

The Effect of Antiepileptic Drugs on Mood and Behavioral Changes In Children Aged 4–10 Years At Dr. Moewardi Regional General Hospital

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Abstract.

Epilepsy in children involves not only the occurrence of seizures but may also be accompanied by mood and behavioral changes potentially linked to the disease characteristics or the use of antiepileptic drugs. Monitoring psychobehavioral changes during therapy is essential to support comprehensive clinical evaluation. This study aimed to analyze mood and behavioral changes in children aged 4–10 years following antiepileptic drug therapy and to evaluate the associations of drug type, dosage, duration of therapy, and treatment regimen with these changes. A quantitative approach using a prospective observational cohort design was employed. The study subjects consisted of 150 children aged 4–10 years with epilepsy receiving antiepileptic drug therapy. Data collected included demographic and clinical characteristics, drug type, dosage, duration of therapy, monotherapy or polytherapy regimens, pre- and post-therapy mood and behavioral scores, side effects, and treatment adherence. Analyses were conducted using paired-samples t-tests or Wilcoxon tests, ANOVA or Kruskal–Wallis tests, Pearson or Spearman correlations, and multiple linear regression, with a significance level of $p < 0.05$. The mean change in mood scores was 1.92 ± 2.30 , and the mean change in behavioral scores was 2.47 ± 2.63 . Statistically significant differences were observed between pre- and post-therapy scores for both mood and behavior ($p < 0.001$). Differences in score changes were observed based on drug type ($p < 0.001$); the levetiracetam group exhibited greater changes in mood and behavioral scores compared to several other drug groups. Multivariate analysis revealed that levetiracetam use and polytherapy regimens were associated with changes in mood and behavioral scores after adjusting for clinical covariates. Changes in mood and behavioral scores occurred in children following antiepileptic therapy, with variations observed based on drug type and treatment regimen. Monitoring mood and behavior should be an integral part of the evaluation of children with epilepsy during therapy. Interpretation of the results must take into account clinical and confounding factors and cannot be used to infer a causal relationship.

Keywords: children, epilepsy, antiepileptic drugs, mood, behavior and antiepileptic therapy.

I. INTRODUCTION

Epilepsy is a chronic neurological disorder in children that is associated not only with the occurrence of seizures but also with impacts on psychological, behavioral, and cognitive aspects, as well as quality of life. Children with epilepsy are known to be at higher risk for mental health issues and neurodevelopmental disorders compared to the general pediatric population. Consequently, monitoring psychological and behavioral aspects is a crucial component of pediatric epilepsy management. Early detection of emotional and behavioral changes is essential, as these issues can affect social functioning, daily activities, family relationships, and treatment adherence [1]. Recent systematic reviews indicate that tools for assessing mental health and neurodevelopment in children with epilepsy remain relatively limited; thus, further research is needed to generate clinical data that can support the systematic monitoring of children's psychological well-being.

The management of pediatric epilepsy generally requires the use of antiseizure medications (ASMs) to control seizures. Although effective in reducing seizure frequency, ASM use can be associated with various side effects, including impacts on psychological and behavioral functioning. Neuropsychiatric manifestations may include irritability, aggression, emotional changes, sleep disturbances, attention deficits, anxiety, and mood swings. These effects can vary depending on the pharmacological characteristics of specific drugs, the patient's condition, and the treatment regimen employed. Reviews regarding the psychobehavioral and cognitive side effects of ASMs in the pediatric population indicate that certain drugs such as levetiracetam and

perampanel are linked to manifestations like aggression and irritability, whereas other drugs may have different effects on cognitive function and behavior [2].

Levetiracetam is an antiepileptic drug that has garnered particular attention regarding its behavioral effects in children. Prospective studies involving pediatric epilepsy patients aged 4–15 years have shown that, following the initiation of levetiracetam, some patients experience behavioral changes measurable via behavioral assessment instruments. These changes primarily relate to hyperactivity, conduct or behavioral issues, and emotional difficulties. Such studies also indicate that pre-existing behavioral problems and a family history of psychopathology may be factors associated with the emergence of behavioral changes during therapy [3]. Although these studies were conducted prior to the last five years, the findings regarding behavioral changes following levetiracetam use remain relevant as a basis for longitudinal research in pediatric populations.

