Migraine Myth of the Month

If you don't have a family history of migraine, then you don't have migraine.

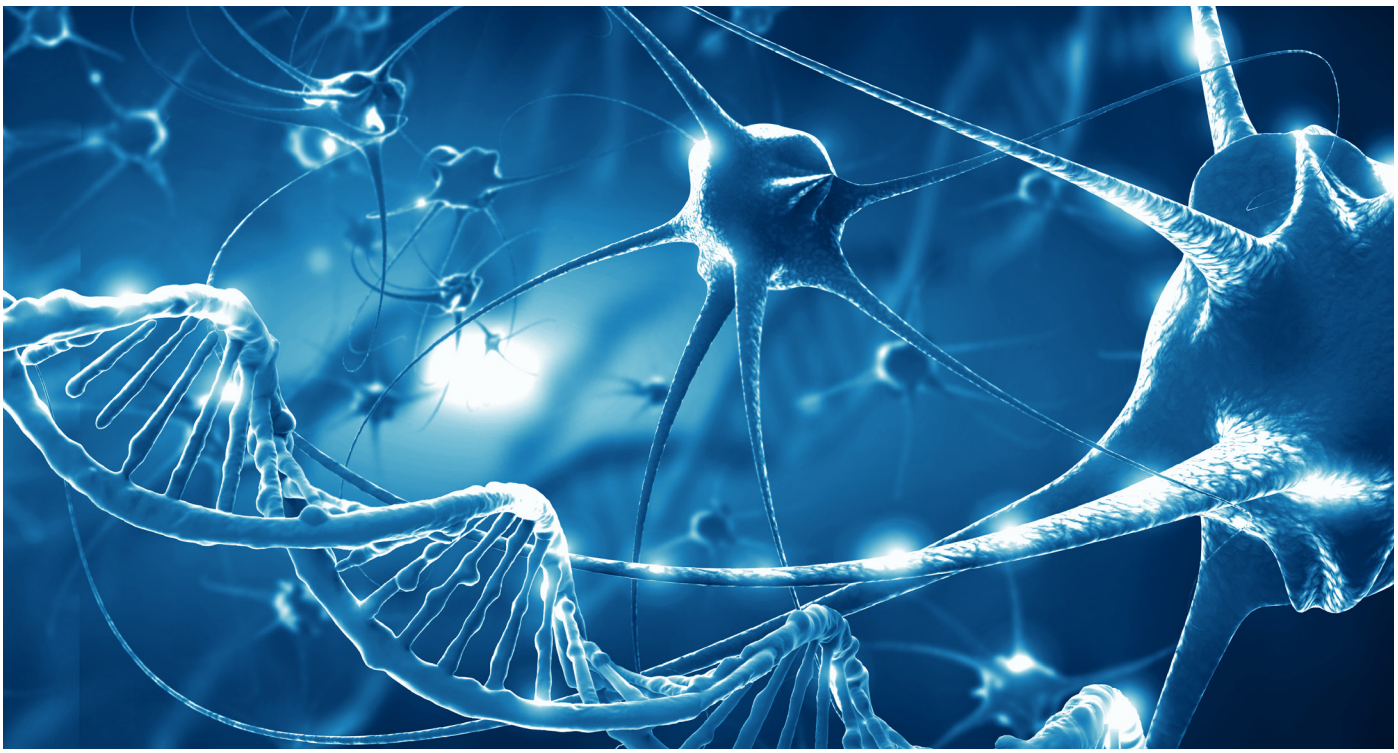
If, as estimated, roughly 40 million Americans have migraine, then almost 300 million don't. What is it about those 12% of us who are susceptible to recurrent attacks of disabling headache that makes us different from those who lack that susceptibility? Is it our personalities? Is it our lifestyles? Is it mold in the apartment, pollen in the air, too much gluten in the diet, too little maternal nurturing, too much maternal nurturing? Is it just random bad luck?

Or is it genetic? The first step in tackling this question involves answering another question: is migraine familial? It only makes sense that if migraine is genetic in origin, then there should be a familial pattern of occurrence and inheritance.

There is compelling evidence that migraine is familial. If you ask migraineur whether he or she has a first-degree relative who also has migraine, 50 to 60% will answer in the affirmative. If you directly interview the first-degree relatives of migraineurs, the frequency of a positive family history increases to around 90%. Looked at another way, if one or both of your parents has migraine, your chance of developing clinical migraine ranges between 50 and 75%.

"Familial" is not synonymous with "hereditary". Theoretically, shared environmental factors could cause a familial pattern of migraine without invoking any genetic contribution. More likely, however, migraine's clear tendency to be familial reflects a genetic inheritance pattern, and how much your genetic predisposition translates into clinical migraine may depend a great deal upon *epigenetic* or, put more simply, *environmental* factors. It's not a question of nature versus nurture; it's nature (genetic predisposition) plus nurture (environmental factors).

If migraine is genetic, why not find the damn gene, fix it, and cure migraine? Were it only that simple. It seems quite clear that in the overwhelming majority of cases it takes more than a single gene defect or mutation to cause migraine. Far more likely is that



migraine may result from any one of many, many genetic permutations that in at least some cases may require an intersection of genes coming from each parent.

The absence of a known family history of migraine does not by any means exclude a diagnosis of migraine.

That said, there are some rare variants of migraine that are caused by mutations in specific genes, and if one has the mutation, it will cause that specific type of migraine. The prototypic example is familial hemiplegic migraine, wherein three specific causal genes have been identified. All three genes influence the movement of certain salts (ions) into and out of brain cells through channels within the walls that surround the cells. The type and level of activity within these channels regulates the nervous system's "excitability", and the clinical disorder we call "migraine" appears to reflect a hyper-excitable nervous system whose increased sensitivity is modulated primarily by the brain.

It may be that mutations or other defects within the genes controlling ion channel activity may predispose not only to hemiplegic migraine, but also to the far more common clinical forms of migraine. This would help explain why migraine is co-morbid with other "excitable" brain disorders such as epilepsy and bipolar disorder and, as well, why medications that "stabilize" nervous system activity and suppress brain hyperexcitability are effective in treating migraine.

All this said, we are still left with that 10% or so of migraineurs who absolutely do not seem to have any family history of migraine. How can this be? One possibility alluded to earlier is that in a given generation the clinical manifestation of the genetic predisposition is so minimal that the afflicted family member simply never has much in the way of migraine symptomotology; perhaps this clinical quiescence occurs as a result of environmental factors. Or perhaps in some cases an intersection of genetic material from both parents is required to produce a particular permutation that will predispose to migraine in the product of their union. Another intriguing possibility is that even if one is born into a family that is entirely free of migraine in both the clinical and genetic sense, *in utero* gene mutations may occur while the fetus is developing in the mother's uterus, with the newborn child - like an Abraham from the Old Testament – begetting a whole new line of migraine.

In any event, the absence of a known family history of migraine does not by any means exclude the possibility that your recurrent headaches fall within the diagnostic category of "migraine".