



NARRATIVE REVIEW

Psychiatric disorders in children and adolescents with temporal lobe epilepsy: A narrative review

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Abstract

People with epilepsy (PWE) are at higher risk of psychiatric disorders (PD), disability, and reduced quality of life than the general population, especially in childhood and adolescence and when seizures originate from the temporal lobe. Temporal Lobe Epilepsy (TLE) is the most common type of focal epilepsy and can be due to structural abnormalities, or non-lesional causes, such as genetic variants. The prevalence of PD is approximately 20%–30% in people with epilepsy in general, and from 40% up to 80% in people with TLE. A higher rate of anxiety and depression disorders has been observed in association with TLE than with extra-temporal epilepsy, or idiopathic generalized epilepsy, or other chronic diseases such as diabetes. However, while the association between psychopathology and TLE has been extensively assessed in adults, only a few studies have focused on its expression in children and adolescents. In this review, we describe the prevalence, characteristics, and risk factors for PD in people with epilepsy in general and with TLE, with a specific focus on the pediatric age. In addition, we provide insights into the current knowledge of the pathophysiological bases of psychiatric symptoms in children and adolescents with TLE.

Plain Language Summary: This review examines the frequency and characteristics of psychiatric disorders in people with temporal lobe epilepsy, with a focus on children and adolescents.

Similarly to adults, younger people with epilepsy have higher rates of psychiatric disorders, such as depression and anxiety, than healthy peers or children with other chronic illnesses such as diabetes and [asthma](#). Contributing risk factors include epilepsy duration and severity, and the effects of antiseizure medications, as well as psychological challenges, sociocultural influences, and family dynamics. Psychiatric disorders associated with temporal lobe epilepsy are relatively frequent, probably in relation to the critical role that some limbic

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structures in the temporal lobe, such as the amygdala and hippocampus, play in regulating emotions and behavior.

KEYWORDS

adolescents, children, comorbidities, psychopathology, temporal lobe epilepsy

1 | INTRODUCTION

Epilepsy is one of the most common chronic neurological disorders and is characterized by variable clinical features and etiologies and temporal lobe epilepsy (TLE) is the most common form of focal epilepsy.¹

TLE can be due to structural abnormalities (both congenital and acquired), or non-lesional causes, such as some genetic variants whose consequences alter neuronal excitability. Among structural causes, hippocampal sclerosis, which is sometimes preceded by a history of prolonged febrile seizures, is considered by some authors as the most common etiology in adults,² while low-grade tumors, especially glioneuronal, and focal cortical dysplasia (FCD), are the most common in children and adolescents.^{3–5} Other possible underlying pathologies are post-infectious, traumatic, and vascular lesions.¹ Genetic causes include autosomal dominant lateral TLE, associated with *LGII* gene mutations,⁶ familial mesial TLE, focal reading epilepsy,⁷ and other polygenic conditions.⁸ In addition, variants in different genes such as *DEPDC5*, *NPRL2*, *NPRL3*, and other genes can cause focal epilepsy arising anywhere in the brain, including the temporal lobe. Available evidence on TLE etiology might be partly biased towards patients with drug-resistant epilepsy who undergo surgery, since neuropathological characterization is certainly more reliable than neuroimaging. In a series dating back to when only low-resolution MRI scan was available,^{9,10} hippocampal sclerosis (HS) and gliotic scars were reported more frequently than developmental problems in children with new-onset TLE and seemingly normal neuroimaging.

The 1989 International League Against Epilepsy classification¹¹ of epilepsies distinguished between mesial temporal lobe epilepsy (mTLE), in which seizures originate in the hippocampus, entorhinal cortex, amygdala, and parahippocampal gyrus,¹² and lateral TLE, in which seizures originate from the temporal neocortex, including the superior, medial, and inferior gyri, the temporo-occipital and temporo-parietal areas.¹³ Mesial temporal lobe and lateral temporal lobe seizures have different ictal clinical manifestations as summarized in Figure 1.