More recent evidence indicates that the behavioral effects of antiepileptic drugs are not limited to a single type of medication. For instance, a prospective study on pediatric patients with newly diagnosed focal epilepsy compared perampanel and lacosamide monotherapy, evaluating efficacy, tolerability, and the patients' emotional and behavioral states. The study highlighted the importance of assessing tolerability and behavioral aspects when comparing antiepileptic treatment regimens in children [4]. Furthermore, a recent analysis based on the Food and Drug Administration Adverse Event Reporting System regarding adverse event reports in children revealed that psychiatric disorders constitute one category of adverse effects associated with the use of various antiepileptic drugs (AEDs). Specific associations between drugs and neuropsychiatric symptoms were identified for both levetiracetam and valproic acid, suggesting that monitoring for psychological and behavioral effects is necessary across various types of antiepileptic medications, not just levetiracetam [5].

Behavioral issues in children with epilepsy cannot always be attributed solely to drug side effects; the epileptic condition itself can contribute to the emergence of behavioral and psychosocial problems. A study of 300 children with epilepsy in Uganda revealed a significant burden of behavioral problems and identified various clinical and psychosocial factors associated with these issues [6]. Consequently, changes in mood and behavior in children undergoing anti-seizure therapy should be understood as a multifactorial phenomenon likely influenced by the type of medication, disease characteristics, seizure frequency, duration of the illness, treatment regimen, and the child's psychosocial condition.

The number of antiseizure medications (ASMs) used is also a crucial aspect when evaluating the impact of therapy. Polytherapy can increase treatment complexity and the likelihood of side effects compared to monotherapy. Furthermore, drug-related side effects can influence the quality of life of children with epilepsy. Research on the relationship between ASM therapy and quality of life in children indicates that ASM usage, treatment duration, and seizure frequency are factors that must be considered to understand the quality of life of pediatric patients with epilepsy [1]. Therefore, evaluating epilepsy therapy in children requires considering not only seizure control success but also the psychological and behavioral changes that may accompany treatment.

Previous studies have provided evidence regarding emotional and behavioral issues in children with epilepsy and their potential link to ASM use. However, research gaps remain. First, some studies focus on a specific drug particularly levetiracetam limiting information on mood and behavioral changes associated with various types of ASMs in the pediatric population. Second, many studies employ cross-sectional designs or analyze adverse event reports, failing to fully capture a structured comparison of mood and behavioral conditions before and after therapy. Third, treatment characteristics such as dosage, duration of use, and the choice between monotherapy and polytherapy are not always analyzed in conjunction with the patients' clinical characteristics.

These gaps are particularly significant given the limitations of instruments used to measure mental health and behavior in children with epilepsy. A systematic review by De Aveiro et al. found that only a small number of patient-reported outcome measures have been specifically evaluated in pediatric and adolescent populations with epilepsy, and some instruments still lack sufficient evidence regarding their validity and reliability [1]. This situation highlights the need for clinical research that systematically measures psychological and behavioral outcomes while simultaneously considering both treatment and patient characteristics.

Consequently, there is a need for research that evaluates in a more structured manner changes in mood and behavior among children aged 4–10 years with epilepsy in relation to antiepileptic drug use, while simultaneously accounting for therapeutic and clinical factors that may act as confounders. Such an approach can help distinguish between patterns of change potentially linked to therapy and those influenced by epilepsy characteristics or the patient's individual condition.

The novelty of this study lies in its approach of evaluating mood and behavioral changes before and after antiepileptic therapy within a specific pediatric age group: 4–10 years. Unlike studies that merely identify the prevalence of behavioral issues or evaluate a single specific drug, this research aims to integrate medication-related characteristics such as drug type, dosage, duration of therapy, and the use of monotherapy versus polytherapy with clinical patient characteristics, including age, sex, epilepsy type, and seizure frequency. This approach offers a more comprehensive perspective, as mood and behavioral changes are not viewed solely as direct drug effects; instead, the study acknowledges that such changes may stem from a combination of pharmacological and clinical factors. This aligns with evidence indicating that the psycho-behavioral effects of antiseizure medications (ASMs) vary between drugs and that patient characteristics play a role in the emergence of neuropsychiatric effects [2].

