

# Problems Regarding Comorbidity of Epilepsy with Depression in Children: A Literature Review

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## Abstract

**Objective:** To review the literature on the comorbidity of epilepsy and depression in children.

**Materials and methods:** The following scientific research systems were used to achieve the set goal: MEDLINE; PreMEDLINE; PubMed Central (PMC); Cochrane Library; Scirus. <http://www.scirus.com/>; Google Scholar; FDA (U.S. Food and Drug Administration); EMA (European Medicines Agency); Rxlist; The New England Journal of Medicine; British Medical Journal; Ovid MD; Best Evidence; UpToDate; Internet Grateful Med; Scientific American Medicine; Clinical Evidence; Harrison's Online.

**Results:** A search of the Internet and scientific journals revealed 21 sources directly or indirectly related to epilepsy and depression in children.

**Conclusion:** An analysis of the literature has shown that despite the literature on the comorbidity of epilepsy and depression, this problem has not been studied in children.

**Keywords:** children; epilepsy; depression; comorbidity

Around 400 BC Hippocrates: "usually melancholy becomes epileptic, and epileptics – melancholic." [1] Recurrent seizures are associated with a number of harmful effects. Seizure-related deaths can account for up to 40% of all deaths in patients with chronic epilepsy. The sudden mortality rate in patients with epilepsy is 7-17% and is reported to be 27 times higher than in patients without seizures. [2]

The neurological dysfunction inherent in epilepsy increases the patient's susceptibility to mental disorders, including depression and psychosis. Depression is the most common comorbid psychiatric disorder in people with epilepsy. However, it is especially difficult to diagnose depression in children. Doctors should consider not only classic depressive symptoms such as anhedonia, but less common symptoms such as unexplained irritability, lack of affection from family members, unfounded somatic complaints, trouble concentrating, and poor school behavior. Depression is more difficult to diagnose in children with epilepsy and mental retardation [3]

Depression and suicide rates increased significantly in patients with epilepsy. Both epilepsy and depression are associated with a decrease in hippocampal volume, but it is unclear if people with both conditions have more atrophy than those with epilepsy alone. Some researchers have

linked depression to right ventricular epilepsy and hippocampal atrophy. At the same time, the author notes that this cannot be explained only by epilepsy. [4]

Depression was found to be most common in patients with epilepsy. These patients have lifelong depression between 30 and 35 years of age.

The variability of many factors plays a pathogenic role in the high comorbidity of both diseases. These variables were critically examined at an international symposium in Chicago in September 2010. Data from structural and functional neuroimaging studies in humans have provided a higher level of understanding of the common pathogenetic mechanisms of depression and epilepsy. The negative effects of depression on seizures have been documented in various studies. Contrary to previous views, the relatively high comorbidity of depression and epilepsy is not only a manifestation of a reactive process, but also leads to the fact that patients face multiple life obstacles with seizures. These data strongly suggest the existence of common neurobiological pathogenetic mechanisms that may play a key role in the high comorbidity of these two conditions. The effect of these pathogenetic mechanisms is not limited to high comorbidity, but plays a decisive role in the deterioration of the pharmacological and

surgical treatment of seizure disorders in patients with a lifelong history of depression. [5]

Cognitive problems in epilepsy can occur early in the disease. Modern technologies make it possible to discover the relationship between the structure and function of cognitive disorders in epilepsy. More and more people are learning about the connection between epilepsy, depression and anxiety. According to the patient, these two comorbid mental illnesses affect the risk of suicide, the side effects of antiepileptic drugs, and quality of life. Mental disorders are less common in patients with epilepsy and do not receive adequate treatment. Physicians treating patients with epilepsy should be aware that cognitive impairment and comorbid mental illness have a major impact on these patients.

