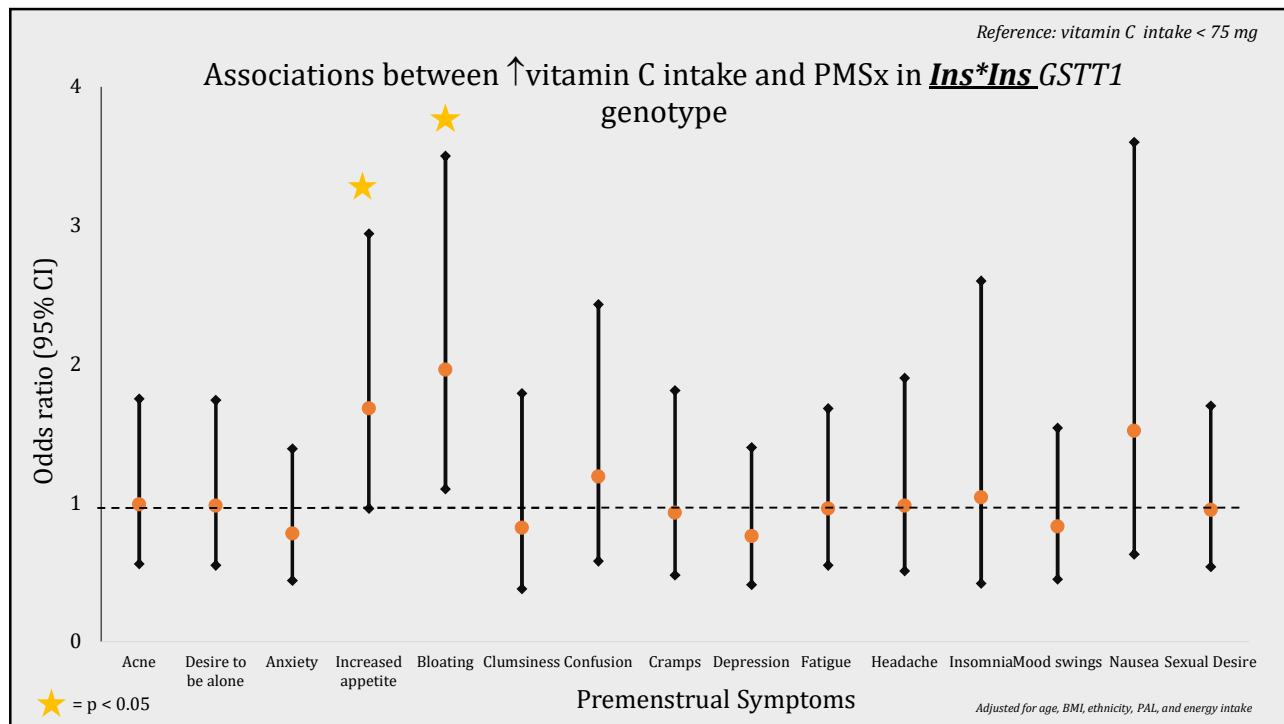
Functional genetic variants of glutathione S-transferase protect against serum ascorbic acid deficiency¹⁻³

Leah E Cahill, Bénédicte Fontaine-Bisson, and Ahmed El-Sohemy

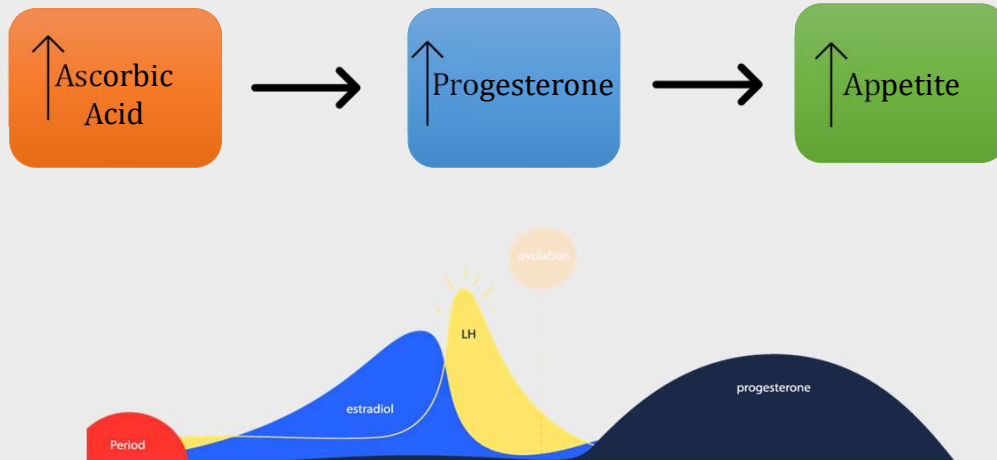
Am J Clin Nutr 2009;90:1411-7.

