Reviewer’s report

Title: Quantitative pedigree analysis and mitochondrial DNA sequence variants in adults with cyclic vomiting syndrome.

Version: 2 Date: 15 April 2014

Reviewer: Robert Issenman

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This paper reports the results of Quantitative Pedigree Analysis (QPA) in 195 patients who were genotyped using Restriction Fragment Length Polymorphism (RFLP) or sequencing. The authors were able to show that there was stronger maternal inheritance for some of symptoms. Unlike previously reported findings in a pediatric population they were unable to show that there was a difference in the prevalence of mitochondrial SNP’s 16519 T, 3010A and the AT genotype in Haplogroup H CVS patients compared to historical controls.

The value of this largely negative study is that it suggests dissimilarity between adult and pediatric patients presenting with similar complaint of episodic bouts of severe debilitating nausea and vomiting. Previous publications have suggested that most pediatric patients tend to become symptomatic at about age 5 with resolution by age 12 in the majority. A minority have established mitochondrial cytopathy or other identifiable metabolic diseases. Though certain mitochondrial sequences occur more frequently about 80% seem to have symptoms which become recognizable as migraine. Many respond to anti-migraine therapy.

By contrast the adult cohort described in this report have onset in late adolescence or early adult life. Those develop these symptoms in association with cannabis exposure are thought to suffer from up-regulation of cannabinoid receptors. In other, there is a high prevalence of anxiety and other psychological morbidities. Far fewer respond to therapies which work for migraine patients.

While disappointing, these results help further delineate subgroups with common symptoms across the age spectrum which ultimate aids in targeting the most effective interventions for different sub-groups.

No particular major or minor revisions are suggested. (This reviewer does not have the expertise to evaluate the validity of the equation used to determine the described maternal inheritance ratio).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I declare that I have no competing interests