In children and adolescents, temporal lobe epilepsy has clinical features that may differ from those observed

Key points

- People with epilepsy, especially children with temporal lobe seizures, are at higher risk of psychiatric disorders (PD).
- The prevalence of psychiatric disorders in people with temporal lobe epilepsy ranges from 40% to 80%.
- The etiology of PD in epilepsy is multifactorial, involving neurobiological, disease-related, iatrogenic, psychological, and social factors.
- Accurate psychiatric assessment is crucial for identifying at-risk patients and providing appropriate and timely interventions.

in adults.¹⁴ Previous studies have documented an inverse relationship between ictal motor manifestations and age, with younger children being more likely to have initial tonic, clonic, myoclonic, and hypermotor phenomena, followed by dystonic posturing. In addition, bilateral and symmetric movements are possible during ictal motor manifestations, despite their unilateral origin, possibly due to incomplete myelination of the central nervous system.^{15,16} In toddlers and infants, it is difficult to fully

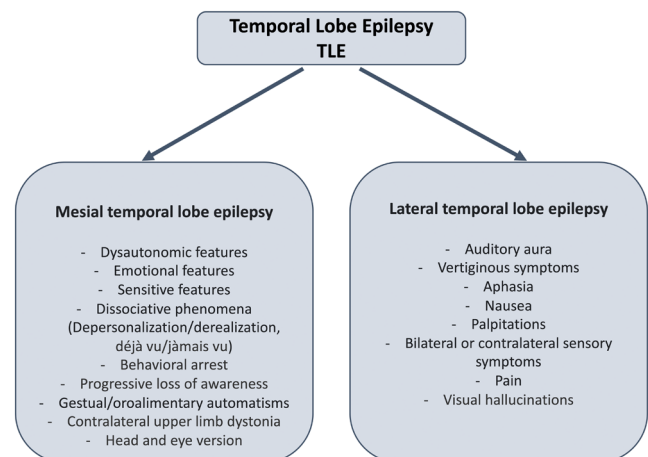


FIGURE 1 Ictal clinical manifestations of mesial and lateral temporal lobe seizures. TLE, temporal lobe epilepsy.

evaluate auras because verbal skills are not fully developed. Automatisms are simpler than in older children,¹⁷ and can be oroalimentary (lipsmacking, chewing, swallowing) and gestural (hand fumbling).¹⁶ Conversely, preschool and early school-age children (age 3–6 years old) develop a better lateralization of ictal motor manifestations,¹⁶ including dystonic posturing, versive or non-versive head turning, eye or mouth deviation, which lateralize to the contralateral hemisphere in 75–100% of cases, and can exhibit more complex automatisms, such as pillrolling, fumbling, grasping, picking at bedclothes, and hand clapping.¹⁸ Auras are easier to evaluate, based on the child's own description. Older children (age >6 years old) and adolescents can experience the same semiology as adults. In addition, in older children loss of awareness may last for several minutes, and be followed by a prolonged postictal state with confusion, disorientation, fatigue, headache, and various types of automatisms, which can be hard to distinguish from ictal manifestations.¹⁹

2 | PSYCHIATRIC DISORDERS IN PEOPLE WITH EPILEPSY

2.1 | Epidemiology

The prevalence of psychiatric disorders (PD) in people with epilepsy is approximately 20%–30%, which is much higher than in the general population.^{20,21}

Psychiatric comorbidities can complicate epilepsy management by reducing adherence to anti-seizure medications (ASM), which, in turn, can result in increased seizure frequency and worsening of cognitive and behavioral outcomes.²² However, in younger children, compliance may be adequate, since parents are usually responsible for administering ASM. Epilepsy has per se a significant impact on quality of life,^{23–25} which can be more compromised due to psychiatric comorbidities than by seizures.²⁶

A population-based study in which a cohort of patients with childhood-onset epilepsy were followed for 35-years confirmed that long term epilepsy is consistently associated with psychiatric and psychosomatic disorders.²⁷

Some studies tried to evaluate and estimate the prevalence and rate of the different PD in epilepsy patients (Table 1).²⁰ A recent meta-analysis of population-based studies has concluded that, in people with epilepsy, psychiatric disorders have a high prevalence, with depression, anxiety, and psychosis being the main conditions.²⁸ These figures are also confirmed by a Danish registry study of people with epilepsy over a 5-year period²⁹ and the Trøndelag Health Study (HUNT).³⁰

TABLE 1 Prevalence of the different psychiatric disorders in people with epilepsy.

