

# Treatment of essential tremor with multi-modal nutritional therapy in a teenage patient

## Abstract

Essential tremor (ET) is common and frequently affects quality of life. Although traditional pharmacotherapy is sometimes effective, patient factors, lack of efficacy, and poor adherence sometimes limit its efficacy. Furthermore, the pathophysiology of ET is not fully understood, but it is increasingly regarded as a highly heterogeneous disorder of cerebellar pathways underpinned by low gamma-aminobutyric acid (GABA) tone. This knowledge and review of recent data prompted the development of a multi-modal nutritional therapy approach to target three putative ET pathways: (i) diet (specifically adopting a Mediterranean diet); (ii) GABA tone (through oral supplementation); and (iii) L-tryptophan/vitamin B pathways (Triptobel oral supplement). The approach is illustrated here with the case of a 13-year-old boy with ET causing severe functional impairment. After two months of therapy, his tremor decreased significantly and he regained normal function. The case identifies and highlights several areas worthy of further investigation, particularly with respect to establishing the role of oral GABA and vitamin B/tryptophan supplementation in ET. Given the safety and positive health benefits of this novel nutritional therapy approach, it can be trialed in patients with ET either with or without concurrent traditional pharmacotherapy.

**Keywords:** essential tremor, nutritional therapy, vitamin b, gamma-aminobutyric acid, mediterranean diet

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**Abbreviations:** 5-HT, 5-hydroxytryptamine (5-HT); BMI, body mass index; ET, essential tremor; GABA, gamma-aminobutyric acid

## Introduction

Essential tremor (ET) the most common movement disorder, affecting 1% of the population across all ages and a significantly higher proportion of older adults.<sup>1</sup> However, ET also affects children, and, although often described as “benign”, the condition interferes with activities of daily living in over 90% of individuals.<sup>2</sup> Pharmacological therapy remains first-line ET treatment, with propranolol (a beta-blocker) and primidone (a barbiturate anti-convulsant) first-choice agents.<sup>3</sup> However, over 50% of patients do not respond to therapy and many experience side-effects including sleepiness and cognitive defects, prompting non-adherence to medication in many cases.<sup>4</sup>

Despite many years of ET research, its pathophysiology remains unknown. However, the most recent evidence suggests that ET is clinically and pathophysiologically heterogeneous, may be caused by abnormal oscillations in the olivo-cerebello-thalamo-cortical loop (as evidenced by electrophysiological and metabolic imaging<sup>5</sup>), and low gamma-aminobutyric acid (GABA) tone is a central feature in most cases.<sup>6,7</sup> Up to 50% of patients with ET have a family history and linkage and sequencing studies have identified associated genomic loci,<sup>8</sup> but non-genetic environmental factors including adherence to a Mediterranean diet<sup>9</sup> and other dietary factors (protein intake,<sup>10</sup>

antioxidant consumption<sup>11</sup>) are also thought to contribute. Furthermore, vitamin B deficiency (especially vitamin B12) can cause involuntary movements via its myriad effects on the central nervous system.<sup>12</sup>

This case is of a teenage boy with ET causing functional impairment who was successfully treated with a multi-modal nutritional therapy targeting diet, GABA tone, and protein synthesis and vitamin B-related pathways. The case outlines a safe and novel approach to

ET treatment that can either be trialed in treatment-refractory cases or used in tandem with traditional therapy.

## Case presentation

A 13-year-old boy presented to neurology clinic with a 24-month history of ET, which was particularly noticeable when performing voluntary tasks (predominantly action-type in character). Prior to onset of the tremor, the boy had been a talented guitar player, and he intended to pursue a musical career; since the onset of ET, he had been unable to play. A full history revealed no exposure to toxins and there was no family history of ET or other movement disorders. Full laboratory work-up (full blood count, biochemistry, thyroid function tests, liver function tests, vitamin B12, serum ceruloplasmin (to exclude Wilson's disease)) revealed no abnormalities, and magnetic resonance imaging of the brain and spinal cord was normal. He was not taking any prescribed medication and he did not use recreational drugs or drink alcohol. Neurological examination was otherwise normal.

The patient was physically active and had a normal body mass index (BMI). However, on taking a nutritional history, it was apparent that he supplemented his normal diet with foods containing large amounts of refined sugars (chocolate, cake, biscuits, ice cream, etc.) on a daily basis. The patient and his parents were reluctant for him to take prescribed medications, not least given his age and the possible side effects. Therefore, he was prescribed a sugar-free, Mediterranean-style diet rich in whole grains as a carbohydrate source and rich in vegetables, fruit, olive oil, and fish. He was also prescribed two nutritional supplements: 150 mg Triptobel (www.triptobel.eu, Croatia) supplement three times daily (8 am, 1 pm, and 6 pm) and gamma-aminobutyric acid (GABA) 750 mg twice daily (10 am and 4 pm) (www.puritan.com, USA). Triptobel capsules contain L-tryptophan, thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), vitamin B6, folic acid (vitamin B9), and cyanocobalamin (vitamin B12).