A further novel aspect is the focus on children aged 4–10 years. This age range encompasses a critical developmental phase during which skills related to emotional regulation, social behavior, attention, and adaptive functioning are evolving. Research targeting a specific age group can yield more focused insights compared to studies that aggregate children and adolescents into a single population cohort. Moreover, evaluating mood and behavioral changes in this age group provides valuable information regarding the need to monitor for neuropsychiatric effects during antiseizure therapy. The study also offers added value through an analysis plan that accounts for potential confounding factors. Drug type, dosage, duration of therapy, and monotherapy or polytherapy regimens were analyzed alongside patients' clinical characteristics to gain a more nuanced understanding of the relationship between antiepileptic therapy and changes in mood or behavior. This multivariate approach is crucial because recent evidence indicates that the psychiatric effects associated with ASM use are heterogeneous and can manifest in various forms in children [5].

Thus, the study's novelty lies not merely in the use of specific medication types, but in the integration of evaluations regarding mood and behavioral changes, medication usage characteristics, and clinical factors among children aged 4–10 years within a single analytical framework. This approach is expected to yield more contextual empirical data regarding the tolerability of antiepileptic therapy in the Indonesian pediatric population.

This study aims to analyze mood and behavioral changes in children aged 4–10 years with epilepsy in relation to antiepileptic medication use at Dr. Moewardi Regional General Hospital (RSUD), and to evaluate the associations of medication type, dosage, treatment duration, and therapy type with these changes, while accounting for relevant patient clinical characteristics.

The study is significant because the success of epilepsy therapy in children is determined not only by seizure control but also by treatment tolerability and the patient's psychological and behavioral status. A more systematic identification of mood and behavioral changes can help provide clinical information on change patterns during therapy, heighten awareness of potential neuropsychiatric effects, and establish a foundation for more comprehensive therapy monitoring. Ultimately, the study's findings are expected to enrich the scientific evidence regarding the relationship between antiepileptic therapy and children's psychological and behavioral conditions, as well as serve as a basis for future research utilizing validated psychometric instruments.

II. METHODS

This study employs a quantitative approach using an observational analytic design—specifically, a prospective cohort design. This design was selected to analyze changes in children's mood and behavior before and after receiving antiepileptic drug therapy and to evaluate the relationship between therapy characteristics and these changes, without administering experimental interventions. A quantitative approach allows variables such as mood scores, behavior scores, dosage, duration of therapy, and score changes to be measured

numerically and analyzed statistically. The prospective cohort design enables the measurement of baseline conditions and follow-up measurements after the therapy period, allowing changes to be observed longitudinally. This design is more suitable than a cross-sectional design, which measures variables at a single point in time, or a case-control design, which focuses on comparing exposure history based on outcome status. Reporting of the observational study adheres to the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) guidelines [7], covering the population, exposures, outcomes, confounding factors, and analysis methods.

The study population consists of children aged 4–10 years diagnosed with epilepsy who are receiving antiepileptic drug therapy at Dr. Moewardi Regional General Hospital (RSUD), Surakarta. Data collection involves structured clinical observation and the recording of patient and therapy characteristics at the study's outset, followed by repeat measurements after the designated therapy period. The study targets 150 subjects matching the sample size of the simulation dataset using a consecutive sampling technique, wherein eligible patients are recruited sequentially until the required sample size is reached. Inclusion criteria comprise children aged 4–10 years with a diagnosis of epilepsy who are receiving antiepileptic therapy and for whom parental or guardian consent has been obtained. Exclusion criteria include incomplete key clinical data, pre-existing neurological conditions or severe psychiatric disorders likely to influence mood or behavior assessments, and failure to complete follow-up measurements. The data collected included age, gender, epilepsy type, seizure frequency, medication type, dosage, duration of therapy, monotherapy or polytherapy status, mood scores, behavioral scores, side effects, and treatment adherence. The study was conducted following ethical approval, and all data were anonymized to maintain patient confidentiality.

Research instruments were used to measure mood and behavioral conditions in a structured manner at two observation points: prior to or at the start of therapy (baseline) and after the therapy period. Changes in mood and behavior were calculated based on the difference between post-therapy and pre-therapy scores. The instruments employed were required to demonstrate evidence of validity and reliability and be suitable for children aged 4–10 years. This is crucial, as systematic reviews indicate that instruments measuring mental health and neuropsychological development in children with epilepsy still lack sufficient psychometric evidence [1]. Furthermore, not all commonly used behavioral screening instruments possess the same level of validation for the pediatric epilepsy population [8].

