By Steven Karceski, MD

What We Do — and Don't — Know About Seizure-Precipitating Factors

Despite numerous patient reports, we still know surprisingly little about the pathophysiology behind seizure triggers.

It has long been recognized that specific stimuli, also called seizure triggers or seizure precipitants, may induce seizures in people with epilepsy. Pierre Loiseau defined a precipitant as "circumstances that precede the onset of the epileptic [seizure], and are considered by both the patient and [doctor] to be a possible explanation" as to why the seizure occurred.[1] Many people with epilepsy report that their seizures are more likely to occur in certain circumstances: under emotional stress, when tired or fatigued, or when they have a febrile illness like the flu. About one third of women report that their seizures are worsened around the time of ovulation of menstruation (called *catamenial* seizures).

In addition, the medical literature is filled with case reports that describe specific kinds of seizure precipitants including music, mental concentration, certain voices, reading, writing, eating, etc. In fact, some have even proposed that there may be "reflexive" forms of seizures: epileptic events that occur in response to very specific stimuli. However, this type of seizure is probably very rare. Though the rare trigger for seizures is very interesting, most doctors will not see patients with these complaints. This column will discuss the most common factors known to precipitate seizures in patients with epilepsy.

Stress, Sleep and Sleep Deprivation

Although many physicians are aware of seizure precipitants, it is interesting to note that there are relatively few studies that address this issue. Most have used patient surveys or survey of patient caregivers to estimate the occurrence of seizure triggers (see Table 1 on p. 24).[2-4] Interestingly, the majority of patients (53 to 92 percent) report at least one seizure precipitant. When the most common precipitants are tabulated, "stress" is at the top of the list. This is followed by sleep deprivation, tiredness (perhaps sleep deprivation and tiredness are nearly the same, and should be "lumped" together), and fever or illness.

When generalized (idiopathic) epilepsy syndromes are independently reviewed, flashing lights, a known activator of both epileptiform discharges and seizures (on EEG) are frequently reported. Supporting this, da Silva found that 15 percent of their patients with juvenile myoclonic epilepsy (JME), a specific idiopathic generalized epilepsy syndrome, reported that flashing lights triggered seizures.[4] Routine EEG takes advantage of this activating effect: it is the reason that photic stimulation is commonly performed in most EEG laboratories.[1]

Of course, these precipitants may not occur independently. Stress, for instance, may also cause sleep deprivation. Stress may lead to overuse of sedatives or alcohol, the withdrawal of which may lead to seizures. An excellent example of how seizure triggers may coalesce is in college students. One can imagine a student who might overuse stimulants (like caffeine) in order to "cram" for examinations. In addition to the stress of the situation, this might lead to sleep deprivation. After finals, the student may celebrate by drinking alcohol. It is likely that *each* of the precipitants played some role in the resulting seizure.

In contrast to this, it is interesting that sleep is sometimes a seizure precipitant. Once called *morpheic epilepsy*, it is now recognized that the seizures in certain epilepsy syndromes are most likely to occur during specific stages of sleep, or during transitions from sleep to wakefulness.[1] For instance, frontal lobe onset partial seizures are brief, tends to cluster, and occur most often during sleep. The hallmark of childhood onset idiopathic localization-related epilepsy (also called benign rolandic epilepsy) is that the centrotemporal epileptiform discharges increase during sleep. In benign rolandic epilepsy, many of the seizures occur during sleep as well. The myoclonic seizures of juvenile myoclonic epilepsy (JME) tend to occur most often upon awakening. As the name would suggest, in the syndrome of *grand mal seizures on awakening*, GTCs occur shortly after waking up. Though this association with sleep is well known, the mechanism by which seizures occur is not.

