

Abstract #482

Symptoms Experienced by Individuals with Methylenetetrahydrofolate Reductase (MTHFR) Mutation

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Introduction

- Chronic overlapping pain conditions (COPCs)** refers to co-occurrence of pain disorders (e.g. fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, interstitial cystitis, chronic pelvic pain, endometriosis, migraine headache, chronic lower back pain, etc.)¹
- Many individuals with COPCs have no unifying diagnosis for these symptoms impacting multiple bodily systems and diminishing quality of life.
- Small Fiber Neuropathy (SFN) has been shown to be prevalent in many individuals with COPCs.¹ This provides a starting point for identifying etiology, treatable causes, and therapeutic options. Yet many cases who meet criteria for work up (absence of large fiber neuropathy, COPCs, autonomic symptoms) are negative for SFN.
- Some SFN (-) patients in our clinic have tested + for MTHFR mutation. MTHFR facilitates a key chemical reaction involving folate (vitamin B9), rendering it more bioavailable in the bloodstream. Mutations in the MTHFR gene disrupts this process, leading to a cascade of adverse effects, including maintenance of nerve health.
- Individuals with MTHFR mutation have reported:
 - Pain sensitivity, neuropathic pain
 - Thrombotic events
 - Cardiovascular complications (e.g. heart attack)
 - Obstetric complications (e.g. miscarriage)
 - Depression/anxiety^{2,3}
 - Fatigue³

However, MTHFR mutation is common and understanding the spectrum of symptoms, diagnostic approaches, and optimal management remains limited.

- Goal of Study:** To elucidate the prevalence of COPCs and associated symptoms within the MTHFR population in comparison to the general population.

Methods

- Institutional Review Board approval was obtained.
- Inclusion criteria was presence of MTHFR mutation by diagnosis codes in our electronic records.
- 77 individuals were identified + for MTHFR mutation.
- Each participant received a mailed survey that asked for the presence or absence of symptoms including anxiety, TMJ, migraines, generalized body pain/joint pain, palpitations, pelvic pain, miscarriage, dysmenorrhea, depression and peripheral nerve pain.
- Data on prevalence and spectrum of symptoms associated with the presence of the MTHFR mutation were collated.
- Wilson’s procedure with continuity correction was utilized to calculate 95% confidence intervals for the percent of respondents with each symptom/diagnosis.
- The National Health Interview Survey and National Comorbidity Survey were utilized to identify the percentage of individuals in the United States with each symptom/diagnosis.

Results

77 individuals were mailed surveys. 3 opted out and 20 responded. Most frequent symptoms are listed in Table 1.

Table 1: Percent of survey respondents versus general U.S. population reporting a symptom/diagnosis.

Symptoms/Diagnoses	Survey Respondents Reporting (%) (95% CI)	Percent of the United States Population Reporting [4] (%)
Anxiety	75% (51%-90%)	19.1%
TMJ	60% (36%-80%)	12.0%
Migraines	55% (32%-76%)	15.3%
Generalized Body Pain/ Joint Pain	55% (32%-76%)	20.9%
Palpitations	45% (24%-68%)	16.0%
Pelvic Pain	45% (24%-68%)	15.0%
Miscarriage	40% (20%-64%)	15.3%
Pain with Menses (Dysmenorrhea)	40% (20%-64%)	71.1%
Depression	40% (20%-64%)	8.3%
Peripheral Nerve Pain	40% (20%-64%)	6.0%

- A significant increase was noted in the percentage of patients with the above symptoms compared to the general United States population. This may indicate a higher prevalence in pain and related diagnoses in individuals with MTHFR mutation.
- Although the etiology of many of these conditions is believed to be multifactorial, MTHFR mutation may explain a unifying etiology pain and autonomic conditions in this select population.
- MTHFR mutations can affect folate metabolism pathways and hinder the ability to maintain nerve fibers over time, causing subsequent irregular pain signaling. Disturbance of these pathways may have a role in chronic overlapping pain syndromes and the autonomic diagnoses surveyed here.

Conclusions

- COPCs are historically regarded to be multifactorial processes with no true known unifying cause.
- Small fiber neuropathy is present in some individuals with MTHFR mutation.
- Our findings suggest there may be an association between MTHFR mutation, COPCs, and associated autonomic symptoms.**

References

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