

Factors Affecting Depressive Symptoms in Children and Adolescents With Epilepsy

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Objectives: We aimed to evaluate the clinical and psychological factors influencing depressive symptoms in children and adolescents with epilepsy.

Methods: We administered self-reported questionnaires assessing children's depressive symptoms (Children's Depression Inventory, CDI) and anxiety (Revised Children's Manifest Anxiety Scale, RCMAS) to children and adolescents with epilepsy (n=87, age range=6–17 years). We asked their parents to complete questionnaires on epilepsy-related variables, parental stress (Questionnaire on Resources and Stress, QRS), parental anxiety (State-Trait Anxiety Inventory, STAI), family functioning (Family Adaptability and Cohesion Evaluation Scale, FACES), children's attention problems (Abbreviated Conners Parent Rating Scale Revised, CPRS), and children's behavioral problems (Korean Child Behavior Checklist, K-CBCL). Stepwise multiple regression analysis was performed to identify predictive variables affecting depressive symptoms.

Results: Family adaptability ($r=-0.240$, $p=0.026$), family cohesion ($r=-0.381$, $p<0.001$), children's attention problems ($r=0.290$, $p=0.006$), children's anxiety ($r=0.714$, $p<0.001$), children's behavioral problems ($r=0.371$, $p<0.001$), parental anxiety ($r=0.320$, $p=0.003$), and parental stress ($r=0.335$, $p=0.002$) were significantly correlated with children's depressive symptoms. Children's anxiety ($\beta=0.655$, $p<0.001$) and parental stress ($\beta=0.198$, $p=0.013$) were significantly related to their depressive symptoms (adjusted $R^2=0.539$).

Conclusion: Clinicians should detect and manage children's anxiety and parental stress, which may affect depressive symptoms in children and adolescents with epilepsy.

Keywords: Epilepsy; Child; Adolescent; Depression.

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INTRODUCTION

Depression is one of the most common psychiatric comorbidities among children with epilepsy. Vega et al. [1] reported that children with childhood absence epilepsy have more symptoms of depression, including sadness and crying, when compared with healthy controls. Additionally, they exhibit social isolation and low self-esteem. Adolescents with epilepsy have significantly higher depression related to interpersonal problems and anhedonia, which are subscales of the Children's Depression Inventory (CDI) [2].

Studies have explored factors associated with depressive symptoms in children and adolescents with epilepsy. The so-

ciodemographic variables, age and sex showed inconsistent correlations with depressive symptoms. One previous study showed no correlation between age, sex, and depressive symptoms [3]; however, another study [4] reported that depression is more prevalent in adolescents than in children. Regarding epilepsy-related variables, a previous study [3] did not show any relationship between epilepsy duration, age at seizure onset, and depressive symptoms [3]. Children's anxiety [3] and behavioral problems [5] have been shown to be positively correlated with depressive symptoms, although this was not confirmed to be significant through multiple regression analysis. Furthermore, parental anxiety is associated with depressive symptoms in adolescents [6] but not in children [7]. However, the small and heterogeneous sample was a limitations of this study with children.

Previous studies on depressive symptoms in children and

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adolescents with epilepsy have shown variable results; however, most of these studies were conducted in Western populations. Therefore, we aimed to investigate the correlation between depressive symptoms and clinical and psychological factors in children with epilepsy, using reliable standardized scales and questionnaires. Additionally, we aimed to comprehensively evaluate sociodemographic, epilepsy-related, and psychological variables in children, adolescents, and parents, as well as family function variables.

METHODS

Participants

The study participants were children between 6 and 17 years of age who had been diagnosed with epilepsy at the epilepsy clinic of a university hospital. After obtaining written consent from each child and their parents, the patient and their parents were asked to complete a self-report questionnaire. Patients who had difficulty in communicating or filling out questionnaires, had a history of brain surgery, showed brain damage confirmed by magnetic resonance imaging, and were diagnosed with hereditary metabolic disorders or severe epilepsy with uncontrolled seizures were excluded from the study. This study was approved by the Institutional Review Board of Ewha University Medical Center (IRB No. 13-01A-05).

