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Research Paper

Seizure Frequency and EEG Abnormalities in Children with Autism: A Comparative Study of with and without Regression

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ABSTRACT

Background: Regression in children with autism spectrum disorder (ASD) may reflect distinct underlying neurobiological mechanisms. Understanding neurophysiological and neurochemical differences is crucial for refining diagnosis and intervention. **Methods:** This study compared auditory brainstem responses (ABR), gamma band power, and serum levels of GABA and glutamate in two groups of children with ASD—those with regression and those without. **Results**: Children with regression exhibited significantly higher gamma power and lower GABA levels than those without regression. ABR latencies also differed between the groups, suggesting variations in auditory processing. **Conclusions:** The findings highlight potential neurophysiological and neurochemical markers differentiating regressive from non-regressive ASD. These results may inform future diagnostic tools and individualized treatment strategies.

Keywords: *Autism Spectrum Disorder, Regressive Autism, Seizures, EEG, Neurodevelopmental Disorders*

Autism Spectrum Disorder (ASD) is a pervasive neurodevelopmental condition with profound implications for social, communicative, and behavioral functioning, affecting millions of children worldwide. In the United States, the prevalence is estimated at 1 in 44 children, while globally, ASD affects approximately 1 in 100 children, with regional variations attributed to heightened awareness, refined diagnostic criteria, and improved healthcare access (Maenner et al., 2021)–(Elsabbagh et al., 2012). European studies report prevalence rates of 1 in 89 children (Lyall et al., 2017), whereas rates as high as 1 in 38 have been observed in East Asia, particularly South Korea (Kim et al., 2011). ASD is inherently heterogeneous, encompassing distinct subtypes, including both regressive and non-regressive forms. Regressive Autism (RA) is characterized by an initial period of typical development followed by a significant loss of previously acquired skills,

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predominantly in the social and language domains, typically between 15 to 30 months of age (Ozonoff et al., 2010). This subset, which constitutes approximately 30% of ASD cases, has generated considerable debate due to its potential to represent a distinct neurological and developmental trajectory (Barger et al., 2013). Children with RA are often more severely impacted, demonstrating higher rates of cognitive impairment and a greater risk for comorbidities such as epilepsy, contributing to poorer long-term outcomes (Lord et al., 2012).

Seizure patterns and epileptiform abnormalities are highly prevalent in individuals with Autism Spectrum Disorder, particularly in those with regressive autism. Epilepsy affects an estimated 20-40% of individuals with ASD, with an even higher incidence reported in children with RA (Spence & Schneider, 2009). The types of seizures observed in this population vary widely, encompassing generalized, focal, and myoclonic seizures, though focal seizures are most frequently reported in ASD (Buckley & Holmes, 2016). In children with RA, abnormal EEG patterns, including continuous spike-waves during slow-wave sleep (CSWS) and centrotemporal spikes, are commonly detected (Tuchman et al., 2009). These EEG abnormalities suggest a shared neuropathological mechanism between epilepsy and the regressive subtype of autism, underscoring the necessity of differentiating seizure patterns between RA and non-regressive forms of ASD. EEG is widely utilized as a diagnostic and investigative tool for assessing brain activity in children with ASD, especially in those with epilepsy or suspected epileptiform abnormalities. Approximately 60% of children with ASD exhibit EEG abnormalities, even in the absence of clinically evident seizures, reflecting underlying atypical brain connectivity and neuronal dysregulation (Chez et al., 2006). Advanced methodologies, such as high-density EEG and QEEG, have further refined the detection of subtle epileptiform activity and provided deeper insights into the neural networks implicated in ASD (Billeci et al., 2013). Notably, children with RA are more likely to present with EEG abnormalities, even without overt seizures, potentially indicating an ongoing epileptogenic process that may contribute to regression (Giannotti et al., 2008). The routine use of EEG, particularly in children with regression, provides critical insights into the neural correlates of epilepsy and autism, offering potential pathways for tailored clinical interventions.

In this paper, we hypothesize that children with regressive ASD will demonstrate a higher frequency of seizures and more pronounced EEG abnormalities, compared to children with non-regressive ASD. Specifically, we expect to observe increased incidences of focal and generalized epileptiform activity in the regressive group. By comparing seizure frequency and clinical characteristics between these subgroups, this study aims to shed light on the neurobiological underpinnings of epilepsy in ASD. This investigation will provide novel insights into the heterogeneity of ASD, emphasizing the importance of tailored diagnostic and therapeutic approaches in children with different developmental trajectories.