Psychiatric disorder	Prevalence
Major depressive disorder	24.2%
Post-traumatic stress disorder	14.2%
General Anxiety disorder	11.1%
Substance Abuse	7.9%
Bipolar disorder	6.2%
Psychotic disorders	5.7%
Obsessive compulsive disorders	3.8%

A higher prevalence of psychiatric symptoms has been described in epilepsies with focal seizures (37.2%), particularly temporal lobe seizures (from 40% up to 80%),^{20,31–33} compared to idiopathic generalized epilepsies (19.2%).^{20,34,35} In particular, a higher rate of anxiety^{36,37} and depression³⁷ has been observed in association with TLE than with extra-temporal epilepsy, idiopathic generalized epilepsy,³² or other chronic diseases such as diabetes, thus supporting the hypothesis that PD do not result from psychopathological consequence of a chronic disease, but rather reflect dysfunction involving limbic structures.^{33,38} Metabolic abnormalities in the amygdala and anterior cingulate gyrus,³⁹ likewise dysfunctional connections between limbic structures and brainstem nuclei⁴⁰ have been associated with depression and TLE.

2.2 | Characteristics of PD in TLE

Studies investigating psychiatric disorders in TLE have focused either on symptoms assessment or clinical diagnosis. Among studies assessing symptoms, Balibey et al.⁴¹ administered Beck Depression Inventory and the Beck Anxiety Inventory and showed higher levels of anxiety and depression in the PWE compared with the healthy control group. In addition, a higher frequency of these symptoms was observed in people with TLE compared with those with extratemporal epilepsy (53% vs. 25% for depression and 38% vs. 21% for anxiety levels).⁴¹

In contrast, Swinkels et al.⁴² suggested that PD in people with TLE are not due to the topography of the seizure onset zone, but to additional risk factors, such as epilepsy duration, seizure frequency, or concomitant frontal lobe dysfunction. In Swinkels's study,⁴² neither an overabundance of psychiatric manifestations in people with TLE compared with those with extra-TLE, nor differences in the frequency of PD between patients with left versus right hemispheric involvement were found.

Among studies based on clinical diagnoses, Ertem et al.⁴³ reported that 57% of patients with mesial TLE

presented psychiatric comorbidities, compared with 37% of patients with juvenile myoclonic epilepsy (JME), with anxiety disorders (23% of patients) and mood disorders (17%) being the most common.

In the context of PD associated with epilepsy, a crucial aspect is represented by the suicide risk. The lifetime prevalence of suicide attempts among PWE has been estimated to be around 9.3% in two studies.^{20,34} The suicide risk is higher in people with epilepsy than in those with other chronic diseases, and in the general population⁴⁴ and increases with greater seizure severity and higher seizure frequency.³⁴ In a cross-sectional study, the authors described psychiatric comorbid conditions (including suicide risk) in 32.5% of PWE (32.50%), compared to 17.5% of patients with asthma and 7.5% of healthy controls.³⁴ As well as for other psychiatric disorders, the suicide risk is higher in TLE patients than in epilepsy in general (25-fold in TLE vs. fivefold in epilepsy in general).⁴¹

Several studies have tried to evaluate the correlation between PD and the lateralization of the seizure onset zone in TLE, with discordant results. Previous studies reported a higher occurrence of psychopathology in individuals with left TLE than in those with right TLE,⁴⁵ in particular depression and anxiety,^{46–48} especially when associated with concomitant frontal lobe dysregulation.⁴⁹

Personality trait disturbances have been observed more frequently in people with left than in those with right TLE or generalized epilepsy, possibly due to a disruption of left-hemisphere language mechanisms.⁵⁰ Other authors have found that left temporal lobe lesions,⁵¹ and left-temporal lobe epilepsy,³¹ can be correlated with higher risk of developing a schizophrenic-like psychosis.⁵² Lower self-estimate of the quality of life has been observed in left compared with right-TLE patients.⁴⁸ However, other studies did not indicate a role of the lateralization of TLE in psychiatric comorbidities^{42,53} or demonstrated a higher prevalence of PD with right-sided epilepsy.³⁶ The above-mentioned reports have focused on the possible causal relationship of epilepsy variables with psychiatric disorders, while others have hypothesized that both PD and epilepsy are caused by a common underlying anatomical-physiopathological dysfunction.³⁸ While cross-sectional studies have not helped clarifying the nature of this association, prospective observational studies have suggested a bidirectional relationship between epilepsy and PD.²⁸ More recently, common pathogenic mechanisms have been hypothesized between seizures and all major psychiatric disorders, which can be considered not as comorbidities but rather as related to the same pathophysiology of epilepsy.⁵⁴ As reported by Vinti and colleagues,⁵⁴ functional and structural changes in the fronto-temporo-mesial circuits implicated in behavioral and emotional manifestations, as well as genetic factors, including epigenomic, transcriptomic,

and proteomic alterations, can influence both epilepsy and cognitive-psychiatric disorders.