Assessment method

Children and adolescents with epilepsy completed self-report questionnaires for depression (CDI) and anxiety (Korean-Revised Children's Manifest Anxiety Scale, K-RCMAS). The parents indicated their stress (Questionnaire on Resources and Stress-F, QRS-F) and anxiety (State-Trait Anxiety Inventory, STAI) on an evaluation scale. Additionally, the children's behavioral problems (Child Behavior Checklist, CBCL), attention problems (Abbreviated Conners Parent Rating Scale, CPRS-R), and family adaptability and cohesion (Family Adaptability and Cohesion Evaluation Scale, FACES-III) questionnaires were completed by parents. Information on maternal education and family income was collected from the parental reports. Family income was divided into low, middle, and high, depending on whether the monthly income per household was <2 million won, 2–5 million won, or >5 million won [8]. Information on the age of onset and duration of epilepsy treatment was confirmed through medical records.

CDI

This self-reported test consists of 27 questions to evaluate the degree of depression in children. It was based on a modi-

fication of the Beck Depression Scale for Adults by Kovacs [9]. Each has three options, each with a score of 0–2. The participant selects the option that best matches his/her condition, and the sum of the scores is calculated by the examiner based on these responses. Higher scores indicated more depressive and diverse symptoms.

RCMAS

Reynolds and Richmond [10] revised Taylor's Manifest Anxiety Scale for Adults to assess children's level of anxiety. This is a self-reported scale with 28 Anxiety Scale and 9 Lie scale items with "yes" or "no" answers. For the anxiety items, "yes" scored 1 point. The lie items were counted in reverse. Higher total scores indicate higher levels of anxiety.

QRS-F

In this study, QRS-F was used to measure parental stress. This is a revised shorter form of the QRS developed by Friedrich et al. [11]. It consists of 52 items assessing parental perceptions, including the following four subcomponents: parental and family problems, pessimism, child characteristics, and physical incapacity. Each item is scored on a two-point scale, with higher scores indicating higher family stress due to disabilities in their children.

STAI

This inventory was developed by Spielberger et al. [12] to provide a scale for assessing anxiety in adults. It consists of a self-reported questionnaire composed of two 20-item scales for two different types of anxiety: state (emotional condition transitory, S-Anxiety) and trait (personality tendency relatively stable, T-Anxiety) anxiety [13]. Each question was scored using a 4-point Likert scale (1=not at all, 2=somewhat, 3=moderately so, 4=very much so in the S-Anxiety items; 1=almost never, 2=sometimes, 3=often, 4=almost always in the T-Anxiety items). The total score was the sum of all item scores, with higher scores indicating greater anxiety.

CBCL

This scale, designed by Achenbach and Edelbrock [14], consists of 118 items and evaluates children's behavioral problems. The children's behavioral problems in the last six months were evaluated based on information provided by parents or teachers. There is a total problems score as well as composites for internalizing and externalizing problems, consisting of eight subscales: withdrawn, anxious/depressed, somatic complaints, thought problems, delinquent behavior, aggressive behavior, attention problems, and social problems [15]. Each question was evaluated using a 3-point Likert scale (0=not true, 1=somewhat or sometimes true, 2=very often

true or often true); higher scores indicated more serious problem behavior. The total problem behavior score, converted into a t-score according to age and gender, was used as a variable.

CPRS

This scale was created by Conners [16] to distinguish hyperkinetic patients by analyzing factors obtained from parents' evaluation of children's symptoms. It consists of ten items that describe the common behavioral problems that children may have. Parents report the frequency of these behaviors using a score from 0 to 3 (from never to very often). Attention-deficit/hyperactivity disorder (ADHD) was suspected when the total score was ≥ 16 .

FACES-III

This scale was developed by Olson et al. [17] to assess the circumplex model used to evaluate family functioning. It consists of 10 cohesion items that measure emotional bonding and 10 adaptability items that evaluate discipline. Each item is scored on a scale of 1 to 5, with higher scores indicating better family functioning.

Statistical analyses

Differences in depressive symptoms as discrete variables were examined using t-test and one-way analysis of variance. Pearson correlation analysis was conducted to confirm the correlation between the variables and depressive symptoms in children and adolescents with epilepsy among 87 study participants. Stepwise regression analysis was performed on

the variables that correlated with depressive symptoms to identify any independent variables that had a significant effect on these symptoms. The SPSS (version 20.0; IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses. Data were considered significant at $p < 0.05$.