Data regarding clinical characteristics and therapy were obtained from medical records, supplemented by structured confirmation from parents or guardians where necessary. Independent variables included drug type, dosage, duration of therapy, and the treatment regimen (monotherapy or polytherapy), while the dependent variable was the change in mood and behavioral scores. Age, sex, epilepsy type, seizure frequency, and treatment adherence served as covariates potentially influencing the relationship between antiepileptic therapy and changes in mood and behavior. These considerations were based on the observed variation in the psychobehavioral effects of antiseizure medications depending on drug type and patient characteristics [2]. Prior to analysis, data were checked for completeness, consistency, and the validity of value ranges. Patient identities were excluded from the analysis dataset, and each subject was assigned a research code.

Data analysis involved univariate, bivariate, and multivariate methods, utilizing a significance level of 5% ($\alpha = 0.05$) and a 95% confidence interval. Univariate analysis was used to describe subject characteristics and variable distributions. Numerical data are presented as mean $\pm$ standard deviation if normally distributed, or as median and interquartile range if not normally distributed, whereas categorical data are presented as frequencies and percentages. Data normality was assessed using the Shapiro–Wilk test and visual inspection of the distribution.

Bivariate analysis was used to compare mood and behavioral scores before and after therapy, employing the paired-samples t-test if parametric assumptions were met, or the Wilcoxon signed-rank test if they were not. Comparisons of score changes across more than two medication groups were conducted using one-way ANOVA or the Kruskal–Wallis test, depending on data distribution and homogeneity of variance, with post-hoc analysis performed where necessary. The relationship between dosage and changes in mood and behavior was analyzed using Pearson or Spearman correlation. Subsequently, multiple linear regression was used to control for confounding factors, with changes in mood and behavior serving as separate dependent variables.

Variables considered included medication type, dosage, duration of therapy, monotherapy versus polytherapy, age, gender, epilepsy type, seizure frequency, and treatment adherence. Regression assumptions including linearity, independence, residual normality, homoscedasticity, and the absence of multicollinearity (assessed via variance inflation factor [VIF]) were evaluated. Regression results are presented as regression coefficients (β), standard errors, p-values, and 95% confidence intervals. Analysis reporting adhered to principles of transparency for observational research, including the handling of incomplete data and the control of confounding factors [9][10]. A p-value < 0.05 was considered statistically significant, with interpretations also taking into account effect sizes and confidence intervals. Analyses were performed using statistical software such as IBM SPSS Statistics or open-source software with equivalent functionality.

III. RESULT AND DISCUSSION

RESULT

Characteristics of Research Subjects

An analysis was conducted on 150 subjects aged 4–10 years. The mean age of the subjects was 6.86 ± 1.90 years. Regarding gender, 77 subjects (51.3%) were male and 73 subjects (48.7%) were female. The most common type of epilepsy was generalized epilepsy (70 subjects; 46.7%), followed by focal epilepsy (65 subjects; 43.3%) and unclassified epilepsy (15 subjects; 10.0%).

Based on seizure frequency, the majority of subjects experienced seizures less than once a month (65 subjects; 43.3%), while 52 subjects (34.7%) experienced seizures 1–3 times per month, and 33 subjects (22.0%) experienced seizures more than three times per month. The most frequently used antiepileptic drug was levetiracetam (66 subjects; 44.0%), followed by valproate (40 subjects; 26.7%), carbamazepine (33 subjects; 22.0%), and lamotrigine (11 subjects; 7.3%).

A total of 100 subjects (66.7%) received monotherapy, and 50 subjects (33.3%) received polytherapy. Regarding adherence, 95 subjects (63.3%) demonstrated good adherence, 41 subjects (27.3%) showed moderate adherence, and 14 subjects (9.3%) exhibited poor adherence. No side effects were reported in 84 subjects (56.0%), whereas the most frequently observed side effects were irritability (31 subjects; 20.7%) and sleep disturbances (19 subjects; 12.7%).