3 | PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS WITH EPILEPSY

3.1 | Epidemiology

Childhood and adolescence are dynamic phases of personal, social, and psychological changes, marked by identity formation and self-concept. Children and adolescents participate in social activities and start to build their social relationships, knowledge, and independence. A chronic disease, and in particular of epilepsy can have significant consequences on emotional and behavioral aspects,^{55,56} as well as on educational, socio-cognitive and neuropsychological domains, including Theory of Mind and executive functions.⁵⁷

Psychiatric and neuropsychiatric disorders occur at higher rates in children and adolescents with epilepsy,^{55,56,58,59} than in healthy controls or pediatric patients with other chronic conditions. For instance, Davies et al.⁵⁹ observed psychiatric conditions in up to 37% of children with epilepsy, compared with 9% of healthy controls and 11% of children with diabetes mellitus.

Population-based studies^{60,61} confirmed the high rate of psychiatric comorbidities in children and adolescents with epilepsy.

A recent retrospective observational study described the relationship between psychiatric comorbidities, investigated by clinical features, and epilepsy, focusing particularly on the age of disease onset.³⁰ The authors considered a sample of 448 individuals with epilepsy, diagnosed between 1987 and 2019 and found that PD were significantly more common in people with childhood-onset epilepsy (45% of cases).³⁰ Depression is one of the most common PD in people with epilepsy of all ages, especially in children and adolescents, with a rate of 23%–33%.^{62–64}

However, in children or adolescents, with or without epilepsy, depression is often underreported and undertreated,^{65–67} probably due to the atypical presentation of its symptoms, consisting in irritability, attention problems, lower levels of school performance, or a high rate of other psychiatric symptoms or comorbidities.^{68,69}

3.2 | Characteristics of PD in children and adolescents with epilepsy

The etiology of PD in people with epilepsy is multifactorial, including not only neurobiological, disease-related

variables, and iatrogenic factors but also psychological and social factors (Figure 2).

Concerning epilepsy variables, potential risk factors for psychopathology include a longer duration of epilepsy, seizure severity,^{70,71} or ASM, especially in polytherapy.^{72,73} A prospective longitudinal study following 224 children for 2 years after epilepsy onset reported that seizure frequency was an additional risk factor for behavioral problems.⁷⁴ In addition, a higher risk of psychopathology has been described in children with focal compared with those with generalized seizures.^{67,75} For instance, Thome-Souza et al.⁷⁵ reported a 90% rate of PD, particularly depression, in children and adolescents with “partial” seizures versus the 10% rate in those with generalized seizures. In addition to the epilepsy variables, social determinants of health may play a role. Family factors have been considered as a relevant risk factor, in particular a family history of psychiatric disorders^{65,75} and family functioning problems⁷⁶ such as a poor parental attention, or high levels of family stress.^{62,77} A longitudinal study using multiple regression analysis to evaluate 127 children with epilepsy for 1 year confirmed that family variables can influence the development of behavioral problems.⁷⁸

Inconsistent and contradictory data have been reported regarding gender differences. Some studies have reported a higher prevalence of depression in girls than in children and adolescent boys,⁷⁸ while other studies found no differences,^{79,80} or described a higher rate in boys than in girls.⁸¹ Demographic or cultural factors appear to have little or no impact on the onset of psychiatric or behavioral issues in children with epilepsy,^{62,82} while an important risk factor for depression is the stigma related to epilepsy. In fact, poor knowledge of this disorder⁸³ can lead to an experience of

even greater discomfort and suffering,⁸² lowering of self-esteem⁵⁶ and reduced quality of life.⁸⁴