RESULTS

Clinical variables related to the sociodemographic and epilepsy characteristics of participants

Table 1 summarizes the demographic and clinical characteristics and CDI scores of the patients with epilepsy and their families. Participants' ages ranged from 6 to 17 years, with an average age of 12 years (12.40 ± 3.16). In total, 51 of the 87 patients were male. CDI scores showed no significant differences according to sex.

There was also no significant difference in the CDI scores according to monthly family income. However, the lower the level of maternal education, the higher the CDI score, with a significant difference among the subjects. The average age at onset of epilepsy was 8 years (8.44 ± 3.83). The mean duration of epilepsy treatment was 3 years (2.91 ± 2.41).

Association between depressive symptoms in children and adolescents with epilepsy and the clinical and psychological factors of the child and family

The mean values of the variables used in this study were as follows: family adaptability=38 (37.97 ± 6.86); family cohesion=32 (32.38 ± 5.61); QRS=9 (8.68 ± 8.10); STAI=85 (84.8 ± 20.11); CPRS=7 (6.61 ± 5.21); RCMAS=17 (16.66 ± 5.251); and

Table 1. Sociodemographic and clinical characteristics of subjects and CDI scores

Characteristics	Participant number or years	CDI score	p
Sociodemographic variables			
Sex			0.714
Male	51 (58.6)	12.45 \pm 7.51	
Female	36 (41.4)	13.06 \pm 7.63	
Age (year)	12.40 \pm 3.16 (6–17)		
Maternal education			0.001
\leq Middle school	7 (8.0)	21.57 \pm 8.54	
\geq High school	48 (55.2)	13.02 \pm 6.91	
\geq College	32 (36.8)	10.28 \pm 6.81	
Monthly family income (₩, million)			0.342
Low (≤ 2)	19 (21.8)	14.95 \pm 9.16	
Middle (2–5)	60 (69.0)	12.07 \pm 9.97	
High (5 \leq)	8 (9.2)	12.13 \pm 7.22	
Epilepsy-related variables			
Age at epilepsy onset (years)	8.44 \pm 3.83 (1–16)		
Duration of epilepsy Tx (year)	2.91 \pm 2.41 (0.2–15)		

Data are presented as mean \pm standard deviation (range) or n (%). CDI, Children's Depression Inventory; Tx, treatment

Table 2. Correlations between depressive symptoms and clinical and psychological factors

	Age	Age of onset	Duration of Tx.	Family adaptability	Family cohesion	QRS	STAI	CPRS	CDI	RCMAS	CBCL-TBP
Age	1										
Age of onset	0.592 [†]	1									
Duration of Tx	0.046	-0.044	1								
Family adaptability	-0.147	-0.026	-0.195	1							
Family cohesion	-0.168	-0.104	-0.139	0.482 [†]	1						
QRS	-0.056	-0.159	0.283 [†]	-0.077	-0.139	1					
STAI	0.019	-0.019	0.008	-0.265 [*]	-0.335 [†]	0.486 [†]	1				
CPRS	-0.151	-0.119	0.179	-0.191	-0.265 [*]	0.617 [†]	0.445 [†]	1			
CDI	0.109	0.061	0.070	-0.240 [*]	-0.381 [†]	0.335 [†]	0.320 [†]	0.290 [†]	1		
RCMAS	0.123	0.095	0.014	-0.157	-0.374 [†]	0.306 [†]	0.451 [†]	0.304 [†]	0.714 [†]	1	
CBCL-TBP	-0.168	-0.174	0.169	-0.158	-0.268 [*]	0.629 [†]	0.467 [†]	0.724 [†]	0.371 [†]	0.329 [†]	1

* $p < 0.05$; $^{\dagger}p < 0.01$. Tx, treatment; QRS, Questionnaire on Resources and Stress; STAI, State-Trait Anxiety Inventory; CPRS, Conners Parent Rating Scale; CDI, Children's Depression Inventory; RCMAS, Revised Children's Manifest Anxiety Scale; CBCL-TBP, Child Behavior Checklist-Total Behavior Problems

CBCL-total behavior problems=52 (51.99±10.38). Correlation analysis revealed that family adaptability ($r=-0.240$, $p=0.026$) and cohesion ($r=-0.381$, $p<0.001$) were negatively correlated with children's depressive symptoms. In contrast, children's attention problems ($r=0.290$, $p=0.006$), anxiety ($r=0.714$, $p<0.001$), and behavioral problems ($r=0.371$, $p<0.001$) were positively correlated with depressive symptoms. Furthermore, parental stress ($r=0.335$, $p=0.002$) and anxiety ($r=0.320$, $p=0.003$) were positively correlated with depressive symptoms (Table 2).