Table 1. Characteristics of Study Subjects (n = 150)

Characteristics	n	%
Age, mean $\pm$ SD	6.86 ± 1.90	—
Sex		
Male	77	51.03.00
Female	73	48.07.00
Type of epilepsy		
Generalized	70	46.07.00
Focal	65	43.03.00
Unclassified	15	10.00
Seizure frequency		
<1 time/month	65	43.03.00
1–3 times/month	52	34.07.00
>3 times/month	33	22.00
Antiepileptic drug		
Levetiracetam	66	44.00.00
Valproate	40	26.07.00
Carbamazepine	33	22.00
Lamotrigine	11	07.03

Duration of therapy		
<3 months	31	20.07
3–6 months	45	30.00.00
>6–12 months	35	23.03
>12 months	39	26.00.00
Treatment regimen		
Monotherapy	100	66.07.00
Polytherapy	50	33.03.00
Medication adherence		
Good	95	63.03.00
Moderate	41	27.03.00
Poor	14	09.03
Side effects		
None	84	56.00.00
Irritability	31	20.07
Sleep disturbance	19	12.07
Aggressiveness	8	05.03
Other mood changes	8	05.03

Changes in Mood and Behavior Scores Before and After Therapy

The mean mood score was 8.71 ± 2.94 before therapy and increased to 10.63 ± 3.97 after therapy, with a mean change of 1.92 ± 2.30 . A normality test on the change in mood scores using the Shapiro–Wilk test indicated that the distribution of the change was not entirely normal ($p = 0.019$). Therefore, the Wilcoxon signed-rank test result was used as the primary analysis, revealing a statistically significant difference in mood scores before and after therapy ($p < 0.001$).

Regarding behavioral scores, the mean score was 9.54 ± 2.90 before therapy and increased to 12.01 ± 4.15 after therapy. The mean change in behavioral scores was 2.47 ± 2.63 . The distribution of the change in behavioral scores showed no significant deviation based on the Shapiro–Wilk test ($p = 0.070$). A paired-samples t-test indicated a difference in behavioral scores before and after therapy ($p < 0.001$). As a sensitivity analysis, the Wilcoxon test also yielded a p-value of < 0.001 .

Table 2. Changes in Mood and Behavioral Scores Before and After Therapy

Variable	Before, mean $\pm$ SD	After, mean $\pm$ SD	Change, mean $\pm$ SD	Test	<i>p</i>
Mood	8.71 ± 2.94	10.63 ± 3.97	1.92 ± 2.30	Wilcoxon signed-rank test	<0.001
Behavior	9.54 ± 2.90	12.01 ± 4.15	2.47 ± 2.63	Paired <i>t</i> -test	<0.001

Categorization results indicate that 86 subjects (57.3%) experienced an increase in mood scores, 46 subjects (30.7%) showed minimal change or remained stable, and 18 subjects (12.0%) experienced a decrease in mood scores. Regarding behavioral scores, 99 subjects (66.0%) showed an increase, 31 subjects (20.7%) showed minimal change or remained stable, and 20 subjects (13.3%) showed a decrease.

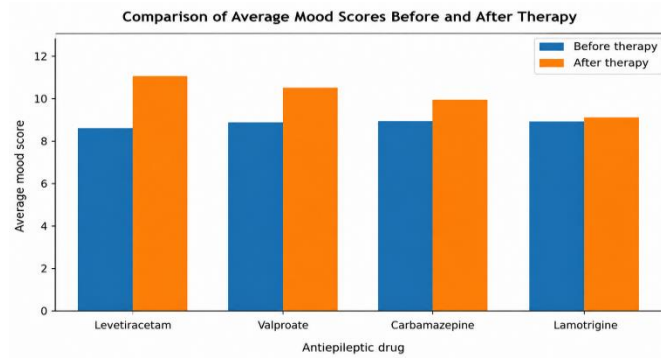


Fig. 1. Comparison of Mean Mood Scores Before and After Therapy

Mood and Behavioral Changes Based on Medication Type

There were variations in the mean change in mood based on the type of medication. The levetiracetam group showed a mean mood change score of 2.73 ± 2.08 ; valproate, 1.68 ± 2.64 ; carbamazepine, 1.15 ± 1.77 ; and lamotrigine, 0.27 ± 1.95 . ANOVA testing indicated a difference in the mean change in mood among the medication groups ($F = 6.661$; $p < 0.001$). The Kruskal–Wallis test yielded consistent results ($H = 18.594$; $p < 0.001$).