Genetic Variability in Vitamin C





Potential Mechanisms



Hemni, H et al. *Fertil Steril*. 80(2):459-61 (2003)
 Gorcyca, AM et al. *Eur J Nutr*. 55(3): 1181-8 (2016)

Folate and PMS

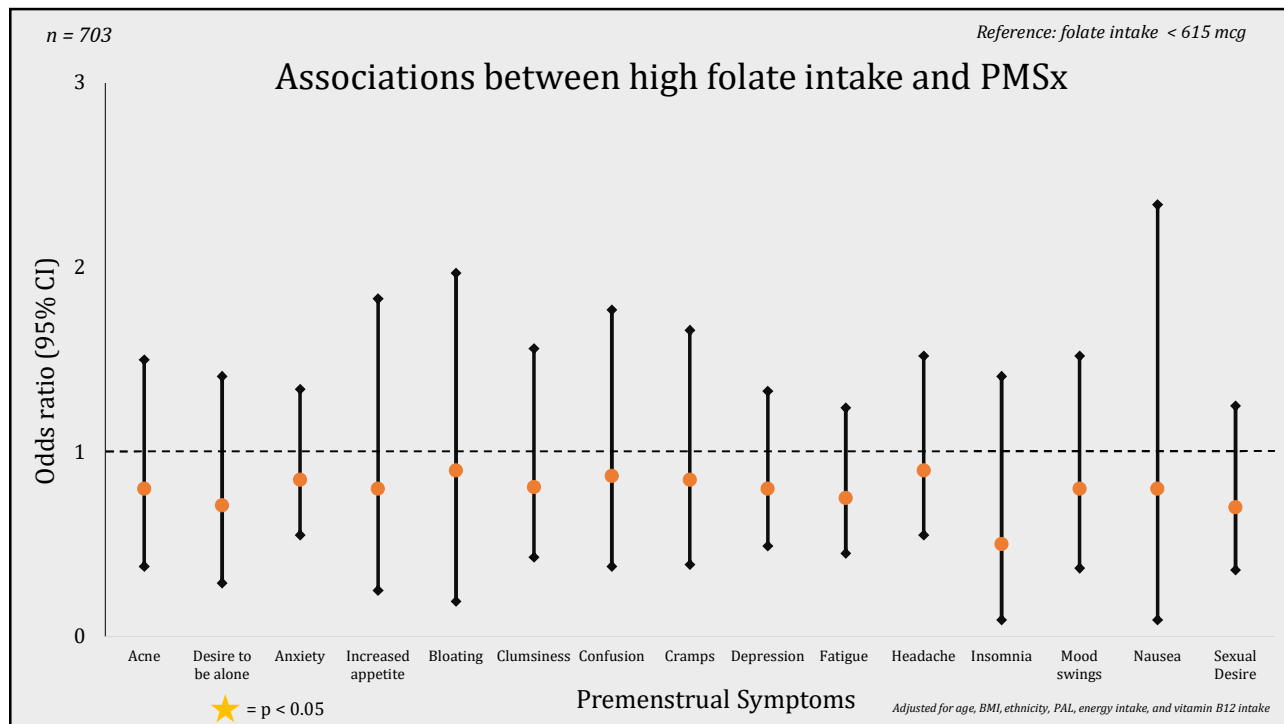
- The role of **folate** from dietary intakes were found to have no associations with PMS¹
 - No studies on genetic variability in folate metabolism

Functions of folate in relation to PMS?

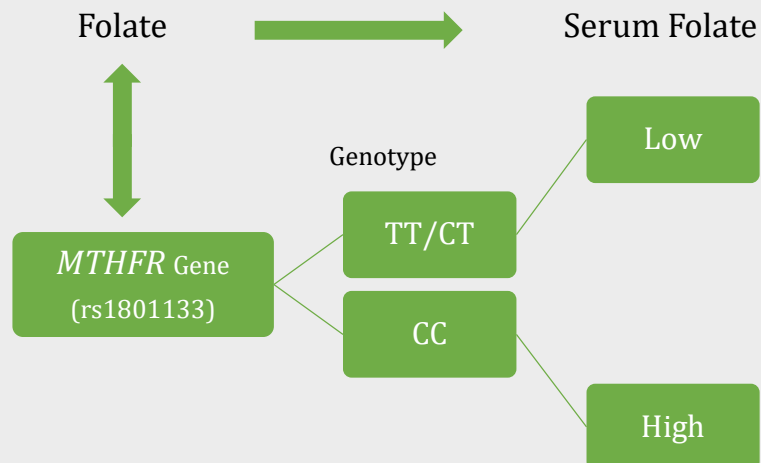
- Folate deficiency → fatigue, irritability, neurological symptoms
- Cofactor required for serotonin and dopamine metabolism²