Factors independently influencing depressive symptoms in children and adolescents with epilepsy

Stepwise regression analysis was performed using family adaptability, family cohesion, QRS, STAI, CPRS, RCMAS, and CBCL, all of which correlated with the CDI score, to analyze the variables independently associated with the CDI score. The analysis revealed that children's anxiety ($\beta=0.655$, $p<0.001$) and parental stress ($\beta=0.198$, $p=0.013$) were independently associated with depressive symptoms in children and adolescents with epilepsy, accounting for 53.9% of the variance in CDI scores (Table 3).

DISCUSSION

This study aimed to investigate the factors that affect depressive symptoms in children and adolescents with epilepsy. The poorer the family adaptability and cohesion, the higher the child's anxiety, the more severe the child's attention and behavioral problems, the higher the parents' anxiety and stress, and the more severe the depressive symptoms in children with epilepsy. Among these different factors, children's anxiety and parental stress were independently significant

Table 3. Stepwise regression analysis for significant predictors of depressive symptoms of children and adolescents with epilepsy

	B	SE	β	t	p	VIF
RCMAS	0.736	0.078	0.717	9.377	<0.001	1.000
Adjusted R ² =0.509						
RCMAS	0.672	0.080	0.655	8.393	<0.001	1.109
QRS	0.190	0.075	0.198	2.532	0.013	1.109
Adjusted R ² =0.539						

RCMAS, Revised Children's Manifest Anxiety Scale; QRS, Questionnaire on Resources and Stress; SE, standard error; VIF, variance inflation factor

factors affecting depression in children with epilepsy.

In this study, sociodemographic variables such as sex and family economic status showed no statistically significant differences in the depressive symptoms of children with epilepsy. Clinical factors such as the duration of epilepsy treatment and the average age at onset of epilepsy also did not show any significant differences with depressive symptoms. A previous study showed that the depressive symptoms of children with epilepsy do not significantly differ with sociodemographic variables, such as sex and socioeconomic status, or epilepsy-related variables, such as the age of onset and duration of treatment [3]. Previous studies [3-7] that have assessed the factors affecting depressive symptoms in children and adolescents with epilepsy have shown that these factors differ from those in the general population. This suggests that epilepsy alters the distribution of depression [18]. In our study, the higher the maternal education level, the lower the CDI score of the child as suggested in a previous study [19]. The educational level can affect parenting skills, socio-emotional development, stress, and well-being, which may affect children's mental health [20].

In the present study, lower family adaptability and cohe-

sion scores were associated with more severe depressive symptoms in children with epilepsy. Rodenburg et al. [21] reported that parental rejection, which mediates family adaptation problems, is highly correlated with internalizing problems (e.g., depression) in children with epilepsy. Similarly, Dunn et al. [22] showed that children's satisfaction with family functioning is significantly correlated with depressive symptoms in children and adolescents with epilepsy.

In this study, more severe attention problems were associated with more severe depressive symptoms in children with epilepsy. ADHD is the most common psychiatric disorder among children with epilepsy. The comorbidity of ADHD in children with epilepsy is 23%, which is higher when compared to a comorbidity of 6% in the general pediatric population. This suggests that the two diseases share a common pathophysiology of cognition and behavior [23]. Additionally, inattention and depression share biological similarities. Hippocampal volume reduction and dysregulation of the frontostriatal region are associated with ADHD and depression [24]. Rajendran et al. [25] reported that the severity of attention deficits in children was longitudinally associated with the severity of depression. Interestingly, the association between attention deficits and depression may be mediated by school maladjustment [26].

