

Micronutrient Deficiencies in Beaumont Integrative Medicine Fatigue Patients

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Introduction

Fatigue is a non-specific symptom described as physical or mental tiredness, weakness or lack of energy¹⁻². It is reported by 25-33% of patients at primary care visits³⁻⁵ and can persist after addressing etiologies such as anemia, infection, malignancy, depression and cardiopulmonary disorders.

Micronutrient deficiencies have been investigated in fatigue patients, particularly individual vitamins such as C, D, B12, E and the mineral zinc⁶⁻¹¹. Nutrient-rich dietary interventions for treating fatigue have shown significant improvements in fatigue scores among children¹², cancer survivors¹³ and multiple sclerosis patients¹⁴.

Fewer studies have investigated broad panels of micronutrients in fatigue patients. Beaumont's Integrative Medicine Clinic evaluates many patients with fatigue and assesses for functional micronutrient deficiencies using SpectraCell Micronutrient Testing (MNT). The MNT measures 31 different vitamin, mineral and metabolite levels concurrently (Table 1).

The SpectraCell MNT is a functional cell-based assay, where lymphocytes are isolated from the patient's blood sample and stimulated to grow in different medias that are replete or deplete in micronutrients¹⁵. Growth is measured by DNA synthesis and compared to a reference range established by assaying thousands of apparently healthy controls¹⁵. The testing reflects the patient's prior 4-6 month nutrient status, based on lymphocyte lifespan.

Objective and Aims

Study Objective: To investigate a broad panel of micronutrient deficiencies in Beaumont Integrative Medicine fatigue patients via chart review and SpectraCell MNT analyses.

Specific Aim 1: Quantify the prevalence of nutrient deficiencies among Beaumont Integrative Medicine fatigue patients.

Specific Aim 2: Assess fatigue-related comorbidities among Beaumont Integrative Medicine fatigue patients.

Methods

Study Design and Inclusion/Exclusion Criteria

The study was a retrospective chart review from 2014 to 2018 of Beaumont Integrative Medicine patients who reported fatigue as their chief concern at initial visit and had SpectraCell MNT data available. Patients younger than 18 years old were excluded from the study, as they are usually evaluated by the Integrative Medicine for non-fatigue related concerns. The study design was approved by the Beaumont Institutional Review Board. 167 charts were reviewed to obtain N = 50 subjects who met the appropriate inclusion criteria. All nutrient status and comorbidity data were de-identified by assigning a unique study ID number to each subject. Chart review and data collection were performed by approved study personnel and compiled into a secure database.

Variables of Interest

The primary variables of interest were the 31 SpectraCell nutrient levels and special functional assays listed in Table 1. Additional variables, particularly those related to fatigue, were also collected:

- Age at time of MNT testing
- Sex
- Comorbidities related to fatigue: depression, anxiety, thyroid disease, obstructive sleep apnea, insomnia, anemia, rheumatic disease, cancer history
- Exercise/activity level
- Medications

Information about supplements, though commonly used among Integrative Medicine patients, was not collected due to time constraints and extreme variability in supplement quality, quantities and durations of use.

Analyses

The characteristics of the study population such as sex and age at time of MNT testing were tabulated (Table 2). The prevalences of fatigue-related comorbidities and exercise levels were calculated, with the comorbidity prevalences compared to that of the general population as per literature review (Table 3). For all 31 micronutrients and special functional assays, the percentages of borderline and frank deficiencies were calculated and graphed in Excel (Figures 1-2).