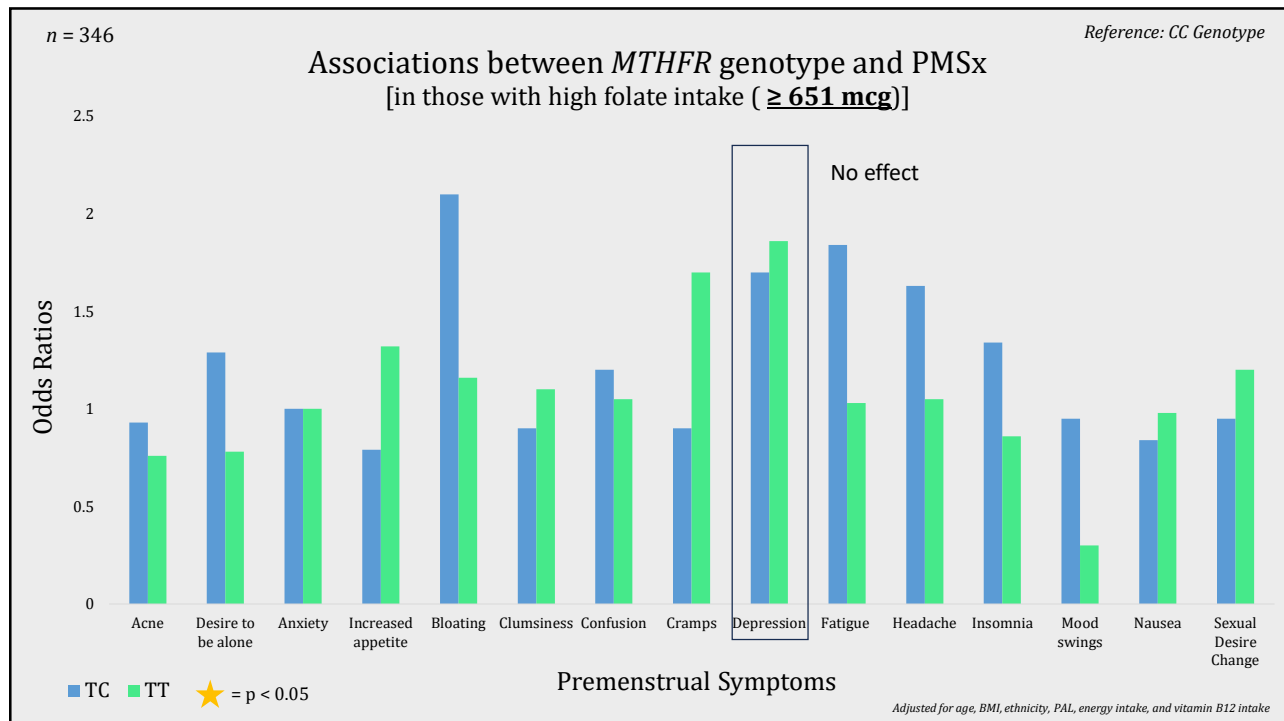
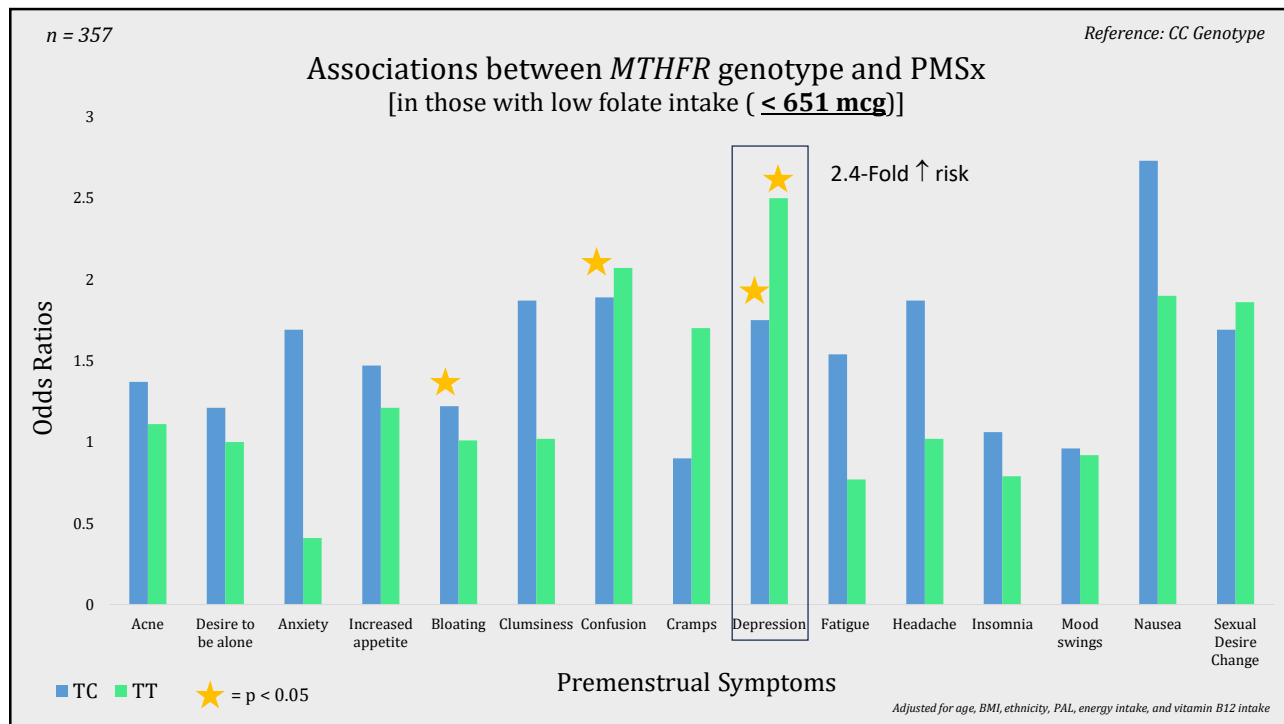