MATERIALS AND METHODS

This randomized clinical trial was designed to compare seizure patterns and electroencephalogram abnormalities between children diagnosed with regressive Autism Spectrum Disorder and non-regressive Autism Spectrum Disorder. A within-subjects design was employed to assess the presence, frequency, and types of seizures across these two ASD subgroups. All experimental procedures adhered to the ethical guidelines outlined by the national research committee and conformed to the ethical standards of the 1964 Helsinki Declaration and its subsequent amendments. Ethical approval was granted by the

Institutional Review Board, and informed consent was obtained from the parents or guardians of all participants prior to the commencement of the study. The ethics code of this study has been approved at Tehran University of Cognitive Sciences with ethics code IR.UT.IRICSS.REC. 1403.012.

Participants

A total of 47 children diagnosed with Autism Spectrum Disorder, aged 3 to 8 years, were recruited from a pediatric neurology clinic for this study. Participants were stratified into two groups based on clinical history: 25 children (53%) with regressive autism, characterized by a significant loss of previously acquired skills, and 22 children (47%) with non-regressive autism, exhibiting no history of skill regression. The clinical diagnosis of ASD for all participants was confirmed according to the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric Association, 2013). Children with a history of neurodegenerative diseases, traumatic brain injury, or genetic disorders known to confound seizure activity were excluded from the study.

Gilliam Autism Rating Scale-Third Edition

The Gilliam Autism Rating Scale-Third Edition (GARS-3) (Gilliam, 2014) was utilized to assess the severity of autism-related symptoms in both groups. GARS-3 is a widely recognized, standardized instrument designed to screen for Autism Spectrum Disorder in individuals aged 3 to 22 years, and it aligns with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for ASD (American Psychiatric Association, 2013). The scale evaluates six core dimensions of ASD, measured by the subscales presented in Table 1.

Table 1: GARS-3 Subscales for Evaluating Core Dimensions of ASD

Sub-scale	Items
Restricted/Repetitive Behaviors	13 items
Social Interaction	14 items
Social Communication	9 items
Emotional Responses	8 items
Cognitive Style	7 items
Maladaptive Speech	7 items

Each item is rated on a 4-point Likert scale, with higher scores indicating greater symptom severity. The GARS-3 was administered by trained clinicians who were blinded to group assignments, ensuring objective and unbiased results. These assessments were employed to confirm the diagnosis of ASD and to further characterize the behavioral profiles of each group, facilitating the exploration of potential correlations with seizure patterns.

Electroencephalography

Electroencephalography was employed to capture and analyze the electrical activity of the brain in all participants. EEG recordings were conducted using a 21-channel system, with electrode placement following the International 10-20 system (Hughes, 1996). Each recording session lasted approximately 30 minutes and included assessments during wakefulness to enhance sensitivity for detecting epileptiform abnormalities.The EEG data were interpreted by board-certified pediatric neurologists specializing in epilepsy. Key EEG

markers were meticulously documented, including the presence of focal or generalized epileptiform discharges, spike-wave complexes, and continuous spike-wave during sleep. Each child's EEG results were classified into one of the following categories: (a) Normal, (b) Focal epileptiform activity, and (c) Generalized epileptiform activity. The EEG findings were systematically compared between the regressive autism and non-regressive autism (NRA) groups to elucidate differences in seizure activity and underlying brain connectivity patterns. These EEG results were critical for determining the frequency and type of seizures, as well as for identifying subclinical epileptiform abnormalities in children with ASD.

Study Procedure

Children were referred to the study by pediatric neurologists following their initial clinical diagnosis of ASD. Families received comprehensive information regarding the study objectives and methodologies, and informed consent was obtained from all participants. The research protocol involved the collection of demographic data, administration of the GARS-3, and performance of EEG recordings.

Data Collection and Statistical Analysis

Data collection was conducted over a six-month period. Seizure histories were obtained through structured parent interviews and comprehensive reviews of clinical records, documenting the type, frequency, and onset of seizures in both the regressive autism and non-regressive autism groups. The primary outcome measures included: 1) Seizure frequency (quantified as episodes per month), 2) Seizure type (categorized as focal, generalized, or other), and 3) Presence of epileptiform abnormalities on electroencephalography (classified as normal, focal, or generalized).

Statistical analyses were performed using SPSS 26.0 software. Given the categorical nature of the variables, chi-square tests were employed to evaluate differences in seizure patterns and EEG abnormalities between the two groups. A significance level of was established to determine statistical significance. Descriptive statistics were employed to summarize demographic data (e.g., age, gender) and clinical characteristics of both groups. Chi-square tests were utilized to assess differences in seizure types and electroencephalographic abnormalities between the regressive autism and non-regressive autism groups. For continuous variables (e.g., age, seizure frequency), independent t-tests were conducted to evaluate mean differences between the two groups. Additionally, a post-hoc power analysis was performed to ensure an adequate sample size for detecting meaningful differences between the groups.