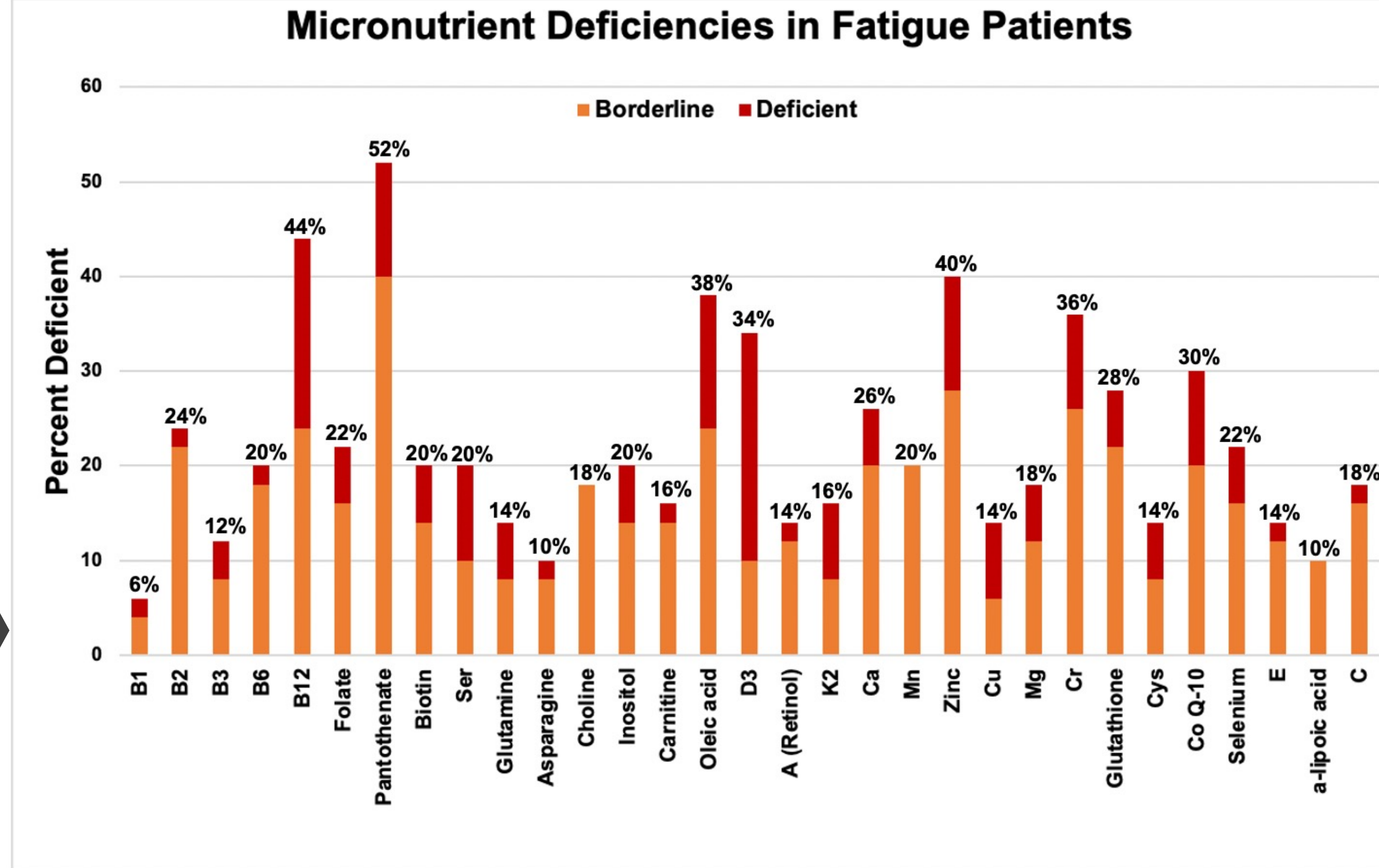
B-Vitamins	Amino Acids and Metabolites	Other Vitamins & Minerals	Antioxidants	Carbohydrate Metabolism
B1	Serine	Vitamins: D3	Vitamin E	Fructose Sensitivity
B2	Glutamine	A	Vitamin C	Glucose-Insulin Interaction
B3	Asparagine	K2	Glutathione	Chromium
B6	Choline	Manganese	Cysteine	Chromium
B12	Inositol	Calcium	Coenzyme Q10	Functional
Folate	Carnitine	Zinc	Selenium	SpectroX® Total Antioxidant Function
Pantothenate	Oleic acid	Copper	Alpha Lipoic Acid	Immunidex Total Immune Function
Biotin		Magnesium		