¹Chocano-Bedoya, P et al. *Am J Clin Nutr*. 93(5): 1080-6 (2011)
²Gao, J et al. *Neurotherapeutics*. 15(1): 156-175. (2018)



Genetic Variability in Folate





Potential Mechanisms

- In the brain, folate is involved in production of dopamine, norepinephrine, and serotonin → implicated in depression¹
- British Women's Heart and Health Study (n=3478):
 - Those with TT (vs CC) genotype of *MTHFR* (C677T) 37% more likely to have depression²



¹Bender, A et al. *J Psych Res.* 95, 9-18 (2017).

²Lewis, S.J et al. *Molecular Psychiatry.* 11(4) 352-60 (2006)

British Journal of Nutrition

cambridge.org/bjn

Research Article

Cite this article: Zeitoun T and El-Sohehy A (2025). Folate intake, *MTHFR* genotype and premenstrual symptoms. *British Journal of Nutrition*, page 1 of 11. doi: [10.1017/S0007114525103620](https://doi.org/10.1017/S0007114525103620)

Folate intake, *MTHFR* genotype and premenstrual symptoms

Tara Zeitoun and Ahmed El-Sohehy

Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, ON M5S 3H2, Canada

Abstract

Premenstrual symptoms are a cyclic set of symptoms that affect women's psychological and physical well-being. Growing evidence suggests that micronutrients may contribute to the risk and severity of premenstrual symptoms such as depression. Yet the relationship between folate