In patients with epilepsy, identifying and treating these comorbidities is just as important as treating seizures [6]

Psychiatric disorders are more common in patients with epilepsy than in the general population. Although researchers have documented a strong link between epilepsy and comorbid mental illness, the nature of this link is still poorly understood. Therefore, mental illness in patients with epilepsy is often not diagnosed or treated, which leads to a further decrease in the quality of life of patients. The authors studied the comorbidity of epilepsy to better understand the relationship between the development of epilepsy and psychiatric disorders in adults and children. There is growing scientific interest in studying the relationship between epilepsy and comorbid mental illness in both adults and children, but they conclude that this is not enough. Further research is needed to create new and improved diagnostic tools for early detection of the onset of concomitant mental illness in adults and children and timely intervention to prevent their negative impact on real life activities. The authors note that physicians should be more careful about the risk of comorbid psychiatric illness in patients with epilepsy, especially the potential death and suicide risk associated with depression. [7]

Depression is a common medical condition that goes hand in hand with epilepsy. However, given the heterogeneity of epilepsy and depression, it is difficult to determine the etiology of depression. However, this overlap is so widespread that a two-way link has been proposed between depression and epilepsy. People with epilepsy and frequent seizures are more prone to depression. Depression varies across pediatrics, but it can be easily identified by understanding the nuances of mental health and the variability in neurovegetative symptoms. There are no clear guidelines for the treatment of epilepsy. Although there have been no clinical trials in pediatrics, anticonvulsants have been shown to improve symptoms of depression. Treating depression on your own can have a positive effect on epilepsy outcomes and quality of life. [8]

Despite the increased risk and prevalence of depression in young people with epilepsy, some researchers have found that only one third receive mental health services. Untreated depression leads to negative consequences and an increase in health care seeking and medical costs. Preventive screening behavioral medicine helps identify symptoms of depression and necessary interventions in efforts to optimize health-related quality of life (HRQOL). The main objectives of the study authors were: a) to study the degree of self-reported depression in young people with epilepsy, b) differences in demographic and medical indicators of depression, c) the effect of depression on HRQOL, and d) changes in subsequent depression and suicidal ideation. Depression was found in 23% of young people, and 14% of them confirmed suicidal thoughts. Depression is highly dependent on age, antiepileptic drugs, and insurance. Finally, the authors conclude that systematic assessment and early detection of depression or suicidal ideation in young people with epilepsy leads to a decrease in depression by improving the quality of life. [9]

Mood disorders, especially depression, are commonly associated with epilepsy. Mental health disorders were extremely common in epilepsy

and are still more common than in other chronic diseases. Fortunately, both medical and non-medical treatments can be very effective. Although the evidence base for treatment is underdeveloped, small samples and observational studies hold promise for positive results. For groin seizures that are not accompanied by generalized seizures, be aware of the possibility of concomitant depression. As the evidence base grows, more information will become available about susceptible subtypes and the optimal use of anticonvulsants and antidepressants. In the meantime, it remains to be determined whether depression will go a long way in improving the quality of life of people with epilepsy and comorbid mood disorders. [10]

Depression is one of the most common mental disorders due to its chronic nature and economic costs associated with society. Several studies have shown that early childhood depression prevention programs are beneficial for healthy children and adolescents.

However, the study notes this. There are still several comparable programs for children and adolescents with chronic conditions. This article discusses the comorbidity of depression with three conditions found in pediatric psychosomatic medicine: diabetes, epilepsy, and inflammatory bowel disease. The authors discuss the situation of adolescents who are chronically ill and at risk of developing depressive symptoms. Each patient group is familiar with specific risk factors and is associated with depression. It also presents existing individual programs and related research on depression prevention. After a literature review, it was shown that research on risk factors and depression prevention for these three patient populations is still in its infancy. While new risk factor models and biomarker approaches for depression prevention are emerging as a promising foundation, research highlights the importance of achieving better tailored preventive interventions for children and adolescents with chronic diseases. [11]

The author investigates some aspects of the relationship between epilepsy and depression, which have recently attracted increasing attention and may become a major research topic in the near future. Epidemiological studies show that in some cases, depression and suicide are premorbid symptoms before the onset of epilepsy. The suicide rate in epilepsy is three times higher than in the general population. Reliable tools already exist for detecting depression and suicide in patients with epilepsy, but real data are needed to develop common clinical pathways between neurology and psychiatry.

