



## Exploring the Connection Between Epilepsy and Migraine

Does one cause the other, or do both stem from a common source? Here's a look at these closely intertwined conditions.

**E**pilepsy and migraine are comorbid disorders. In other words, the occurrence of migraine in people with epilepsy is greater than would be expected based on the usual prevalence of migraine. Not only do they often occur together, but they share common features, including the fact that both are episodic. In both illnesses, a person is often completely unaffected between the paroxysms. Recent evidence has shown that the mechanisms by which each “attack” occurs may be similar. Finally, there is overlap between the treatments of these illnesses: several of the antiseizure medications also are effective in both the treatment of acute migraine and in migraine prevention.

Epilepsy and migraine are both common neurological illnesses. Twenty percent of patients in a general neurology practice complain of migraines, epilepsy or both.<sup>1</sup> Of the two, migraine is far more common. For epilepsy, the incidence rates are highest in the very young and the elderly. Unlike epilepsy, in migraine the incidence is lowest in the extremes of age, and peaks in adolescence.<sup>1</sup>

There are many reasons for this difference, including the fact that headaches in infants and children are difficult to diagnose. Not only may the child be unable to communicate his or her symptoms clearly, but the manifestations may be atypical (for instance, abdominal migraine), and therefore under-recognized as such. In older adults, headaches are often ascribed to alternative causes such as stroke, brain tumor and vasculitis; here again, the true incidence of migraine may be underestimated.<sup>1</sup>

Not only are the illnesses common, they often occur together. Ottman at Columbia University looked at the association between epilepsy and migraine and showed that the prevalence of migraine in people with epilepsy was 24 percent; the prevalence was 26 percent in relatives of people with epilepsy.<sup>2</sup> This was compared to the prevalence of 15 percent in the control group (no epilepsy), a rate which is similar to quoted rates of migraine in the general population. In other words, when compared to people without seizures, both the persons with seizures as well as their relatives were at increased risk of having migraines.

Ottman proposed several theories to explain this phenomenon;<sup>2</sup> Sacco discussed similar possibilities.<sup>3</sup> First, one disorder may simply cause the other. If true, when a population of people with epilepsy was studied, we would expect to see that they had developed epilepsy first and, later, migraine. Similarly, if the opposite were true, we would expect to see that migraineurs developed headaches first and then seizures. Careful study of these groups, however, did not support this hypothesis.<sup>1,2</sup>

A second possibility is that there is an environmental factor that causes both illnesses. For instance, migraine and seizures can be post-traumatic; perhaps there are other shared environmental factors that might account for this association. Third, a genetic factor might lead to a susceptibility to both migraine and epilepsy.<sup>2,4</sup> For instance, people with idiopathic generalized epilepsy (a syndrome that often starts in childhood or adolescence, and causes myoclonic, absence and generalized tonic-

clonic seizures) frequently also have migraine. In other words, the same gene (or perhaps groups of genes that are co-inherited) that predisposes the individual to one illness also causes the other illness. Finally, Ottman proposed that both disorders are due to *brain excitability*: though perhaps a simplified way of looking at these disorders, this would also explain why treatment options overlap in these disorders.

There is another interesting association between migraine and epilepsy: in some seizure patients, migraines occur immediately before, during or after the seizure. There are also reports that migraine aura can induce seizures. Similarly, there are case reports wherein the seizure induces a migraine. Because of this overlap, some people have used the term *migrainepoly* to encompass symptoms of both disorders which seem to overlap.<sup>1,3</sup> However, the association between the two does not have to be a temporal one: many people with seizures will experience migraine headaches that are unassociated with the occurrence of their seizures.

In addition, both migraines and seizures can occur with greater frequency during certain phases of a woman's menstrual cycle. In epilepsy, the seizures occur most often during ovulation or menstruation, at times when estrogen is at its peak. In migraineurs, the trigger for headache seems to be related to decreases in estrogen.<sup>1,5</sup> In women with catamenial seizures, regulation of the hormone cycle with exogenous hormones, can help to reduce the number of seizures the woman experiences. Similarly, migraines that are worsened by changes in hormone levels may



## Table 1. Possible Explanations for Comorbid Conditions

*Comorbidity is defined as a second condition which occurs with greater frequency than can be explained by pure coincidence:*

- One illness causes the other: for instance, migraines cause seizures or vice versa.
- The conditions share a common underlying mechanism.
- The conditions share a common underlying genetic factor.
- The conditions share a common causative environmental factor (trauma, virus, etc.)