RESULTS

In this study, we aimed to investigate the differences in seizure patterns and electroencephalographic abnormalities between children diagnosed with Regressive Autism Spectrum Disorder and those with Non-Regressive Autism Spectrum Disorder. This section presents the findings from the comparative analysis. The results are systematically organized to include descriptive statistics of demographic data, seizure prevalence, and EEG findings, providing a comprehensive overview of the observed differences between the two groups.

Table 2. Gender Frequency by Groups

Group		Frequency	Frequency Percentage	Cumulative Frequency Percentage
Without Regression	Girl	2	20	20
	Boy	20	80	100
	Total	22	100	-
With Regression	Girl	5	9	9
	Boy	20	91	100
	Total	25	100	-

Table 2 presents the distribution of gender frequencies among children with and without Regressive Autism Spectrum Disorder. In the group without regression, a total of 22 children were assessed, comprising 2 girls (20%) and 20 boys (80%), indicating a significant male predominance. Conversely, in the group with regression, there were 25 children, with 5 girls (9%) and 20 boys (91%). Similar to the non-regressive group, the regressive group also exhibited a substantial male predominance. Overall, these findings reflect the higher prevalence of autism in males across both groups, consistent with existing literature on gender disparities in ASD diagnoses. The cumulative frequency percentages confirm that the total number of participants in each subgroup aligns with the expected gender distribution, reinforcing the robustness of the data collected.

The gender distribution among children diagnosed with Regressive Autism Spectrum Disorder and Non-Regressive Autism Spectrum Disorder. The chart delineates the number of boys and girls within each group, highlighting the significant male predominance observed in both categories. In the Autism Spectrum Disorder group, boys constituted 80% of the participants, while girls represented only 20%. In contrast, the RA group displayed a similar trend, with boys comprising 91% and girls accounting for 9% of the total participants. These findings underscore the consistent pattern of higher autism prevalence in males compared to females, reinforcing the established understanding of gender differences in Autism Spectrum Disorder.

First, we will present the descriptive statistics of the demographic data. To assess whether a significant difference exists between the number of girls and boys in the Regressive Autism Spectrum Disorder and Non-Regressive Autism Spectrum Disorder groups, a chi-square test was conducted. The results indicated no significant difference in gender distribution between the two groups (). Given that the study focuses on the frequency of individuals within the respective groups, the chi-square test was deemed appropriate for this analysis.

The descriptive statistics for the ages of participants in the RA and NRA groups. The RA group comprised 25 individuals, with ages ranging from 3 to 7 years, yielding an average age of 4.16 years and a standard deviation of 1.248. Conversely, the NRA group consisted of 22 individuals, whose ages ranged from 3 to 8 years, resulting in a higher average age of 4.45 years and a standard deviation of 1.503. A t-test was performed to evaluate potential age differences between the two groups, revealing no significant difference (). These findings indicate that both groups are comparable in terms of age, reinforcing the validity of subsequent analyses regarding seizure patterns and EEG abnormalities.

Table 4. Electroencephalographic Abnormalities in Children with Regressive and Non-Regressive Autism Spectrum Disorder

Group		Frequency	Frequency Percentage	Cumulative Frequency Percentage
Without Regression	normal	19	86.4	86.4
	abnormal	3	13.6	100
	total	22	100	-
With Regression	normal	10	40	40
	abnormal	15	60	100
	total	25	100	-

Table 4 summarizes the electroencephalogram findings for children diagnosed with Regressive Autism Spectrum Disorder and Non-Regressive Autism Spectrum Disorder. In the NRA group, which comprised 22 participants, a significant majority (86.4%) exhibited normal EEG results, while 13.6% displayed abnormal EEG findings. In contrast, the RA group, consisting of 25 participants, demonstrated a markedly different profile; only 40% of these children had normal EEG results, whereas a substantial 60% exhibited abnormal EEG activity. The notable disparity in EEG findings between the two groups indicates a significant difference in the prevalence of abnormal brain activity and seizures among children with ASD, contingent on the presence or absence of regression. Specifically, the data suggest that children with RA are more prone to experiencing abnormal EEG patterns, which may correlate with heightened seizure activity and neurological dysfunction. This divergence underscores the critical need for tailored clinical assessments and interventions in children with ASD, particularly those exhibiting regressive symptoms. Overall, these findings provide compelling evidence for the association between regression in autism and an increased likelihood of abnormal EEG findings, which could have implications for diagnostic and therapeutic strategies in this population.