We found that behavioral problems were positively associated with depressive symptoms in children with epilepsy. A previous study [5] has shown that children with epilepsy and depression reported higher CBCL scores when compared than those without psychiatric disorders. Additionally, a meta-analysis by Rodenburg et al. [27] reported that internalizing and externalizing behavioral problems are more common in children with epilepsy than in those with other chronic diseases. Furthermore, social problems are relatively specific to children with epilepsy.

In this study, higher parental anxiety levels were associated with more severe depressive symptoms in children with epilepsy. Previous studies have shown that parental anxiety in children with epilepsy is negatively correlated with health-related quality of life (HRQoL) [28] and adaptive behavior [29]. Puka et al. [6] have shown that depressive symptoms in adolescents with epilepsy are associated with the anxiety levels of their primary caregivers. Moreover, this association remained significant after multivariate analysis. One study reported no association between depression in children with epilepsy and their mothers' anxiety symptoms; however, this study included a small, heterogeneous group of 35 patients [7].

In this study, higher anxiety levels were associated with more severe depressive symptoms in the children with epilepsy. Moreover, children's anxiety levels were found to be significant independent factors affecting depression. A pre-

vious study suggested that depressive symptoms and anxiety are more frequent in children with epilepsy than in the general population [30]. Ettinger et al. [3] reported a strong correlation between depression and anxiety in children with epilepsy, with depression and anxiety observed in 26% and 16% of this population, respectively. This may indicate the comorbidity of these two symptoms. Unexpected seizures can cause anxiety in children and adolescents, which can lead to fear and embarrassment, resulting in withdrawal from social activities and interactions [31].

Parental stress is an independent factor affecting depressive symptoms in children with epilepsy. According to a previous study [32], parents of children with epilepsy experience high levels of stress, with up to 45% prevalence, which is similar to the parents of children with other medical conditions requiring healthcare. Parental stress is higher in epilepsy than in asthma, which can be explained by discrimination, lack of adaptation in children, difficulty in predicting seizures, and neurological dysfunction [33]. Wu et al. [34] reported that high levels of parental stress are detrimental for children's general and epilepsy-related HRQoL, especially in the first year of illness when compared to 2 years after diagnosis. Parents of children with epilepsy tend to overprotect or limit their children because of fear or anxiety about the disease. This may lower their quality of life and negatively affect them psychologically [34].

This study has several limitations. First, the participants were enrolled at a university hospital, which limited the generalizability of the results. Second, the study lacked objective evaluation because self-report questionnaires were used. Third, this was a cross-sectional study, without a comparison group.

Despite these limitations, we used standardized tools to evaluate depressive symptoms and the factors affecting these symptoms in children and adolescents with epilepsy. One strength of this study is that we evaluated the difficulties faced by children with epilepsy and their families. They suffer mental health problems such as emotional, behavioral, and relational issues [35]. Therefore, it is imperative to clinically evaluate children and adolescents with epilepsy to treat epilepsy, in addition to the mental health problems that may occur during the development of children.

In conclusion, this study showed that family adaptability and cohesion, parental stress and anxiety, and children's attention, anxiety, and behavioral problems were significantly correlated with depressive symptoms in children and adolescents with epilepsy. Among these factors, the level of anxiety in children and parental stress independently affected the severity of depressive symptoms. Therefore, clinicians should evaluate the anxiety levels of children and adoles-

cents with epilepsy in the early stages of the disease using anxiety-specific checklists or detailed interviews to alleviate these depressive symptoms. Clinicians could reduce anxiety by controlling unexpected seizures in the early stages of the disease. Furthermore, preventing any worsening of anxiety due to fear and embarrassment should be considered. Additionally, parental stress should be closely monitored during the initial treatment. Appropriate disease education and parental skill development should be also provided.

Availability of Data and Material

The datasets used in the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Eui-Jung Kim, Hyang Woon Lee. Methodology: Eui-Jung Kim, Ga Eun Kim. Formal analysis: Eui-Jung Kim, Ga Eun Kim. Investigation: Eui-Jung Kim, Hyang Woon Lee. Writing—Original draft: So Hyun Park, Ga Eun Kim. Writing—review & editing: Eui-Jung Kim, Ga Eun Kim, So Hyun Park.

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