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Results

Figure 1. SpectraCell assay results of Beaumont Integrative Medicine fatigue patients showing the percentage of borderline and frank deficiencies 31 micronutrients. The SpectraCell MNT is a functional cell-based assay, where lymphocytes are isolated from the patient's blood sample and stimulated to grow in different medias that are replete or deplete in individual micronutrients. Growth is measured by DNA synthesis and compared to a reference range established by assaying thousands of apparently healthy controls. The testing reflects the patient's prior 4-6 month nutrient status, based on lymphocyte lifespan.

	Median Age	Age Range
Total Study	N = 50	55.5
Female	40/50	80%
Male	10/50	20%



Study Comorbidity	Study Prevalence	General Population Lifetime Prevalence (per literature review)
Depression	23/50	46%
Anxiety	20/50	32%
Thyroid Disease	16/50	32%
Insomnia	16/50	32%
OSA	5/50	10%
Rheumatic Disease (excluding diagnosed with osteoarthritis)	6/50	12%
Cancer History	5/50	10%
Anemia	3/50	6%
Diabetes Mellitus, type 2	3/50	6%
EBV History (symptomatic)	3/50	6%
Vegetarian or Vegan Diet	5/50	10%
Bariatric Surgery	1/50	2%
Exercise		
Sedentary	14/50	28%
Mildly Active	15/50	30%
Very Active	21/50	42%