Data on children with epilepsy are still limited, although, in addition to epilepsy, about 50% of children with adults with mood and anxiety disorders have a history of mood and anxiety disorders. Despite the increased attention to the problem, the additional stigma associated with mental health problems remains one of the main obstacles to timely diagnosis and treatment. The new research will focus on developing common clinical pathways in neurology and psychiatry for treating mental illness and preventing suicide. New global campaigns to combat double stigma will support the disease in regions where it is still equally ill and poorly treated. [12].

Anxiety and depression in children and adolescents with epilepsy is a common comorbid condition that places a serious burden on patients and their families and complicates the clinical management of epilepsy. In this study, the authors provided an analytical review of the etiology, phenomenology, assessment, and treatment of depression and anxiety in pediatric patients with epilepsy. Recognition of effective comorbidities in childhood epilepsy is currently limited, and clinicians must consider the adjuvant role of antiepileptic drugs in such comorbidities. Recognition of comorbid mental illness in children and adolescents with epilepsy remains limited. Although rarely a single cause, the effects of anticonvulsants must be considered by clinicians in this context and appropriately addressed. [13]

Researchers have found that epilepsy is associated with a significantly increased risk of depressive disorders during adolescence. On the other hand, depression is more common in adolescents with epilepsy. These results highlight the importance of early detection and appropriate treatment of depression in adolescence. The prevalence of depressive episodes in adolescents with epilepsy is 8-35% higher than in the population of the same age. The relationship between epilepsy and depression is complex and potentially two-way, indicating a common pathophysiological mechanism between the two diseases. In addition, failure to identify and treat depressive disorders, especially during adolescence, leads to a number of negative consequences, such as increased suicidal ideation or behavioral risk and decreased quality of life. It is important to use psychiatric or psychological ratings, structured or semi-structured rating scales to identify depressive disorder. According to the authors, physicians should be able to regularly check for signs of depression in young people with epilepsy. The first step to consider when treating adolescent epilepsy depressive disorder is to consider possible reversible causes of anxiety and depression (i.e., controlling seizures with anticonvulsants). On the other hand, great attention should be paid to the education of children and adolescents and their families, and efforts should be made to improve knowledge about epilepsy, while reducing parental stress and increasing the competence of the child. Consideration should also be given to medical treatment for adolescents diagnosed with depression. [14]

In this presentation, the authors discuss specific and general risk factors for epilepsy in childhood epilepsy, prevention, clinical symptom assessment, and suicide risk and treatment. Epidemiological data on the detrimental effect of depression on the course of epilepsy and its long-term consequences are presented. Depression is an important risk factor for long-term negative outcome of epilepsy, regardless of the frequency of seizures, the type of epilepsy and the amount of antiepileptic drugs used. Despite a decrease in the number of epileptic seizures and an improvement in diagnosis and treatment, the incidence of comorbid psychopathology has not changed over the past 30 years. Patients with epilepsy have a higher risk of depression than patients with diabetes and asthma. The comorbidity of epilepsy and depression increases the risk of suicide compared to the general population: 20% of children with epilepsy commit suicide. Patients with epilepsy should have a mental health screening as part of their daily epilepsy treatment. Depression is common in childhood epilepsy and is associated with a high risk of suicide, severe epilepsy, and long-term sequelae. [15]

The fact that epilepsy goes hand in hand with a wide range of diseases is already accepted as a fact. Although epileptic seizures are an important element of epilepsy in children, there are a number of neurological, mental and cognitive disorders that lead to a decline in quality of life, which increases the burden of epilepsy in childhood. The most common comorbid conditions of childhood epilepsy include depression, anxiety, autism spectrum disorders, sleep disturbances, attention deficit disorder, cognitive impairment, and migraine. Although epilepsy can lead to comorbidities, many childhood illnesses have a two-way relationship, and the risk of epilepsy and epilepsy increases. The dual nature of epilepsy and comorbidities is likely to be a common pathophysiological mechanism of both seizures and comorbidities. While the recognition of co-morbid conditions in childhood epilepsy is increasing, the development of effective treatments has been delayed by concerns that drugs used to treat co-morbid conditions may increase the susceptibility to seizures. There is now some evidence that most drugs used for comorbid conditions are safe and do not relieve seizures. Unfortunately, data on medications for many diseases associated with epilepsy in children are very limited. There is a great need for randomized, placebo-controlled trials of drugs for efficacy and safety in the treatment of childhood epilepsy-related diseases. [16]

Depression is common and negatively affects the quality of life of patients with epilepsy. While many studies have looked at relevant predictors, the results are mixed. The goal of this meta-analysis is to examine risk factors that may increase the likelihood of depression in this population. The search was conducted by Medline, The Cochrane Library, Web of Science and Embase for a comprehensive study of the incidence of epilepsy and depression.

