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Epilepsy

Changes in gut microbiome can be associated with abrupt seizure exacerbation in epilepsy patients

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Purpose

Seizures can be triggered by a variety of endogenous or exogenous factors. We hypothesized that alterations in the gut microbiome may be a seizure precipitant and analyzed the composition and characteristics of the gut microbiome in epilepsy patients who experienced an abrupt seizure exacerbation without a clear seizure precipitant.

Methods

We prospectively enrolled 25 adult patients with epilepsy and collected fecal samples on the admission and after seizure recovery for next-generation sequencing analysis. We performed nonparametric paired t-test analysis to evaluate changes in the gut microbiota as seizures worsened and when it recovered and also estimated alpha and beta diversities in each category.

Results

A total of 19 patients (13 males) aged between 19 and 78 years (mean 45.2 years) were included in the study. The composition of the gut microbiota underwent a significant change following an abrupt seizure exacerbation. At the phylum level, the relative abundance of Fusobacteria and Synergistetes was decreased in the seizure recovery state compared to the acute seizure exacerbation. A similar trend was observed at the lower hierarchical levels, with a decrease in the relative abundance of Fusobacteria, Tissierellia, and Synergistia at the class level, and that of Synergistales, Tissierellales, and Fusobacteriales at the order level. At the family level, the relative abundance of Fusobacteriaceae and Staphylococcaceae was decreased, whereas that of Leuconostocaceae was increased. No statistical differences were observed in alpha and beta diversity between the pre- and post-acute seizure exacerbation periods.

Conclusion

Our study suggests that the changes in Fusobacteriaceae and Lecuonostocaceae may be associated with acute seizure exacerbation in epilepsy patients. Given that Fusobacteriaceae are associated with various systemic diseases due to their invasive properties and that Leuconostocaceae are known to produce GABA, our results may suggest a gut microbiome-based treatment option for epilepsy patients.

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Epilepsy

Septic shock and convulsive status epilepticus in a patient with MELAS syndrome: A case report

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Background

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is one of the most common maternally inherited mitochondrial disorders. While it is a heterogeneous syndrome with diverse clinical features, the most frequent presentation of central nervous system (CNS) involvement are epileptic seizures which can develop into status epilepticus (SE), often refractory.

Case presentation

A 29-year-old male patient, who had been diagnosed with MELAS two years prior, was transferred to our clinic due to convulsive status epilepticus. On admission, he was in a state of septic shock, with an altered mental state, verbally unresponsive, and was immediately admitted to the neurological intensive care unit. After a failure of seizure termination with intravenous antiepileptics, and due to respiratory insufficiency, he received analgosedation, after which he was intubated and mechanically ventilated. Brain MRI findings included irregular T2/FLAIR hyperintensities most prominent in the right parietal and temporooccipital region and the left occipital and temporal region, as part of the underlying condition. Initial EEG showed generalized slowing of background activity, with diffuse epileptiform abnormalities and an epileptic focus in the right fronto-centro-temporal regions. After the stabilization of his condition, correction of antiepileptic therapy (AET) was performed and physical therapy was initiated. He was discharged fully conscious, mobile with assistance, with right peripheral facial palsy.

Conclusion

Although we presented a patient whose condition improved significantly after status epilepticus, its onset in mitochondrial encephalopathies is usually associated with poor prognosis. Unraveling the mechanisms of epileptic seizures in MELAS is needed to develop more effective treatments.

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The effect of ventral tegmental stimulation on the course of local seizure reactions induced by hippocampal stimulation.

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Mood disorders are the most frequent psychiatric comorbidity in epilepsy, and in particular in temporal lobe epilepsy. Emotional disturbances in patients with epilepsy can be: preictal - which develops before the onset of seizures, and interictal - which develops between seizure manifestations. It is especially noteworthy that pre- and interictal emotional disorders in patients with epilepsy can have both negative and positive manifestations. Clinical and especially experimental research shows that the factors that alter the emotional state of humans or animals affect the development/course of seizure activity. The results of such studies are contradictory. The limited number of studies does not allow us to conclusively establish whether there is a relationship between these emotional disorders and epileptogenesis. The dopaminergic system of the brain stem is involved in the implementation of positive emotional reactions. Therefore, the influence of stimulation of the ventral tegmental area in the development of convulsive reactions caused by irritation of the hippocampus was studied. It was shown that electrical stimulation of the ventral cover blocks local convulsive reactions in the hippocampus. At the same time, it was shown that the inhibition of convulsive reactions lasts for several tens of minutes.