Tukey post-hoc analysis revealed differences primarily between levetiracetam and carbamazepine ($p = 0.005$) and between levetiracetam and lamotrigine ($p = 0.004$). The difference between levetiracetam and valproate did not reach statistical significance ($p = 0.079$). Regarding behavioral changes, the greatest mean change was observed in the levetiracetam group (3.58 ± 2.35), followed by carbamazepine (1.85 ± 2.56), valproate (1.48 ± 2.52), and lamotrigine (1.36 ± 2.62). ANOVA testing showed significant differences among the medication groups ($F = 8.058$; $p < 0.001$), and the Kruskal–Wallis test produced similar results ($H = 20.579$; $p < 0.001$).

Table 3. Changes in Mood and Behavior Based on Medication Type

Drug	n	Mood swings, mean $\pm$ SD	Behavioral change, mean $\pm$ SD
Levetiracetam	66	2.73 ± 2.08	3.58 ± 2.35
Valproat	40	1.68 ± 2.64	1.48 ± 2.52
Karbamazepin	33	1.15 ± 1.77	1.85 ± 2.56
Lamotrigin	11	0.27 ± 1.95	1.36 ± 2.62
Between-group test		$p < 0.001$	$p < 0.001$

In the levetiracetam group, 69.7% of subjects showed an improvement in mood scores, and 83.3% showed an improvement in behavioral scores. In contrast, the proportion of subjects with improved mood scores was 27.3% in the lamotrigine group and 57.5% in the valproate group. These differences in distribution must be interpreted with caution, as the lamotrigine group was relatively small and differences in clinical characteristics among the drug groups could act as confounding factors.

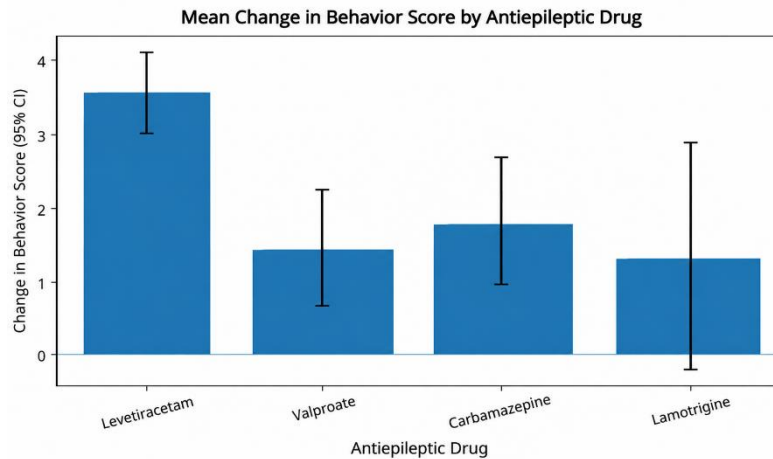


Fig. 2. Average Change in Behavior Scores by Drug Type

Relationship of Dosage and Therapeutic Regimen to Mood and Behavioral Changes

Correlation analysis revealed a weak positive correlation between drug dosage and changes in mood scores, based on both Pearson ($r = 0.197$; $p = 0.015$) and Spearman ($\rho = 0.179$; $p = 0.029$) tests. Thus, within this dataset, higher dosages correlated with greater changes in mood scores, although the strength of the association was relatively weak. Conversely, the relationship between dosage and changes in behavioral scores was very weak and not statistically significant (Pearson $r = 0.029$; $p = 0.726$; Spearman $\rho = 0.014$; $p = 0.869$).

Regarding treatment regimens, the mean change in mood was 1.60 ± 2.27 in the monotherapy group and 2.56 ± 2.23 in the polytherapy group ($p = 0.015$). For behavioral changes, the mean change was 2.18 ± 2.81 for monotherapy and 3.06 ± 2.14 for polytherapy ($p = 0.035$).

Multivariate Analysis

Multiple linear regression was used to evaluate the relationship between treatment characteristics and score changes, after adjusting for age, gender, epilepsy type, seizure frequency, and medication adherence.

The mood change model explained approximately 24.4% of the variation in score changes ($R^2 = 0.244$; adjusted $R^2 = 0.153$; $p = 0.001$). After adjusting for covariates, the levetiracetam group showed a β coefficient of 1.606 compared to the carbamazepine reference group (95% CI 0.623–2.590; $p = 0.002$). The polytherapy regimen also showed a β coefficient of 1.160 (95% CI 0.409–1.912; $p = 0.003$). Variables such as dosage, age, gender, epilepsy type, seizure frequency, adherence, and other treatment duration categories did not show statistically significant associations in the model.

