

## Comorbidites of epilepsy

Historically, epilepsy was defined as a condition with the occurrence of seizures. However, in more recent times, the scientific and medical community has realized that epilepsy can be so much more than seizures. The presence of accompanying conditions (also known as ‘comorbidites’) is frequently recognized now. Today, epilepsy is defined as a neurological condition where individuals have an increased propensity to epileptic seizures and can have psychiatric comorbidites as well. Epilepsy can be genetic or acquired (as a result of stroke, meningitis or brain injury) and seizures can be of various types. Some are partial (when only part of the brain is involved) and generalized (the entire brain is involved in seizure generation and propagation). Seizures could also be classified as ‘simple’ seizures where there is no loss of consciousness and ‘complex’ seizures where there is a loss of consciousness. The exact mechanism causing seizures is not fully understood; however, an imbalance between excitation and inhibition leading to hyperexcitability has been shown to contribute.

A few comorbidites seen with epilepsy are mental retardation, learning disabilities, cognitive impairment, depression, anxiety and autism. It is important to study these accompanying disorders because they could profoundly impact quality of life. For example, someone with epilepsy might have seizures once a year, or once every six months but the psychiatric comorbidities may be present throughout the person’s life. It is for this reason that the National Institute for Neurological Disorders and Stroke ([NINDS](#)) has listed as the study of comorbidites in its [benchmarks](#) that scientists use to guide research. There are a few issues that come into play when studying comorbidities of epilepsy. One is that both – seizures and the psychiatric comorbidites involved- are extremely complicated disorders to understand individually. One can imagine the complexity when studying the disorders together. Also, some anti-epileptic drugs can exacerbate psychiatric conditions – this makes it difficult to tease apart the effects of seizures vs. those of the medication. In addition, there is the possibility that epilepsy and psychiatric comorbidites will evolve over time. How the pathophysiology changes is an interesting, albeit unanswered question. In this article, we will go over a few comorbidities and some details about them.

**Cognitive impairment** in epilepsy can be found in epilepsies of a wide range e.g. frontal and temporal lobe epilepsy, and if the cause is genetic or acquired. Studies in experimental rodents have found that animals given drugs to produce seizures also causes cognitive impediments – a test used to measure this is the Morris Water Maze test. Here, rats or mice are placed in a pool of colored water and they have to find their way to an invisible platform by using spatial cues. Animals made epileptic experimentally show deficits in this task and studies have found that the hippocampus may show structural and morphological deficits that may lead to poor performance in this task.

For more information about cognitive comorbidities in epilepsy,

<http://www.ncbi.nlm.nih.gov/books/NBK98139/>

**Migraine** is another comorbid condition seen with epilepsy. A commonality between seizures and migraine is a phenomenon known as cortical spreading depression which is a wave of profound hyperexcitability of neurons followed by intense inhibition. It is suggested that spreading depression can explain the headache in migraine and auras in epilepsy. The risk of migraine in people with epilepsy is twice what is seen in the normal population. Both epilepsy and migraine are episodic disorders, meaning that the seizures and headaches appear sporadically and between attacks, individuals are seizure free. However, perhaps another way of looking at it is that the brain of someone with epilepsy or migraine or both is fundamentally different from someone who doesn't have these disorders. Certain stimuli like lack of sleep or drugs of abuse or intense stress may precipitate seizures (in epilepsy) and headaches (in migraine). Another point of similarity between migraines and epilepsy is the sequence of events – the prodromal phase where initial symptoms occur, an aura, the actual event (which could be a seizure or the migraine headache) and the postdromal phase (the phase when seizures or headache have subsided). It is probably not surprising that a few drugs used in epilepsy have been shown to be useful in migraine as well. The neurotransmitter glutamate has been suggested to be linked to migraine and epilepsy is the excitatory neurotransmitter glutamate, and some genes involved are those that code for calcium channels, sodium-potassium transporter and for sodium channels.

For more details, read <http://www.ncbi.nlm.nih.gov/books/NBK98193/>

Depression in people with epilepsy can be constant (as opposed to the episodic nature of seizures) and can be quite debilitating. Depression is the most common comorbidity seen in epilepsy and it has been noted that the incidence of depression in someone with seizure disorders can be as many as 3.7 times higher than someone who doesn't have a seizure disorder. An animal model used in the lab to study depression uses the phenomenon anhedonia which is the inability to feel pleasure. Normal rats have a preference towards sweetened water over normal tap water, but rats that have a genetic mutation that renders them with depressive symptoms do not show this preference. Experimental rodents that have been given convulsants to simulate epilepsy also show anhedonia suggestive of depressive symptoms. A neurotransmitter named 5-HT or serotonin, the hypothalamic-pituitary axis and inflammation have been implicated in depression comorbid with epilepsy. You can find more information here

<http://www.ncbi.nlm.nih.gov/books/NBK98131/>

An important question in this field is who with epilepsy will go on to develop a particular comorbidity. Not everyone with epilepsy shows comorbidities, so it would be interesting to find out what

could make someone susceptible to one comorbid condition over another. If we know this, we could perhaps design novel therapies to decrease the impact of these comorbidities.