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Effects of stimulation of emotiogenic central structures on the development of seizure activity of the brain

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Emotional disturbances such as anxiety, fear, depression and aggression are often experienced by patients with temporal lobe epilepsy. These psychiatric symptoms may occur during or just after (postictal) a seizure; however, in some patients, they occur interictally (i.e. between seizures) and may profoundly change the individual's personality. There is a lack of evidences regarding the influence of activation of emotiogenic structures and emotional behavior on development of seizures. The interrelation between emotional and seizure reactions was studied in Wistar albino rats. In our study we tried to elucidate: can emotional behavior evoked by stimulation of the emotiogenic zones of the hypothalamus or of induction of acute pain stress modify manifestations of generalized seizures within the period where a "full" epileptic syndrom has been stable formed earlier? Our leading hypothesis is as follow: the emotional disturbances can be considered as the emergence of instinctive behavior with an adaptive significance of defense and as a by-product of the inhibitory processes that build up to protect against the future occurrence of seizures.Our experiments for the first time gave direct proofs of the statements that activation of the DMH resulting in initiation of emotional behavior (anxiety and fear) interferes with the development of seizure activity initiated by the kindling procedure.

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The effect of dorsomedial hypothalamic stimulation on the course of status epilepticus induced by hippocampal stimulation

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A few clinical observations allow one to suppose that patients manifesting seizures that result from hyperactivation of the limbic structures are especially predisposed to interictal behavioral emotional disorders. The respective shifts in the emotional sphere can significantly modify the patient's personality. The mechanisms responsible for susceptibility to mental disorders in subjects suffering from epilepsy remain mostly obscure. In our study, we tried, to elucidate whether induction of emotional behavior resulting from stimulation of the dorsomedial hypothalamus (DMH) influences the development of seizure activity in the course of epileptogenesis within the framework of self-sustained status epilepticus (stimulation of the hippocampus). To induce hippocampal self-sustained status epilepticus, the animals (n=8) were subjected to the stimulation of ventral hippocampus with 10 sec train of stimuli, according to the following time schedule for total of 9 epochs (10 min each). The 10 min epoch consisting of 9 min stimulation and 1 min rest period, repeated 9 times within 90 min. In the trial group, the animals were subjected to the DMH along with hippocampal stimulation, only the DMH was stimulated (100-150 μA, 50-60 Hz) continuously (1 min) during the silence (hippocampal stimulation-off) period. Stimulation of the DMH in the above experimental situations resulted in significant suppression of both electrographic and behavioral manifestations of seizure activity.

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The effect of ventral tegmental stimulation on the course of generalized convulsive reactions induced by hippocampal stimulation.

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Emotional disturbances in patients with epilepsy can be: ictal - which accompany seizures, peri ictal - which develop after the seizures, preictal - which develop before the onset of seizures, and interictal - which develop between seizure manifestations. The relation between emotions and epileptic activity relies largely on exiguous clinical investigations. Consequently, the empiric and/or neurophysiological evidence for the possible relation between emotions and epileptic activity remains poorly known to date. Therefore, the effect of stimulation of the ventral tegmental area on the development/course of hippocampal stimulation evoked kindling was studied. It has been shown that stimulation of the ventral tegmental area inhibits the development of kindling induced by hippocampal stimulation. Stimulation of the ventral tegmental area also inhibits the development of epileptogenic foci by irritation of the hippocampus in the presence of an already formed epileptogenic focus. The results obtained may be caused by the potentiation of dopaminergic neurons in the ventral tegmental area. It is also possible that neurons of the reticular nucleus of the thalamus participate in the blockade of seizure responses. It has been shown that activation of neurons of the reticular nucleus of the thalamus leads to a blockade of the development of generalized seizure responses.

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Interaction between Seizure and Theta Rhythm

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Recently it was shown by us that combined stimulation of hippocampus and dorsomedial hypothalamus resulted in suppression of the electroencephalographic seizure reactions and, respectively, manifestations of behavioral seizures reduced. It is expected, that augmentation of inhibitory processes in hippocampal neurons in the course of dorsomedial hypothalamus stimulation can trigger mechanisms preventing the development of epileptiform activity. Because of two important characteristics of the hippocampus—theta rhythm and epileptogenesis—these appear to be interrelated in respect of their cellular substrates, and as far as theta rhythm may modulate hippocampal excitability, a study of the functional relationship between theta rhythm and seizure activity was endeavored. The purpose of this study is to test this proposal by determining the effects on seizures of induction or suppression of hippocampal theta activity. Our findings show that 1) the frequency of hippocampal interictal epileptiform dischargers increased with the transition from the awake state to drowsiness and a slow-wave sleep phase. After the animal came from slow-wave sleep to paradoxical sleep, epileptiform activity completely disappeared; 2)When at hypothalamus stimulation instead of theta rhythm the electrical activity is desynchronized, there occurs a considerable intensification of seizure activity. Therefore, seizure-theta antagonism in our experiments could be interpreted as an adjustment of the inhibitory mechanisms when the theta rhythm is evoked.