The behavioral change model explained 25.8% of the variation in score changes ($R^2 = 0.258$; adjusted $R^2 = 0.168$; $p < 0.001$). Levetiracetam had a β coefficient of 2.402 compared to carbamazepine (95% CI 1.287–3.518; $p < 0.001$). Polytherapy had a β of 0.859 (95% CI 0.007–1.711; $p = 0.048$), whereas treatment duration of less than three months had a β of -1.316 compared to the 3–6 month reference group (95% CI -2.463 to -0.169 ; $p = 0.025$). Dosage showed a trend toward a negative association but did not reach statistical significance ($p = 0.065$). The VIF values for all predictor variables ranged from approximately 1.05 to 2.04, indicating no significant multicollinearity issues within the model. Residual analysis also revealed no major deviations from normality based on Jarque–Bera statistics.

Table 4. Multiple Linear Regression Analysis of Mood and Behavioral Changes

Variable	Δ Mood β (95% CI)	<i>p</i>	Δ Behavior β (95% CI)	<i>p</i>
Levetiracetam vs karbamazepin	1,606 (0,623– 2,590)	0,002	2,402 (1,287– 3,518)	<0,001
Lamotrigin vs karbamazepin	–0,542 (–2,146–1,063)	0,506	–0,547 (–2,366– 1,273)	0,553

Valproat vs karbamazepin	0,426 (−0,607– 1,460)	0,416	0,044 (−1,128– 1,217)	0,941
Polytherapy vs. monotherapy	1,160 (0,409– 1,912)	0,003	0,859 (0,007– 1,711)	0,048
Dose (mg/day)	0,0003 (−0,001–0,002)	0,731	−0,0019 (−0,004–0,0001)	0,065
Age (years)	−0,068 (−0,262–0,126)	0,487	−0,111 (−0,331– 0,109)	0,322
model R²	0,244		0,258	
Adjusted R²	0,153		0,168	

Discussion

The study results indicate changes in mood and behavioral scores between measurements taken before and after antiepileptic therapy. The mean mood score changed by 1.92 points, while the behavioral score changed by 2.47 points. These findings suggest that the psychobehavioral status of children with epilepsy can shift during the course of treatment. However, these score changes cannot be immediately interpreted as clinical improvement or deterioration without first establishing the direction of interpretation for the instruments used. This is significant because children with epilepsy face a higher risk of mental health disorders, behavioral issues, and neurodevelopmental problems compared to the general pediatric population. De Aveiro et al. also demonstrated that selecting measurement instruments for the pediatric epilepsy population remains challenging, as not all instruments possess adequate psychometric evidence [1].

The statistically significant differences in scores observed before and after therapy must be understood within a broader clinical context. The mood and behavior of children with epilepsy are influenced not only by medication but also by epilepsy characteristics, seizure frequency, sleep patterns, neurodevelopmental comorbidities, the family environment, and psychosocial conditions. Consequently, longitudinal changes cannot automatically be attributed to the direct pharmacological effects of the medication. Strzelczyk and Schubert-Bast emphasize that disentangling the effects of the epilepsy itself, neurodevelopmental comorbidities, and the psychobehavioral effects of antiseizure medications poses a challenge in research involving children with epilepsy [2].

A key finding of the study is the variation in mood and behavioral changes based on the type of medication. The levetiracetam group exhibited a greater mean change in scores compared to several other medication groups, and this association persisted even after adjustment in the regression analysis. These findings align with existing literature regarding the psychobehavioral profile of levetiracetam. Strzelczyk and Schubert-Bast reported that levetiracetam is an antiepileptic drug associated with psychobehavioral effects such as irritability and aggression, particularly in the pediatric population [2].