Recently, a study investigated the determinants of Health-Related Quality of Life (HRQOL) in 88 pediatric patients with TLE through parental ratings on the Behavior Rating Inventory of Executive Function (BRIEF), Behavior Assessment System for Children (BASC-2) and Quality of Life in Childhood Epilepsy (QOLCE) questionnaires and showed that depressive characteristics, related to low executive function, current ASM, and hippocampal sclerosis, were indirectly correlated with HRQOL.⁸⁵

Anxiety, the second most common PD in young people with epilepsy, occurs in 5%–18% of children and 0.6%–7% of adolescents.⁶⁷ Among anxiety disorders, GAD is the most common. Similar to adults, anxiety problems in children and adolescents with epilepsy have been associated with clinical variables such as seizure frequency, polytherapy, and duration of epilepsy.⁷² As with depression, the role of psychological, family-related or social factors has also been investigated in anxiety disorders. Psychological variables such as the unpredictability of seizures, feelings of helplessness experienced by patients, fear of future seizures, and low levels of self-esteem have also been considered relevant risk factors, especially in adolescents. Other risk factors including socio-cultural aspects, for example, a low level of knowledge about epilepsy, misinformation, stigma,^{55,56} and family context, such as parental stress or reaction to fear and distress, can also contribute to child's anxiety.⁷⁶ Some studies described a higher rates of anxiety in adolescents compared with younger children,⁸⁶ while other studies indicated higher prevalence in younger children.⁶⁷ High levels of anxiety have been found at all ages, and the contrasting results between studies may be due to differences in how these symptoms are manifested in children and adolescents. For instance, young children more frequently exhibit autonomic and agitation symptoms, while adolescents manifest cognitive and socially avoidant symptoms.⁵⁵ Regarding gender differences, despite a female predominance for anxiety disorders in the general population, no significant correlation between gender and anxiety has been found in children with epilepsy.^{72,87,88}

The contribution of the seizure type to anxiety has never been clearly confirmed in children and adolescents.^{55,72,87} Williams and colleagues⁸⁷ observed similar rates of anxiety disorders among children with complex partial (CPS) and absence seizures (CAE). Oguz and colleagues⁷² also reported similar rates of anxiety disorders in children with generalized tonic-clonic, simple partial, complex partial, and absence seizures. Only Caplan et al.,⁶⁷ comparing 100 children with complex partial seizures and 71 children with absences, reported a higher rate of anxiety disorders in those with CAE and

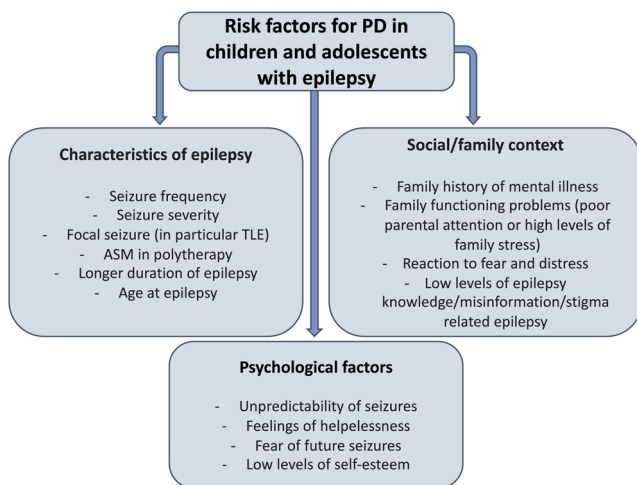


FIGURE 2 Main risk factors for PD in children and adolescents with epilepsy. ASM, anti-seizure medications; PD, psychiatric disorders; TLE, temporal lobe epilepsy.

a higher rate of depression in those with CPS. This could be due to the older age of the patients with complex partial seizures compared with those with absences but also be related to the anatomic basis of epilepsy with focal seizures.