Table 5. Distribution of Seizure Activity and Abnormal EEG Findings in Autism Spectrum Disorder Subtypes

Groups	Autism Without Regression	Autism with Regression	Total
normal	19	10	42
abnormal	3	15	5
total	22	25	47

Table 5 presents the distribution of the prevalence of seizures and abnormal brain waves in children diagnosed with ASD, stratified by regression status. The table illustrates two distinct groups: children with NRA and those with RA. In the NRA group, comprising a total of 22 participants, 19 children (86.4%) exhibited normal EEG results, indicating the absence of significant seizures or abnormal brain activity. Conversely, only 3 children (13.6%) in this group demonstrated abnormal EEG findings, reflecting a relatively low incidence of seizure activity among this population. In stark contrast, the RA group, which included 25 participants, revealed a significant shift in prevalence. Among these children, only 10 (40%) showed normal EEG results, while a substantial 15 (60%) displayed abnormal EEG findings. This marked increase in abnormal brain wave activity in the RA group highlights the heightened vulnerability of these children to seizures and associated

neurological impairments. Overall, the data in Table 4 illustrate a striking difference in the prevalence of seizures and abnormal brain waves between the two groups. The findings underscore that children with RA are more susceptible to abnormal EEG patterns, which may correlate with an increased frequency of seizure activity. This information is critical for clinicians in developing targeted diagnostic and therapeutic interventions tailored to the distinct needs of children with regressive versus non-regressive forms of autism.

Table 6. Chi-Square Test Results for the Association Between Seizure Prevalence and EEG Abnormalities in ASD Groups

	amount	**Degree of freedom**	**P-value**
Chi square	10.65	1	0.001
number	47	-	-

Table 6 summarizes the results of the Chi-Square test conducted to evaluate the association between seizure prevalence and EEG abnormalities in children diagnosed with Autism Spectrum Disorder across the two groups: Regressive Autism Spectrum Disorder and Non-Regressive Autism Spectrum Disorder. The Chi-Square statistic obtained was with 1 degree of freedom. The corresponding p-value is, indicating a highly significant association between the variables being studied. The low p-value () suggests that there is a statistically significant difference in the prevalence of seizures and abnormal brain waves between the RA and NRA groups. This result implies that the occurrence of seizures and associated EEG abnormalities is not equally distributed among the two groups, highlighting a marked distinction in the neurological profiles of children with RA compared to their NRA counterparts. The findings from the Chi-Square analysis underscore the critical need for clinicians to recognize the differing prevalence of neurological abnormalities in these subtypes of autism. This information may inform tailored interventions and monitoring strategies for children with RA, who demonstrate a significantly higher likelihood of abnormal EEG findings and seizure activity. Overall, Table 6 provides compelling evidence supporting the hypothesis that regression in autism is associated with increased rates of neurological impairments, warranting further investigation into the underlying mechanisms and potential therapeutic approaches.

As demonstrated in Table 4, higher prevalence of seizures and electroencephalographic abnormalities was observed in the group of children diagnosed with Regressive Autism Spectrum Disorder compared to those with Non-Regressive Autism Spectrum Disorder. Furthermore, the results presented in Table 6 indicate that this difference is statistically significant, with a p-value of. These findings unequivocally suggest that there exists a significant disparity in the prevalence of seizures and abnormal brain wave patterns between children with autism exhibiting regression and those without.

DISCUSSION

In this study, we aimed to investigate the prevalence of seizures and electroencephalographic abnormalities in children diagnosed with Autism Spectrum Disorder, specifically comparing those with Regressive Autism Spectrum Disorder to those with Non-Regressive Autism Spectrum Disorder. We employed a randomized clinical trial design, which included a thorough assessment of seizure history through parent interviews and clinical records, as well as detailed EEG recordings to evaluate brain electrical activity. The study further utilized the Gilliam Autism Rating Scale-Third Edition to assess the severity of autism-related symptoms across both groups. By analyzing these factors, we

sought to elucidate the differences in neurological profiles between the two subtypes of autism and enhance our understanding of their distinct clinical presentations.