These findings are also consistent with more recent pharmacovigilance studies. Gui et al., using data from the FDA Adverse Event Reporting System covering the period 2004–2024, identified reports of psychiatric adverse effects associated with various antiepileptic drugs in children; they noted that levetiracetam was frequently linked to reports of behavioral and impulse control disorders [5]. However, as that study relied on a spontaneous reporting system, it lacked exposure denominator data and could not be used to calculate incidence rates or establish a causal relationship. In the current study's dataset, the most frequently recorded adverse effects were irritability, sleep disturbances, and aggression. This pattern generally aligns with existing literature regarding the psycho-behavioral effects of antiepileptic drugs. Previous systematic reviews on levetiracetam use in children have also reported aggression, hostility, and nervousness as behavioral side effects, although observational studies have yielded heterogeneous results, showing either worsening or improvement in behavior.

Differences between drug types must be interpreted with caution. The levetiracetam group in the dataset comprised 66 subjects, whereas the lamotrigine group included only 11. Such imbalances in group size can affect the precision of estimates, particularly for smaller groups. Furthermore, drug selection in clinical practice is not randomized; factors such as epilepsy type, disease severity, response to prior therapy, and patient

characteristics influence the choice of medication. Consequently, the regression findings indicate a statistical association following adjustment, rather than evidence that the drug type directly causes changes in mood or behavior. In this study, the association between dosage and mood changes was positive but weak, while the association between dosage and behavioral changes was not statistically significant. These findings suggest that psycho-behavioral changes cannot be explained solely by dosage levels. A drug's effect profile may be influenced by the specific medication, individual sensitivity, neurological conditions, combination regimens, and other clinical factors. Studies on the psychobehavioral effects of antiepileptic drugs also highlight the heterogeneity among drugs and individuals, as well as the complexity of treatment regimens.

In the regimen-based analysis, the polytherapy group exhibited greater changes in mood and behavioral scores compared to the monotherapy group. Even after adjustment, polytherapy remained associated with changes in mood and behavior. These results should be interpreted as an association rather than a direct effect of polytherapy, as patients receiving multiple medications may have more complex or difficult-to-control epilepsy. Literature on pediatric levetiracetam use also indicates that adverse events occur more frequently with polytherapy regimens than with monotherapy; however, this does not in itself prove that drug combinations are the sole cause of behavioral changes. Another crucial aspect is the choice of measurement instruments. Wagner et al. demonstrated that the various behavioral health screening instruments used for children with epilepsy vary in their level of psychometric support (Wagner et al. 2022). Therefore, future studies should explicitly report the instrument name, language version used, the respondent, score ranges, direction of score interpretation, cut-off points, and evidence of validity and reliability within the relevant population. Such information is vital to ensure that changes in scores observed during the study can be interpreted as clinically meaningful changes rather than mere numerical fluctuations.

Overall, the dataset results indicate changes in mood and behavioral scores following the treatment period, alongside variations in these changes based on drug type and treatment regimen. Multivariate analysis reveals that drug type and treatment regimen remain associated with score variations even after accounting for various clinical characteristics. However, given the observational study design and the use of a simulated dataset, these results should be viewed as preliminary analytical findings and not used to draw causal conclusions regarding drug efficacy or safety. In actual clinical studies, interpretation must take into account baseline characteristics, indications for drug selection, seizure control levels, comorbidities, standardized instruments, and subject attrition during follow-up.

IV. CONCLUSION

Analysis revealed changes in mood and behavioral scores among children aged 4–10 years following a period of antiepileptic drug therapy. Mean mood scores shifted by 1.92 points, while behavioral scores changed by 2.47 points; the differences between pre- and post-therapy scores were statistically significant. Furthermore, variations in mood and behavioral score changes were observed depending on the type of antiepileptic drug used. The levetiracetam group exhibited greater score changes compared to other drug groups, and this association persisted after adjusting for various clinical and therapeutic characteristics.

Polytherapy regimens were also associated with changes in mood and behavioral scores after accounting for covariates. In contrast, the relationship between drug dosage and changes in behavioral scores did not reach statistical significance. These findings suggest that mood and behavioral changes in children with epilepsy require a multidimensional approach, taking into account drug type, therapeutic regimen, clinical characteristics, and other patient-related factors.

These results cannot be interpreted as evidence of a causal relationship due to the study's observational design. Moreover, as the analysis relied on a simulated dataset, the findings require confirmation through studies utilizing actual patient data, validated mood and behavioral instruments, methodologically determined sample sizes, and more comprehensive control of confounding factors. Prospective studies with standardized follow-up periods are needed to gain a more robust understanding of mood and behavioral changes associated with antiepileptic drug use in children.

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