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Effect of Negative Emotional Reactions on the Development of Seizures in a Kindling Model in Rats

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We studied the effect of acute stress induced by nociceptive stimulation of the limbs on the duration of electroencephalographic epileptiform activity and manifestation of generalized motor convulsive reactions under conditions of a kindling model of epilepsy in rats. Two and four weeks after termination of the kindling procedure, test stimulations of the hippocampus evoked intense attacks of epileptic activity. Short-lasting pain-inducing stimulation (intense electrical stimulation of the limbs) resulted in noticeable limitation of both ECoG and motor behavioral manifestations of epileptic activity determined by the formation of an epileptogenic nidus. The antiepileptic effect of acute stress was limited in time; manifestations of this effect reached their maximum about 3 h after painful stimulation, while about 6 h after such stimulation they became smoothed to a considerable extent.

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Epilepsy

Epilepsy in patients with depression after hemorrhagic stroke

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Objective: Depression and epilepsy are recognized complications following hemorrhagic stroke. This study aimed to evaluate the risk of epilepsy in patients with post-stroke depression.

Methods: This is a retrospective cohort study including hemorrhagic stroke patients diagnosed with depression in our center from April 2022 to November 2023. Patients with a prior diagnosis of depression or epilepsy were exluded. They were followed-up for a 12-month period with quarterly screening for clinical seizures. All patients had been started antidepressant treatment with either a SSRI or SNRI. Depression severity was evaluated using Hamilton Depression Rating scale (HAM-D). Statistical analysis included Chi-square test and logistic regression.

Results: A total of 103 patients was included who were diagnosed with depression after brain hemorrhage. Average mRS was 2.5 (SD 0.8) and HAM-D 13.1 (SD 4.5). Of these 63% were treated with a SSRI, 34.1% with a SNRI and 2.9% of patients had refused treatment or interrupted it due to early side effects. 19.4% of patients manifested seizures in the follow-up period, of which 45% focal seizures, 35% bilateral and 20% focal to bilateral. There was an increased frequency in the SSRI vs the SNRI group (22% vs 11%) which could suggest a trend towards a higher seizure risk with SSRI antidepressant however not statistically significant (p-value 0.057).

Conclusion: Post-stroke depression could be a risk factor for epilepsy. Study was limited by sample size, larger number studies needed to assess prevalence as well as differences among patients with different antidepressant medications or without therapy.

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Epilepsy

Suicidality in persons with epilepsy: under the radar of depression screening

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Introduction:

It is often assumed that most people at risk of suicide have depression, and therefore the use of valid depression screening tools, such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), is sufficient to effectively identify PWE at risk. The aim of our study is to assess whether scoring Item 4 of the NDDI-E separately from the total score of the NDDI-E adds value to screening for suicidality.

Methods:

A consecutive sample of Russian PWE admitted to the Center for Neuropsychiatry completed the NDDI-E and were assessed for suicide risk using the Columbia Suicide Severity Rating Scale (C-SSRS). Statistical methods used were Fisher`s exact test, Mann-Whitney test, Benjamini-Hochberg procedure.

Results:

A total of 372 PWE were enrolled (mean age 42.9 years, 64.8% female), of whom 42 (11.3%) were at risk for suicide according to the C-SSRS. In our sample, 31% of all suicidal patients had a total NDDI-E score below the cut-off for depression (12). With a cut-off of 1, Item 4 of the NDDI-E correctly identified suicide risk in 9 out of 13 PWE who scored positive for severe suicide risk on the C-SSRS but scored below the cut-off for depression on the NDDI-E.

Conclusion:

In routine practice, if decisions to refer a patient for psychiatric consultation were based solely on the total NDDI-E score, approximately 1/3 of at-risk PWE would not have access to appropriate psychiatric assessment and treatment. Our data support the utility of scoring Item 4 separately from the total NDDI-E score.

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Epilepsy

Stress and seizures: The October 7th experience

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Background:

Stress is among the most frequently self-reported seizure-promoting stimulus of seizures in patients with epilepsy. Stress is a vague subjective concept that is hard to quantify or define empirically. Moreover, it often coexists with other seizure triggers, such as fever or sleep deprivation. To date, studies that investigated the prevalence of seizures during stressful events had conflicting results.

On October 7th, 2023, a large-scale terrorist invasion accompanied by massive rocket launching against Israel took place. These traumatic life-threatening events with widespread exposure, undoubtedly qualifies as a stressful crisis and provide an opportunity to investigate the possible role of stress in provoking seizures.

Methods: All adults who presented to the emergency department (ED) of Tel Aviv Sourasky Medical Center between January 1st 2017, and February 29th, 2024, and were diagnosed with seizures were included. Demographic and clinical parameters were collected using MDClone, a data acquisition tool. We compared the number of new and recurrent cases after the traumatic exposure between October 2023 and February 2024 to prior years.

Results: A diagnosis of seizure was given to 351 patients who presented to the ED after the traumatic. There was no difference regarding demographic variables compared to patients who presented in the same period the year before. A predictive model based on the number of ED presentations in previous years showed no difference in the period above compared to previous years. The results are unchanged when adjusted to the overall ED admissions from any cause.