Vitamin D and PMS



Journal of the Academy of Nutrition and
Dietetics

Volume 119, Issue 1, January 2019, Pages 115-123



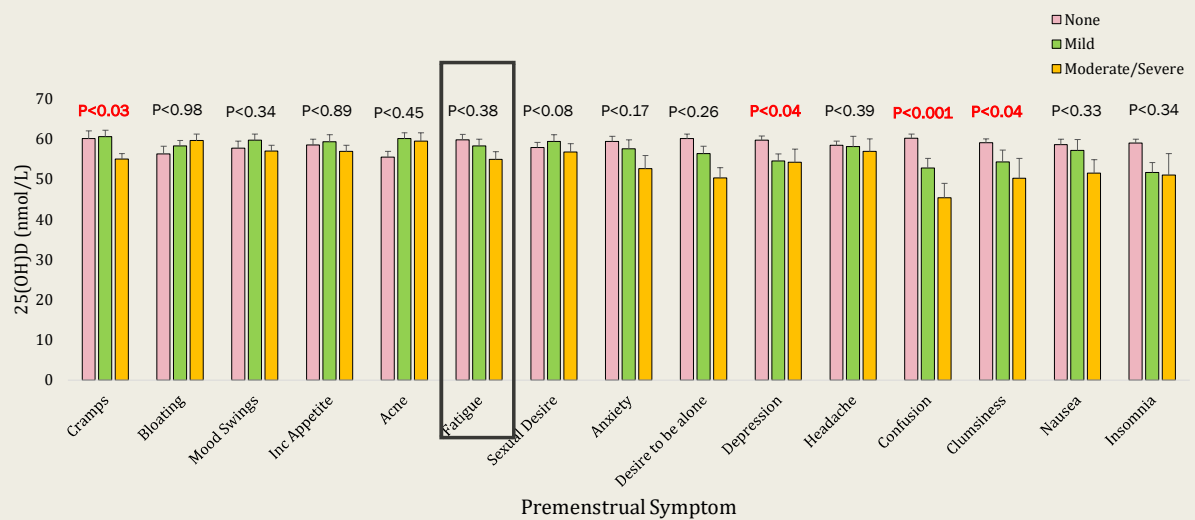
Research

Original Research: Brief

Association between Vitamin D Status and Premenstrual Symptoms

Alicia C. Jarosz MSc, Ahmed El-Sohehy PhD

Association between 25(OH)D and Premenstrual Symptoms



Vitamin D, VDR Genotype and PMS

Jarosz et al. *Genes & Nutrition* (2021) 16:35
<https://doi.org/10.1186/s12263-021-00696-2>

Genes & Nutrition

RESEARCH

Open Access

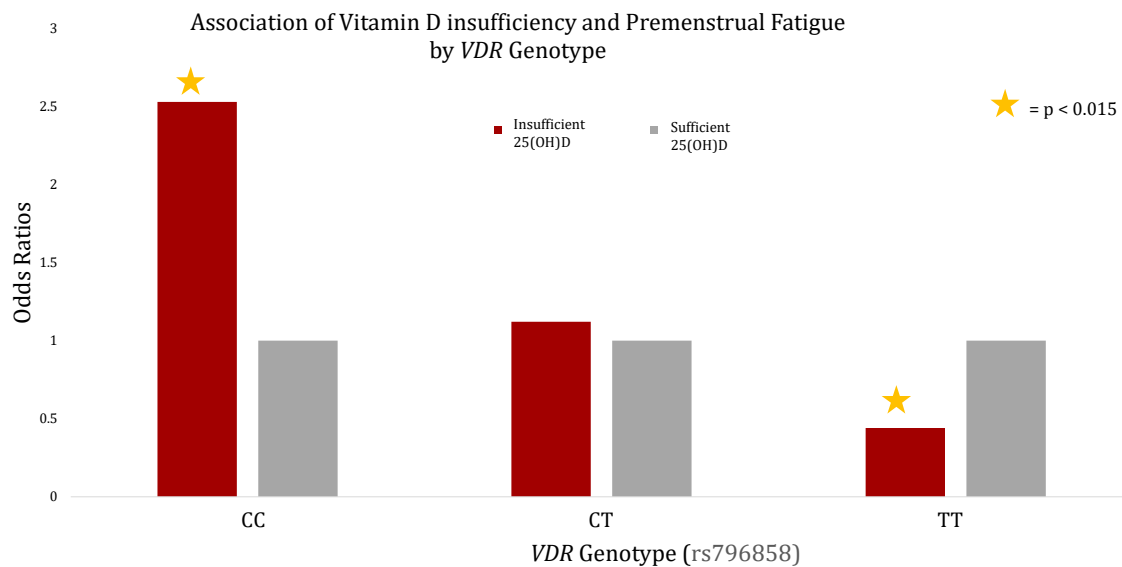
Variation in the vitamin D receptor gene, plasma 25-hydroxyvitamin D, and risk of premenstrual symptoms