In addition to psychiatric symptoms, an increased risk for suicide attempts has also been observed in children and adolescents.⁴⁴ Some studies have reported that the suicide risk is significantly higher in children and adolescents with epilepsy compared the general young population.⁵⁵ Caplan et al. reported the suicide risk rate up to 20%, although, in that study, only 33% of pediatric patients were receiving some form of mental health service.⁶⁷ However, Jones et al. reported that the lifetime rate of suicide attempts or ideation ranges from 5% to 14%.⁸⁹ Conclusive data are lacking and further studies are necessary to identify the most appropriate type of intervention.^{44,90}

4 | PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS WITH TEMPORAL LOBE EPILEPSY

While the association between psychopathology and TLE has been extensively assessed in adults,^{20,31–33,36,37,91} only a few studies have focused on its expression in children and adolescents.^{55,92–98}

In a study including 100 children with TLE, 85% experienced psychiatric problems.⁹² In another study on 132 children and adolescents with various epilepsy syndromes, the rates of internalizing disorders (41% of the sample) were similar between patients with generalized epilepsy and those with focal epilepsy. Conversely, other studies reported higher rates of depression and anxiety in young people with TLE compared to those with extra-temporal epilepsy.⁹⁷ Temporal lobe epilepsy was related with a twofold increased risk of clinically significant depression ratings compared with frontal lobe and generalized epilepsy.⁹³

Shukla et al.,⁹⁴ when comparing children with TLE with those with generalized epilepsy, also described a significantly higher number of emotional disturbances (18% vs. 6%) and PD (79% vs. 47%) in TLE; in particular, the “neuroses” rates were 37% versus 16%, personality disorders rates 23% versus 21% and psychoses 19% versus 10%. The same author,⁹⁵ some years later, demonstrated a higher incidence of PD, especially schizophrenia, in 25 patients who had TLE in childhood, compared with those with “grand mal epilepsy.” Temporal lobe seizures, in particular those with loss of awareness, are assumed to be at risk for important mental health illnesses.⁹⁶

Recently, Schraegle and colleagues⁹⁸ assessed the clinical and psychological pattern of behavioral and

psychiatric disorders in 81 children with TLE, and identified three distinct behavioral phenotypes that is, no behavioral concerns (43% of patients), externalizing issues (41% of patients), and internalizing disorders (16% of patients). These behavioral phenotypes were associated with relevant differences in clinical epilepsy and psychosocial variables. Externalizing problems correlated with younger child age, lower maternal educational level, and higher rates of single-parent households, while internalizing problems were linked to older age at seizure onset and higher prevalence of hippocampal sclerosis and family history of psychiatric disorders. In addition, among the studies assessing symptoms, a cross-sectional single-center study administered the Youth Self Report (YSR) to assess psychopathological symptoms and the Weinberger Adjustment Inventory (WAI) to evaluate personality aspects in 28 adolescents with pharmaco-resistant symptomatic TLE and frontal lobe epilepsy (FLE) aged 14–18 years. The authors observed higher rates and wider ranges of psychopathological symptoms, with high prevalence of internalizing symptoms in patients with TLE, but not in those with FLE. When assessing personality aspects, a significantly higher mean score for distress and repressive defensiveness, and a significantly lower mean score for positive emotion and confidence were observed in adolescents with TLE.⁹⁹ In contrast, Kaminer et al.¹⁰⁰ found similar prevalence of depression in adolescents with TLE compared to those with chronic asthma, thus indicating that PD in adolescents with epilepsy are due to the chronic health condition rather than to epilepsy itself.

Although the evidence for an association between seizure type or lateralization and psychiatric symptoms in children is weak,⁶² a major involvement of the left TLE has been suggested.^{81,92,101} A study⁸¹ evaluating the risk for learning and behavioral problems in a group of schoolchildren with epilepsy found a correlation between persistent left temporal spikes on the EEG and a higher rate of “disturbed behavior,” especially compared with children with generalized epilepsy or persistent right temporal spikes. Another study described the association between left TL seizures with loss of awareness and interictal schizophrenia-like psychosis.¹⁰¹ Finally, an association was observed between persistent TLE and the onset of psychosis, in particular in patients with left-sided EEG abnormalities during childhood.⁹²

Camfield¹⁰² did not confirm significant behavioral or cognitive differences (such as depression, anxiety, psychosis, on a clinical scale of a Personality Inventory for Children), between children with left and right EEG abnormalities. However, the sample size was too small to definitively exclude behavioral differences correlated with the lateralization of TLE. Other studies described how TLE etiology may have different prognostic

implications on psychological problems, concluding that children with significant antecedents/hippocampal sclerosis are expected to have the greatest risk of psychological disorders.¹⁰³

Finally, some authors have tried to establish the impact of TLE surgery on psychiatric comorbidities.