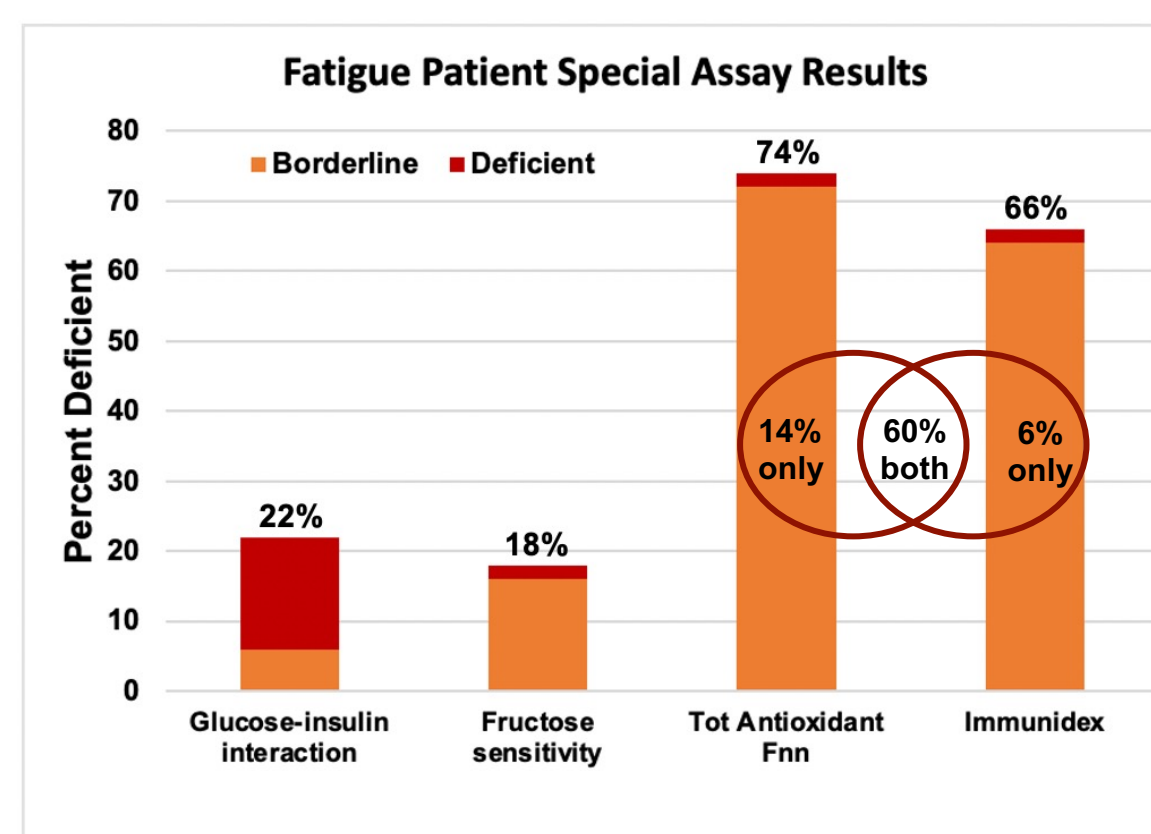


Figure 2. SpectraCell assay results of Beaumont Integrative Medicine fatigue patients showing the percentage of borderline and frank deficiencies in glucose-insulin interaction, fructose sensitivity, total antioxidant function and Immunidex score. The glucose-insulin interaction assay measures lymphocyte growth in the presence or absence of insulin¹⁵. Decreased cell growth may indicate either a functional deficiency of insulin *in vivo* or a metabolic defect in intracellular glucose utilization. The fructose sensitivity assay measures changes in lymphocyte growth after a fructose challenge¹⁵. Reduction in cell growth indicates a poor ability to metabolize fructose due to genetic and/or nutritional deficiencies (e.g. copper, zinc). The total antioxidant function assay measures the cellular ability to resist damage in response to an oxidative challenge with H₂O₂¹⁵. The Immunidex score measures T lymphocyte proliferation in response to stimulation with phytohemagglutinin¹⁵. In general, the higher the total antioxidant function, the higher the Immunidex score, since antioxidant function is important for promoting optimal T lymphocyte function.

Discussion

The most prevalent nutrient deficiencies, seen in nearly one third of the Integrative Medicine fatigue patient population, were in vitamins B5 (pantothenate), B12 and D along with coenzyme Q10, zinc, oleic acid and chromium (each with prevalences of ≥ 30% when including both borderline + frank deficiencies). All of these nutrients except for oleic acid have been previously linked to fatigue³³⁻³⁹ and are already included on the SpectraCell fatigue nutrient wheel for clinical education⁴⁰ (Figure 3). Seventy four percent of fatigue patients had deficient total antioxidant function and two thirds had impaired lymphocyte proliferation. Since antioxidant function is important for lymphocyte proliferation, co-deficiencies were expected. Since no controls were included in the study, it is unknown whether these deficiencies are otherwise common among all Beaumont Integrative Medicine patients or the wider population. Further work would be necessary to determine this. Comparing these results to other methods of testing nutrient status, instead of the functional intracellular SpectraCell assay approach, would also be informative.

The prevalences of depression, anxiety and insomnia tended to be higher in the fatigue patient study population and the prevalences of cancer history and anemia tended to be lower. The prevalences of thyroid disease, OSA, diabetes and symptomatic EBV history tended to be similar among the fatigue patients as compared to the general population. Although the prevalence of rheumatic disease tended to be lower in the fatigue patient study population, this is likely related to the fact that osteoarthritis information was excluded from our study in order to focus more on inflammatory arthritides, whereas the comparison CDC statistic does include osteoarthritis. Although exercise programs are considered one of the evidence-based treatments for chronic fatigue, our chart review found that only 28% of the Integrative Medicine fatigue patients self-reported as completely sedentary. 30% of the fatigue patients were "mildly active" indicating 2+ days/week of gentle walking, chores or yoga. 42% of the fatigue patients were "very active" indicating consistent/daily walking or 2-3+ days per week of running, going to a gym/trainer or fitness classes.

