Sleep and stress give clues to understanding epileptic seizures

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Sleeping patterns and stress hormones could be the key to understanding how and when people with epilepsy are likely to experience seizures, a new study reveals.

Researchers used mathematical modeling to understand the impact of different physiological processes, such as sleep and changes in concentration of the stress-hormone cortisol, on key signatures of epilepsy—known as epileptiform discharges (ED).

Epilepsy is a serious neurological disorder characterized by a tendency to have recurrent, spontaneous seizures. Classically, seizures were assumed to occur at random, until the discovery of ED activity with timescales that vary from hours and days through to months.

The scientists analyzed 24-hour EEG recordings from 107 people with idiopathic generalized epilepsy and discovered two subgroups with distinct distributions of epileptiform discharges: one with highest incidence during sleep and the other during daytime.

Publishing their findings in *PLOS Computational Biology*, the international research team led by the University of Birmingham, reveal that either the dynamics of cortisol or sleep stage transition, or a combination of both, explained most of the observed distributions of ED.

Lead author Isabella Marinelli, from the University of Birmingham's Center for Systems Modeling & Quantitative Biomedicine (SMQB), said, "Some 65 million people have epilepsy worldwide, many of whom report specific triggers that make their seizures more likely—the most common of which include stress, sleep deprivation and fatigue.

"Our findings provide conceptual evidence that sleep patterns and changes in concentration of cortisol are underlying physiological drivers of rhythms of epileptiform discharges. Our mathematical approach provides a framework for better understanding what factors facilitate the occurrence of ED activity and potentially trigger the seizures which can be so debilitating for epilepsy sufferers."

The researchers' mathematical model describes the activity of connected brain regions, and how the excitability of these regions can change in response to different stimuli—either transitions between sleep stages or variation in concentration of cortisol.

ED frequency increases during the night, early in the morning, and in stressful situations in many people with epilepsy. The team discovered that sleep accounted for 90% of variation in one subgroup and cortisol around 60% in the other subgroup.

Cortisol is one of the primary stress hormones in humans, with production and secretion controlled by the hypothalamic-pituitary-adrenal (HPA)-axis. In stressful situations, HPA-axis activity increases, resulting in a higher secretion of cortisol.

"Sleep alone cannot account for the changes in ED likelihood during wakefulness observed in our first subgroup," explained Dr. Marinelli. "There is a reduction in ED likelihood during the sleep time after an initial sharp increase during the first hours.

"This can be explained by the fact that deep sleep, which is linked to an increase of EDs, is predominant during the first third of the sleep period. We found an increase in ED occurrence before waking, which—given that the level of cortisol is known to increase around waking—suggests a combined effect of sleep and cortisol."

More information: Circadian distribution of epileptiform discharges in epilepsy: Candidate mechanisms of variability, *PLoS Computational Biology* (2023).

Provided by University of Birmingham