The results of the meta-analysis showed that several factors were associated with an increased risk of depression in epilepsy. This can help develop more effective strategies for prevention and selection of group depression. In addition, the mechanisms underlying these diseases require further study to determine appropriate and targeted interventions on a case-by-case basis. [17]

The authors used the following search methods: Cochrane Epilepsy Group Specialized Registry; Cochrane Central Registry for Controlled Trials (CENTRAL 2014 Issue 5), MEDLINE (Ovid), SCOPUS, PsycINFO, www.clinicaltrials.gov.

Research findings: There is very limited evidence that antidepressants are effective in treating depressive symptoms associated with epilepsy. Results from only a small randomized controlled trial show that venlafaxine has a statistically significant effect on symptoms of depression. No high quality evidence was found for the choice of antidepressants or drug class in the treatment of depression in patients with epilepsy. The review presents evidence of the low quality of security in terms of escalating tensions with the SSRI. However, I have no comparative data on antidepressant classes and seizure safety. There are no comparative data on antidepressants and psychotherapy in the treatment of depression in epilepsy. The researchers believe that comparative clinical trials of antidepressants in large populations of epilepsy and depressed patients are needed to better inform future treatment strategies. [18].

L.R. Zenkov [19] notes that depression requires special attention in epilepsy. According to the author, 10-30% of patients with epilepsy suffer from depression. This is primarily due to brain dysfunction in epilepsy and limited stigmatization of educational, professional and social contacts.

## Conclusion

Depression is one of the mechanisms explaining the comorbidity of epilepsy. Post Author: R.M. theory. Kindling in the classical sense is a gradual increase in sensitivity to intermediate repetition of stimulation of the same subelectric neuron over time. In this sense, the amygdala has been studied in more detail. This is due to the stimulation of repetitive excitation: a decrease in the seizure threshold after an electrical discharge; high blood pressure; progression of the seizure phase, ending with full-scale tonic-clonic seizures of the forelimbs with raising and lowering; it is a manifestation of evolutionary stimuli for spontaneous seizures. This evolving process is immediately accompanied by changes in the spatio-temporal expression of early genes, neurotrophic factors, and late-acting genes, as well as changes in the model of the effectiveness of various pharmacological interventions in time and space. Since remembering this pattern is a paradigmatic manifestation of behavior, some pharmacological seizures result from local anesthesia such as cocaine and lidocaine, and some epileptic syndromes are likely homologous modeled by this phenomenon. However, since non-epileptiform syndromes such as recurrent episodes of affective disorders and some pain syndromes contain heterogeneous evolutionary elements similar to sedation, some of the principles involved in the burning sensation may be related to the understanding and treatment of these syndromes. For example, one can try to distinguish between secondary and adaptive genes involved in the initial pathological processes in the evolution of the syndrome. This differentiation can have a significant impact on the development of

therapeutic approaches to suppress or enhance changes, respectively. In these cases, the results obtained using the kindling model are necessarily indirect and limited, since various neuroanatomical and biochemical processes can influence the development of each neuropsychiatric syndrome. Given the limitations of well-known non-homologous models, relapse can provide information on the longitudinal course, progression, and treatment of several neuropsychiatric syndromes that can be clinically tested directly [20]. The great Russian scientist I.P. Pavlov once used the following phrase about a patient with alcoholic delirium: “This is not a state of drowsiness, the hallucinations observed in a patient are a manifestation of neuronal awakening” [20]. Thus, the study of the comorbidity of epilepsy and depression in children is of great theoretical and practical importance. First, it will help identify depression early. Second, it can prevent suicide. Third, the number of resistant forms of epilepsy treatment will decrease. Finally, it will have a positive effect on improving the quality of life of patients with epilepsy.

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