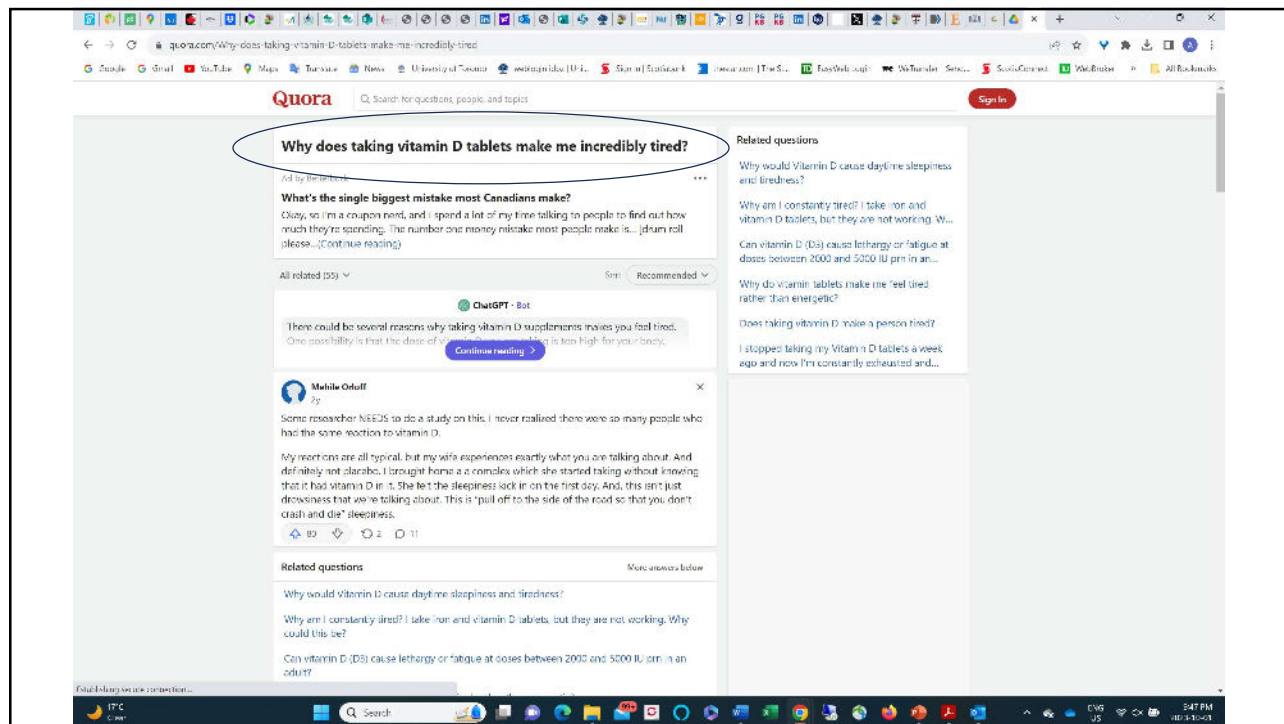
Alicia C. Jarosz[†], Daniel Noori[†], Tara Zeitoun, Bibiana Garcia-Bailo and Ahmed El-Sohemy^{*}

Jarosz et al 2021 Genes & Nutrition

Vitamin D and PMS

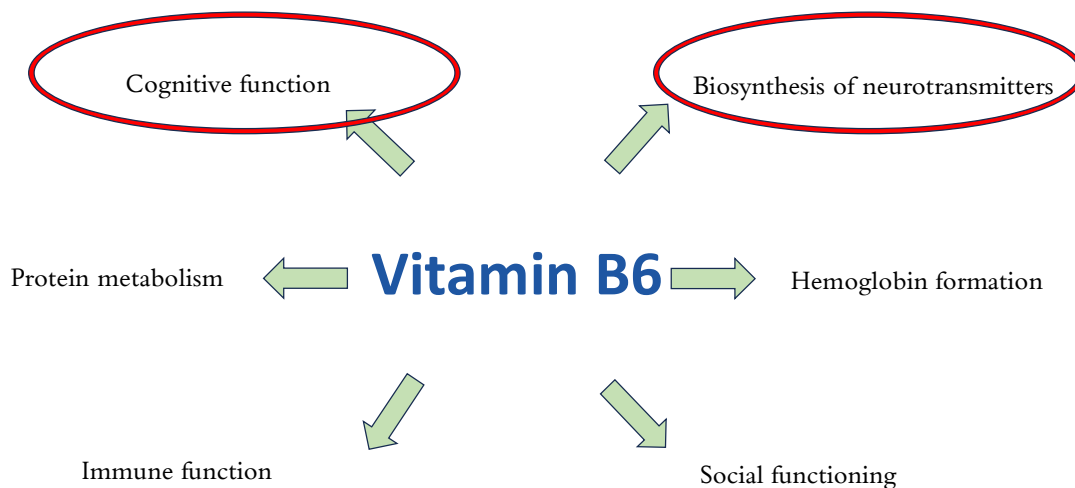


Jarosz et al 2021 Genes & Nutrition



Unpublished Studies (2026)

Vitamin B6



National Institutes of Health. (2023). Office of Dietary Supplements - Vitamin B6. Nih.gov

Tomioka et al., (2018). Decreased serum pyridoxal levels in schizophrenia: meta-analysis and Mendelian randomization analysis. *Journal of Psychiatry and Neuroscience*, 43(3), 194-200.