McLellan and colleagues¹⁰⁴ tried to establish the prevalence and spectrum of PD in 60 pediatric patients (25 females, mean age at surgery:10years and 7 months) with TLE before and after epilepsy surgery. These authors found one or more psychiatric disorders in 72% of patients and two or more PD in 45% of them, with similar rates after surgery. A recent systematic review and meta-analysis¹⁰⁵ of 10 surgical series investigated the psychiatric outcomes of TLE in patients (both adults and children) with psychiatric comorbidities. The percentage of patients whose PD resolved or improved after surgery varied widely among studies, resulting between 15% to 57%, at last follow-up. While psychiatric symptoms improved in a substantial percentage of people with TLE after surgery, 7%–36% of patients may worsen, especially children. In general, outcome reports including symptom scores are scarce and predictive factors for favorable outcomes remain to be identified.

5 | THE ROLE OF TEMPORAL LOBE IN PSYCHIATRIC DISORDERS: PHYSIOPATHOLOGICAL ASPECTS

Temporal lobe is deeply linked with the limbic system,³³ which plays a crucial role in emotions and behavior.¹⁰⁶ During infancy or early childhood, ictal and interictal epileptiform discharges can negatively influence the normal development of neuronal integration, leading to plastic changes, with possible deleterious consequences on normal brain functioning.³⁹ Given the fundamental role of the temporal lobe in regulating emotions and behavioral aspects, PD can develop when epilepsy involves this anatomic area, and in general the limbic system.^{38,106}

Some studies have not confirmed the hypothesis of a specific role of TLE in the pathogenesis of PD, blaming other factors, such as epilepsy duration, seizure frequency, frontal lobe dysfunction, or multifactorial aspects,⁴² or simply deeming them as a psychological react and effect of poor adaptation to a chronic disease.^{75,100}

Finally, another theory suggests that epilepsy and PD can be caused by the same underlying pathological process.³⁹ However, this is an unsolved question: whether the onset of psychiatric symptoms is secondary to epileptic seizures, or both the PD and

epilepsy are directly caused by a common underlying anatomical-physiopathological dysfunction.³⁸

6 | CONCLUSIONS

The association between PD and temporal lobe epilepsy has been widely studied in the adult population. However, only a few studies have addressed this topic in children and adolescents, with inconclusive evidence.

Considering the high prevalence and possible consequences of PD in children and adolescents with TLE, an accurate assessment of the psychological and psychiatric aspects should always be performed during the routine clinical evaluation to identify patients at risk and provide appropriate and timely intervention. The potential overlap of some seizure symptoms (e.g., fear, anxiety, autonomic manifestations) with common psychiatric manifestations such as panic attacks, can complicate the diagnostic process, especially in non-specialized settings.^{107,108}

There are major gaps in our understanding of the causal relationships between antecedents, MRI epileptogenic lesions, TLE, and cognitive and psychiatric disturbances. The role of initial precipitating injuries such as febrile status epilepticus, viral infections or autoimmune dysfunctions remains speculative. Given the relevance and the negative implications of the phenomenon, future longitudinal studies using timely EEG recordings, advanced MRI techniques, and comprehensive assessment of comorbidities are needed to address the pathophysiological mechanisms underlying the bases and risk factors for psychiatric symptoms in children and adolescents with TLE.

Age at seizure onset, disease duration, PD and impaired intellectual functioning have been correlated with a poor outcome in social abilities, communication, occupation, social engagement, and life skills.¹⁰⁹ If seizures are well controlled and basic education is successful, young people with epilepsy have a social functioning comparable to that of their healthy peers.¹¹⁰ Therefore, in addition to conventional epilepsy treatment, it is crucial to provide all available social and educational support, including cognitive training, meta-cognitive therapy, psychotherapy, or work/social training, to promote intellectual, functional, and social development in later life.

AUTHOR CONTRIBUTIONS

Pietro Cappelletto: Writing—original draft. **Claudia Accolla:** Writing—original draft. **Martina Preti:** Writing—original draft. **Tiziana Pisano:** Review and editing. **Renzo Guerrini:** Conceptualization, review and editing. **Carmen Barba:** Conceptualization, Review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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