At follow-up after 14 days of treatment, the tremor had markedly subsided and by two months had almost completely resolved. The patient continues on long-term therapy and has resumed playing his guitar to pursue his chosen career.

## Discussion

Here, a teenage boy was successfully treated with a holistic, rational, and multi-modal nutritional therapy for ET. He showed rapid symptomatic improvement after only two weeks including being able to play his guitar and thus avoiding significant psychosocial impairment.

The approach was designed to target three main mechanisms known to participate in the pathophysiology of ET and involuntary movement disorders, the reasoning being that these mechanisms could be simply but effectively modulated through relatively simple dietary changes and safe dietary supplementation. These were adopting a Mediterranean diet, GABA supplementation, and vitamin B/L-tryptophan supplementation.

First, and given that the patient's composite dietary pattern was rich in refined sugars and saturated fats and low in vegetables, fruits, and cereals, adopting a Mediterranean diet was reasoned to be of benefit because: (i) the risk of ET is inversely proportionally related to adherence to a Mediterranean diet<sup>9</sup> and (ii) adherence to a Mediterranean diet is associated with a lower risk of other neurological diseases including Alzheimer's disease.<sup>13,14</sup> A Mediterranean diet typically consists of: (i) high vegetable, legume, fruit, cereal, fish, monounsaturated fatty acid intake; (ii) low saturated fatty acid, dairy product, meat, and poultry intake; and (iii) mild to moderate ethanol use. It is not entirely clear whether withdrawal of refined sugar and saturated fats or introduction of the Mediterranean diet was contributory in this case. Indeed, the effects of high-fat high-sugar diets on the risk and pathogenesis of ET have yet to be studied. However, the Mediterranean diet is thought to exert its beneficial effects through vascular, inflammatory, and oxidative mechanisms that might contribute to ET pathogenesis,<sup>14</sup> and serum and brain levels of the neurotoxin hormone derived from meat consumption are elevated in patients with ET vs. controls,<sup>10,15</sup> which may have been modified by the Mediterranean diet here. Regardless of causality, the introduction of a Mediterranean diet in patients with ET is a relatively easy intervention that in addition to helping control tremor has overall beneficial health effects.

Second, since low GABA tone is a central feature of ET, twice daily oral GABA supplementation was prescribed. GABA is the main inhibitory neurotransmitter in the human cortex, and nearly all effective pharmacological interventions for ET enhance the GABA-ergic neurotransmitter system, whether barbiturates, primidone, benzodiazepines, gabapentin, or topiramate.<sup>16</sup> Even the beta-blocker propranolol may act by enhancing central GABA receptivity in addition to its peripheral effects.<sup>16</sup> There is now evidence to suggest that GABA crosses the blood-brain barrier, although results are conflicting and there remains controversy in this area.<sup>17</sup> However, there have been differences in physiological readouts (electroencephalography, heart rate, chromogranin A levels) in GABA recipients in placebo-controlled trials, supporting its central role.<sup>17</sup> There has yet to be a study of oral GABA supplementation in patients with ET and, given both the fairly robust pathophysiological basis for GABA tone in the pathophysiology of the disease and our current findings, further investigation of dietary GABA supplementation in patients with ET is warranted.

Third, a combined L-tryptophan-vitamin B complex supplement (Triptobel) was prescribed, the reasoning being that: (i) the B group of vitamins are critical to brain function including neural development, energy production, DNA/RNA synthesis and repair, and neurochemical signaling;<sup>18</sup> and (ii) 5-hydroxytryptamine (5-HT), the amino acid tryptophan's main biosynthetic product, is implicated in the pathophysiology of diverse neurological conditions including movement disorders.<sup>19</sup> Although serum B12 levels were normal in this case, vitamin B12 supplementation has been shown to resolve tremor and involuntary movements.<sup>12</sup> The causative role for L-tryptophan and B vitamins in ET again requires further study.

## Conclusion

In conclusion, ET is a common disorder that affects quality of life and is often treatment-refractory. Given the age of this patient and his preference not to take long-term traditional pharmacotherapy, a rational, multi-modal nutritional treatment approach was developed that successfully resolved his ET and returned normal function. This approach can be trialed in patients with ET either with or without concurrent pharmacotherapy since it is both safe and has positive health benefits regardless of efficacy.

## Patient consent

The patient and his parents provided informed consent for publication of this case report.

## Conflicts of interest

None.

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