

When the following article linked stress to CLOCK, we had a basis from which to formulate a model that could use epigenetics based on physical science to assay the variables that regulate the circadian rhythm.

The results of the process are attached to this article.

<https://www.sciencedaily.com/releases/2017/09/170904093810.htm>

Financial stress is associated with migraine, if you have specific circadian gene variants

September 4, 2017

Date:

European College of Neuropsychopharmacology (ECNP)

Source:

People with a specific variation in the CLOCK gene have more migraines under financial stress. This work shows the effect of the genetics of circadian rhythms on migraine.

Summary:

People with a specific variation in the CLOCK gene have more migraines under financial stress. This work, the first time that the genetics of circadian rhythms has been shown to have an effect on migraine, is presented at the ECNP conference in Paris.

Migraine is a serious and debilitating neurological disease affecting 1 billion people worldwide. Migraine has been estimated to cause a financial cost of around €27 billion every year in the European Union, and \$17 billion every year in the USA. In the UK, 1 in 4 women and 1 in 12 men are migraine sufferers.

The background of migraine is highly complex involving a large number of genes and their interaction with environmental effects, and acting via multiple pathways in the central nervous system. Variations of circadian genes (which affect how the body controls and responds to environmental changes -- such as changes in light) have previously been shown to affect mood disorders, so it was thought it would be interesting to see if they were associated with migraine.

The group of researchers from Hungary and the UK checked 999 patients from Budapest and 1350 from Manchester, for two variants (single nucleotide polymorphisms, SNPs) of the CLOCK gene, and how these are associated with migraine. The CLOCK gene has an important role in regulating many rhythmic patterns of the body, including body temperature or level of cortisol, the primary stress hormone. They found that there was no significant direct connection between the gene and migraine, but when they factored in stress (financial stress, measured by a financial questionnaire), they showed that the investigated gene variants increased the odds of having migraine type headaches in those subjects who suffered from financial hardship by around 20%. (odds ratio -- see abstract for details).

The researchers looked at functional single nucleotide polymorphisms within the CLOCK gene that are able to influence how much protein is transcribed from the gene. Because this protein controls the body clock machinery these variants may impair processes that can prevent migraine in the face of stress.

Researcher Daniel Baksa (Semmelweis University, Budapest) said:

"This work does not show what causes migraine -- there is no single cause -- but it does show that both stress and genetics have an effect. In the work presented here, we were able to show that stress -- represented by financial hardship -- led to an increase in migraine in those who have a particular gene variant. What we need to do now is to see if other circadian gene variants in association with different stress factors cause the same effect.

The strength of our study is that we saw the same effect in two independent study groups, in Budapest and Manchester, so we think it is a real effect. The investigated gene variants are present in around 1/3 of the population, so they are common variants with small effect size. Our results shed light on one specific mechanism that may contribute to migraine. What it does mean is that for many people, the stress caused by financial worries can physically affect you. Migraine involves a huge health and financial burden each year, so any steps we can take to help patients understand their condition will be really welcome."

Commenting, Professor Andreas Reif (University Hospital, Frankfurt) said:

"This is a really interesting study on the interaction of genetics with stress in migraine. The studied gene is involved in the circadian system, which has previously been shown to be implicated in mental disorders such as bipolar disorder, which intriguingly is comorbid with migraine. Thus, this study might provide a clue how these diseases might be linked on the genetic level which is interesting as such. But even beyond this, the study demonstrates how an environmental risk factor exerts its effect only in the presence of a given genetic risk factor. This has not been done to a great extent in migraine, making this study an exciting new lead."

Story Source:

Materials provided by [European College of Neuropsychopharmacology \(ECNP\)](#). Note: Content may be edited for style and length.

We have performed preliminary reviews of CLOCK and interactions with BMAL1, PER1 - 3 and CRY1 and 2 without being able to develop an explicit model for interactions.

When the following article linked stress to CLOCK and circadian rhythm, knowing that stress stimulates iron - sulfur based aldosterone and the nine DNA repair signaling molecules can be proven to be byproducts of aldosterone, we had a foundation to use to revisit CLOCK.

Extensive details for DNA repair and copy error mutation are outlined in the following link for discussion purposes.

<http://www.mcfip.net/upload/Entanglement%20of%20Genes%20and%20DNA.pdf>

It should be noted that our explanation for DNA repair intentionally avoided reference to the roles of micronutrients (aka vitamins) to prevent cynicism. The following has used the designations of vitamins and all facets of the model can be verified.

It must be noted that natural “vitamins” are the forms that exist within cells of fruits and vegetables that have the molecular size to enter the extracellular matter. Over the past several decades; synthetic nutritional supplements are evolved for use as nutritional supplements have molecules of sizes that render them ineffective as signaling mechanisms to regulate DNA repair and gene entanglement.

Research must revisit the definition and application of natural cellular micronutrients.

MCFIP provides explicit and verifiable explanations for how these micronutrients are formed and how they function for cellular activities. This explanation for circadian neurobiology is only one example.

The following results were derived from our modeling process:

PER has 3 forms 1 - 3 and their amino acids are leucine - isoleucine and valine; making them bioidentical to the three forms of vitamin B1

BMAL1 has three forms; NPAS1 - 3 with the amino acids being glutamic acid - proline - glycine; making them bioidentical to vitamin B2

CRY has 3 forms 1 - 3 and they are known to be photosensitive. Their amino acids are phenylalanine - tyrosine and tryptophan; making them bioidentical to vitamin B3. This finding is noteworthy because these three amino acids are the aromatic amino acids that are activated by light

in the range of UVB 256 - 280 nm. This fact attributes to why they are photosensitive.

Careful review of many studies links glutamate decarboxylase (GAD) to these members of the CLOCK family. GAD has three forms and it can be established as the three forms of vitamin B6 that performs catabolic activity (autophagy) on amino acids.

Summary

We have just unlocked the mysteries of the circadian neurobiology (rhythm).

We assert that neuroplasticity establishes the circadian rhythm in cells in the hippocampus.

With near certainty, disruption of the mechanism can result in copy error mutations that can account for why shift work and sleep abnormalities can result in cancers and CVD.