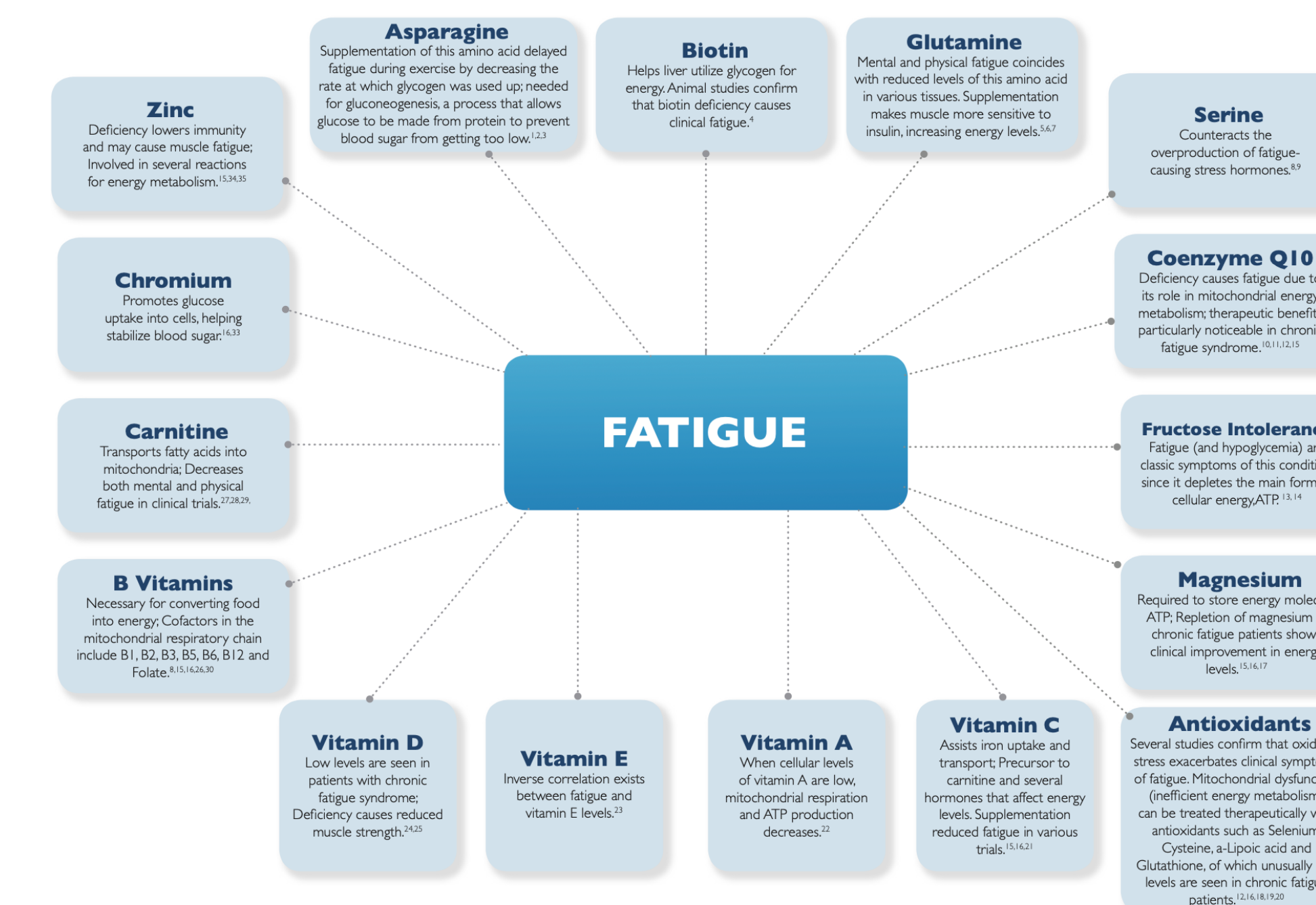


Figure 3. SpectraCell fatigue nutrient wheel for clinical education⁴⁰ and MNT results interpretation. The physiology of each fatigue-related nutrient is provided along with references to the scientific literature.

References



Acknowledgements

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