Hyperventilation and Exercise

Hyperventilation has been reported to trigger seizures, and to activate epileptiform discharges on EEG, especially in the idiopathic generalized epilepsy syndromes.[1] For instance, hyperventilation can provoke absence seizures in kids who have childhood absence epilepsy (CAE, a juvenile-onset type of idiopathic generalized epilepsy). This can be recorded on routine EEG, and as a diagnostic "test," can be performed in the doctor's office to

(Continued on p. 24)

Table 1. Common Seizure Triggers Reported by Epilepsy Patients

Seizure Triggers	Epilepsy Type	Study Population	Author
53% reported one precipitant 30% reported two or more precipitants Most common were: 1. emotional stress (20.9%) 2. sleep deprivation (11.6%) 3. tiredness (9.5%) 4. alcohol (5.7%) 5. fever (5.1%)	Mixed: "generalized" localization related, and "unclassified"	data derived from twin registries in the USA, Denmark, and Norway; 1677 subjects	Nakken et al., 2005
62% reported one precipitant Most common were: 1. stress (30%) 2. sleep deprivation (18%) 3. sleep (14%) 4. fever or illness (14%) 5. fatigue (13%)	Mixed	400 patients	Frucht et al., 2000
92% reported at least one precipitant Most common were: 1. stress (83%) 2. sleep deprivation (77%) 3. Mental concentration (23%) 4. Flashing lights (15%) 33% of women reported that menses triggered seizures	Juvenile Myoclonic Epilepsy (JME)	75 patients	Sousa et al., 2005

(Continued from p. 18)

confirm the clinical diagnosis. Hyperventilation causes a respiratory alkalosis and vasoconstriction of the central blood vessels. Whether it is the alkalosis that is the direct cause of the seizures remains unknown.

Exercise, which causes a person to hyperventilate, does *not* seem to cause seizures. A prospective study in 2001 demonstrated that exercise improved quality of life in people with seizures, but did not have an impact on seizure frequency.[5] Data derived from patient surveys indicate that exercise-induced seizures occur either infrequently or rarely.[6] Though rare, exercise-induced seizures have been reported, and have been associated with several epilepsy syndromes.[7] Whether it is the hyperventilation due to exercise that actually induces the seizures in these rare instances is unknown.

Alcohol

The August 2006 Epilepsy Essentials (available at www.avondalemedical.com/archive_PNAugust2006.htm) covered this particular topic in more detail; however, it is an important issue to discuss with people who have seizures. Up to 10 percent of heavy drinkers will experience convulsions. Usually, the seizure occurs within 48 hours of the last drink. In other words, the seizure is usually related to alcohol *withdrawal* as opposed to a direct effect that alcohol has on the central nervous system.

Most people, however, are not heavy alcohol users. Instead, patients with epilepsy will typically ask, "Can I have an occasional glass of wine or beer? Will it cause me to have seizures?" The answer to these questions has never been clearly answered. The observation that alcohol-related seizures occur in the setting of overuse, abuse and withdrawal has led to the widespread thought, shared by most neurologists, that the occasional alcoholic drink is unlikely to cause seizures.

Missed Medication Doses

Perhaps the most common precipitant for seizures is poor medication compliance. One factor that contributes to this is frequency of dosing. It has long been recognized that more frequent medication dosing results in poor compliance: once-a-day or twice daily dosing is best. Studies have shown 33 to 50 percent of people do not take their antiseizure medications in the way that they are prescribed. For most patients, if one or two doses are inadver-

tently omitted, no harm results. However, for individuals who frequently "forget" or for those who do not take their medications for extended periods of time, there is an increased risk of seizures and subsequent injury.

Sudden discontinuation of medication may cause status epilepticus, a potentially life-threatening condition. Poor seizure control can also result in death (sudden unexplained death in epilepsy also known as SUDEP; see Epilepsy Essentials July 2005 at www.avondalemedical.com/archive_PNJuly2005.htm). It continues to be my opinion that patients should be informed of the possible consequences of poor medication compliance.

Conclusions

More than half of patients with epilepsy report at least one seizure trigger. Stress is the most commonly reported seizure precipitant. However, sleep deprivation, missed doses of medication, alcohol and illicit drugs often are reported to induce seizures. When it comes to seizure precipitants, an old joke comes to mind. A patient goes to the doctor's office, saying, "Doctor, when I raise my arm like this, it really hurts. What should I do?" The doctor's reply is, "Well, don't do that!"

Where seizure triggers are concerned, counseling about avoidance of precipitants is needed. For some triggers, like sleep deprivation, the answer may be clear. For others, like "stress," a straightforward solution may not be evident. However, the best degree of seizure control occurs in instances where seizure precipitants are minimized while at the same time administering a carefully selected therapeutic regimen. **PN**

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