Pyridoxine (Vitamin B6)

- ✓ Water-soluble vitamin
 - ✓ Absorbed in the jejunum
 - ✓ Activated in the liver to pyridoxal-5'-phosphate (PLP)
- ✓ RDA: **1.3 mg/day** for adults aged 19 to 50
- ✓ One-carbon metabolism
 - ✓ Involved in over 100 enzymatic reactions

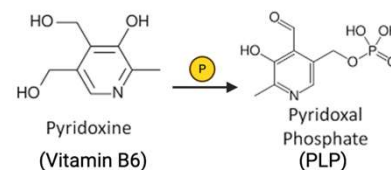


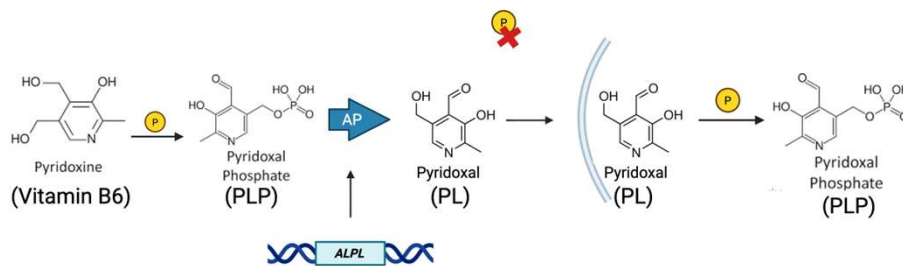
Figure created by BioRender & Curva

National Institutes of Health. (2023). Office of Dietary Supplements - Vitamin B6. Nih.gov

Tomioka et al., (2018). Decreased serum pyridoxal levels in schizophrenia: meta-analysis and Mendelian randomization analysis. *Journal of Psychiatry and Neuroscience*, 43(3), 194-200.

ALPL

- ✓ alkaline phosphatase, biomineralization associated (ALPL) → Alkaline phosphatase (AP)
- ✓ Important for **vitamin b6 clearance & neurodevelopment**



ALPL alkaline phosphatase, biomineralization associated [Homo sapiens (human)] - Gene - NCBI. (2025, September 27). ncbi.nlm.nih.
 Tournis, S., Yavropoulou, M., Polyzos, S., & Doulgeraki, A. (2021). Hypophosphatasia. Journal of Clinical Medicine, 10(23), 5676.
 rs4654748 Report. NCBI. (2024). Nih. gov.
 Figure created by BioRender
 Hazra et al., (2009). Genome-wide significant predictors of metabolites in the one-carbon metabolism pathway. Human Molecular Genetics, 18(23), 4677-4687.

Vitamin B6 and PMSx

JOURNAL ARTICLE

Effect of nutritional interventions on the psychological symptoms of premenstrual syndrome in women of reproductive age: a systematic review of randomized controlled trials

Jazz Robinson, Amy Ferreira, Marina Iacovou, Nicole J Kellow ✉

Nutrition Reviews, Volume 83, Issue 2, February 2025, Pages 280–306,

<https://doi.org/10.1093/nutrit/nuae043>

Published: 29 April 2024

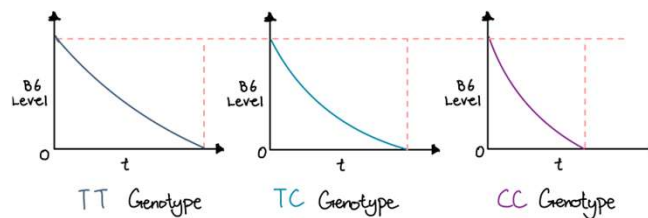
- Vitamin B6 ~ significant positive effects on the psychological PMSx in women with PMS

Acne in Caucasians stratified by vitamin B6 intake and genotypes

Unpublished Results

Potential Mechanisms

- ✓ Lower vitamin B6 intake x C allele ~ ↓ Acne
- ✓ High vitamin B6 ~ ↑ Acne
- ✓ C allele ~ More efficient clearance activity = Less circulating vitamin B6 → ↓ Acne



Zamil et al., (2020). Acne related to dietary supplement. *Dermatol Online J.* 15(25), 8.

PMSx Management

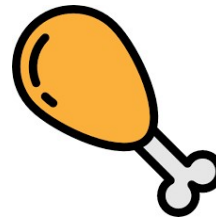
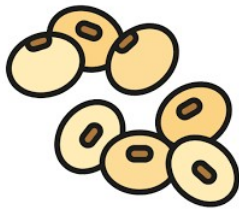
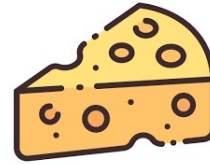