Source: Sacco S, Oliveri L, Bastianello S, and Carolei A. Comorbid neuropathologies in migraine. *J Headache Pain* 2006;7:222-230.

respond to similar type of therapies.<sup>1</sup>

Finally, both disorders share common provocative factors or triggers. Food substances such as chocolates, aged cheese, and red wine may trigger migraine headaches: alcohol (or more specifically alcohol withdrawal) provokes seizures in many individuals. Poor sleep is often reported as a trigger for both seizures and headaches. Patients often describe “stress” as an important trigger for headaches or seizures. Although they usually are referring to unusual emotional or work stresses, physical stressors, such as an intercurrent illness, can sometimes lead to headaches or seizures.

### Treatment

In both epilepsy and migraine, the goal of treatment is the same: prevent the “attacks” while causing no side effects. In both conditions, this goal may not always be attainable. In people whose illnesses are difficult to control with medications, the goal may be to reduce the frequency of the events (seizure or migraine) while simultaneously minimizing side effects. In short, the goal of treatment is to improve the person’s ability to function or their quality of life. Because both epilepsy and migraine share the mechanism of *neuronal hyperexcitability*, it is not surprising that there are treatments common to both illnesses.

The acute treatment of seizures differs from that of migraine. If a person has a prolonged seizure, or is prone to clusters of events, benzodiazepines such as oral lorazepam or rectal diazepam may be administered. These agents have little or

no effect on migraine. Instead, triptans, non-steroidal anti-inflammatories and other analgesics may be used as abortive therapies for acute migraine. The agents useful for acute treatment of migraine have no effect on seizures and in some cases may actually worsen a person’s epilepsy.

Where the illnesses share common ground is in the preventative therapies. Although many factors are weighed before a medication is selected (in either illness), there are several agents that have been shown to reduce the frequency of both migraines and seizures. Valproate and topiramate are perhaps the best examples of this. Each has undergone extensive, randomized, placebo-controlled trials in both epilepsy and migraine. Each has achieved approval from the FDA for both migraine and epilepsy. However, there are several other antiepileptic drugs that have also been shown to attenuate migraine headaches by case series, most notably gabapentin, levetiracetam and zonisamide. Of note is the fact that the dose of AEDs in the treatment of migraine is usually lower than that used in the treatment of epilepsy.

When a person has both illnesses, it seems logical to try to consolidate medical treatments in order to reduce polypharmacy. This almost certainly results in fewer side effects. However, the doses that are used in the treatment of seizures are usually higher than those proposed in migraine. As such, “epilepsy” doses may be needed in order to achieve good control of both. In other words, when using one medication to treat two illnesses, one must be careful

not to undertreat one of the two conditions.

The use of non-prescribed medications, such as herbal remedies and nutrition supplements, has recently grown considerably. This is true for people with both seizures and migraines as well. Unfortunately, there are limited studies as to the effectiveness of these remedies in these illnesses. Further, there is concern that some “natural herbs” might worsen the condition. Drug-to-drug interactions may occur, potentially limiting the effectiveness of prescribed medications. Until further studies are completed, these agents must be used cautiously in people with either seizures, migraines, or both.

### Conclusions

Epilepsy and migraine share many common features. They are both episodic, often with normal thinking and function between events. They share common etiologies such as head injuries, stroke, or central nervous system neoplasm. Both are disorders of neuronal excitement. Interestingly, both share common treatment options as well. The goal of treatment for both is to improve a person’s quality of life. Often, this means eliminating the events while preventing side effects. Because polypharmacy often leads to frequent side effects, when a person has both epilepsy and migraine, it is logical to try to “consolidate” treatments. In other words, it might be possible to treat both illnesses with one medication. **PN**

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