SSRIs

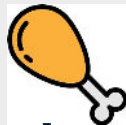
Serotonin

5-HT

Dietary Tryptophan Sources



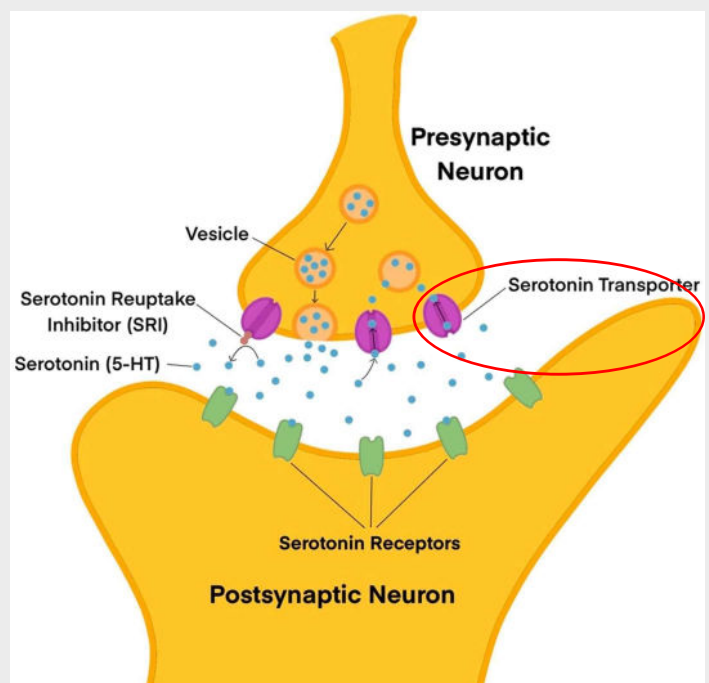
Tryptophan



5-HTP

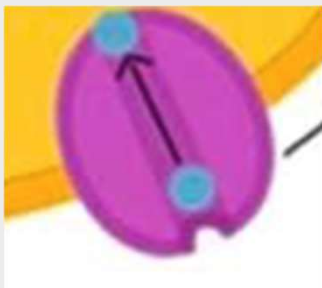
Serotonin

5-HT



Huang, C., van Wijnen, A. J., & Im, H.-J. (2023). *The Journal of Pain*, 25(3).

Genetic Variation in the Serotonin Transporter



- ✓ Serotonin transporter (5-HTT)
- ✓ Gene: *SLC6A4*
- ✓ rsXXXX
- ✓ rsXXXX

Serotonin, Tryptophan and PMSx



Biological Psychiatry

Volume 64, Issue 6, 15 September 2008, Pages 498-504



Archival Report

New Evidence for the Association of the Serotonin Transporter Gene (*SLC6A4*) Haplotypes, Threatening Life Events, and Depressive Phenotype

Judit Lazary^a, Aron Lazary^b, Xenia Gonda^a, Anita Benko^a, Eszter Molnar^a, Gabriella Juhasz^c, Gyorgy Bagdy^{a,d} 



Journal of Affective Disorders 32 (1994) 37–44

**Journal of
AFFECTIVE
DISORDERS**

Acute tryptophan depletion aggravates premenstrual syndrome

David B. Menkes^{*}, Diane C. Coates, J. Paul Fawcett

Department of Psychological Medicine and School of Pharmacy, University of Otago, Dunedin, New Zealand

Received 20 October 1993; revision received 5 April 1994; accepted 6 April 1994

Depression stratified by tryptophan intake

Unpublished Results

Anxiety stratified by tryptophan intake

Unpublished Results

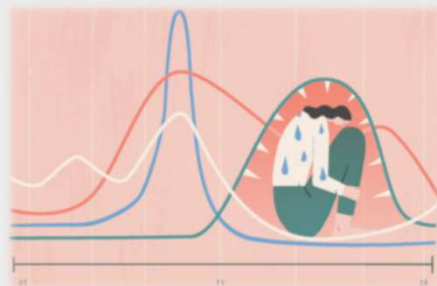
OR = 2.04
(0.91, 4.56)

Mood swings stratified by tryptophan intake

Unpublished Results

Implications

- Potential benefits of micronutrient intake in PMSx
- Understanding of genetic variation
- Precision Nutrition Recommendations



Is DNA-Based Advice Ready for Prime-Time?

- Scientific evidence is robust (for some markers)
- Independent of ethnic background
- Improved compliance (evidence from RCT)
- Information is actionable and “personalized”
- Increasing consumer awareness and demand
- More effective through HCPs, rather than DTC

Benefits of Genetic Testing

- ✓ Improved nutritional status
- ✓ Greater weight loss
- ✓ Improved compliance
- ✓ Enhanced motivation
- ✓ Better understanding of dietary advice



Thank you

Q&A



Email: a.el.sohemy@utoronto.ca



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