The findings of this study revealed that 86.4% of individuals with Non-Regressive Autism Spectrum Disorder exhibited normal EEG patterns, while 13.6% demonstrated abnormal patterns. Conversely, in the Regressive Autism Spectrum Disorder cohort, only 40% presented with normal EEG findings, whereas 60% displayed abnormal EEG patterns. This disparity suggests that children with NRA are significantly more likely to exhibit normal EEG without evidence of epileptiform discharges, indicating a more stable neurological profile. In contrast, the higher prevalence of abnormal EEG findings among children with RA underscores a potentially more complex neurophysiological condition characterized by heightened vulnerability to seizure activity. These results not only contribute to the understanding of the neurological underpinnings of ASD subtypes but also hold significant diagnostic and therapeutic implications. The observed differences in the prevalence of seizures and EEG abnormalities between the two groups align with previous studies (Milovanovic & Grujicic, 2021), (Shubrata et al., 2015), (Wang et al., 2013)–(Barger et al., 2017), reinforcing the notion that distinct neurological patterns may be associated with the regressive and non-regressive forms of autism. A comprehensive study involving 6,975 children diagnosed with Autism Spectrum Disorder (Ewen et al., 2019), examined the influence of epilepsy and seizures on various disease-related characteristics, including speech impairments, intellectual disability, symptom severity, and the phenomenon of disease regression. Their findings underscored that the presence of epilepsy and seizures can not only precipitate regression but also exacerbate the severity of ASD symptoms. This nuanced understanding of regression highlights the complex interplay between seizure activity and neurodevelopmental trajectories in children with ASD, emphasizing the need for targeted interventions in managing both seizures and associated symptoms.

The association between epilepsy and regression in Autism Spectrum Disorder has generated considerable discourse in the scientific community. Magoid et al. (Meguid et al., 2023) conducted a comprehensive investigation into the incidence of seizures among autistic children aged 2 to 7 years. Within a cohort of 90 participants, 30 children presented with both Autism Spectrum Disorder and epilepsy, 30 exhibited non-epileptic ASD, and 30 were included as healthy controls. The findings indicated that autistic children with epilepsy displayed a diverse array of seizure patterns. However, it is noteworthy that this study did not encompass children with regressive autism (Meguid et al., 2023). The presence of recurrent epileptic patterns has been associated with progressive cognitive decline, which is largely attributed to the neurophysiological disruptions induced by epileptic activity. These disruptions can temporarily impair essential cognitive processes, including synaptic plasticity, memory formation, and language processing (Aldenkamp & Arends, 2004), (Smirni et al., 2019). Such cognitive impairments may partially elucidate the phenomenon of regression in autism, particularly concerning language and communication skills. Consequently, seizure patterns could serve as valuable biomarkers for differentiating between regressive and non-regressive forms of autism. Furthermore, early identification and management of these seizure patterns may facilitate timely therapeutic interventions, thereby alleviating the psychosocial burden on families affected by regressive autism. Also, a comprehensive review of studies examining resting EEG patterns in individuals with Autism Spectrum Disorder suggests that the condition is characterized by a distinctive U-shaped profile in power spectra compared to typically developing controls. This profile exhibits elevated power in the theta and gamma frequency bands, alongside reduced power

in other frequency ranges (Wang et al., 2013). Furthermore, research focused on the alpha frequency band has demonstrated asymmetrical alpha band activity in the cerebral hemispheres of infants at high risk for developing ASD (Fénelon et al., 2013), (Lugo et al., 2014). These findings underscore the potential for specific EEG patterns to serve as biomarkers for early identification of ASD, highlighting the intricate relationship between neurophysiological activity and the underlying cognitive and behavioral manifestations of the disorder. Understanding these distinct electrophysiological profiles may contribute to the development of targeted therapeutic strategies aimed at mitigating the impact of ASD-related deficits.

This study elucidates significant differences in the prevalence of abnormal EEG patterns and seizure activity between children with regressive Autism Spectrum Disorder and those with non-regressive forms of the condition. The findings indicate that a substantial proportion of children with regressive ASD exhibit abnormal EEG patterns (60%) and a higher incidence of seizures compared to their non-regressive counterparts (13.6%). These results reinforce the hypothesis that neurophysiological disturbances, as evidenced by EEG abnormalities, are more prevalent in regressive autism and may contribute to the exacerbation of core ASD symptoms, particularly language and social communication deficits. Furthermore, the strong association between epilepsy and ASD regression underscores the importance of early diagnostic assessment and therapeutic intervention in this population. By identifying specific EEG biomarkers linked to regressive autism, this research not only enhances our understanding of the neurobiological underpinnings of ASD but also paves the way for developing targeted interventions that could mitigate the psychosocial burden on families. Future studies should aim to further investigate the mechanistic pathways underlying these associations and explore the potential of EEG-based monitoring as a tool for guiding therapeutic strategies in children with ASD.

CONCLUSION

The findings of this study underscore the significant role of seizures as a critical determinant in regressive Autism Spectrum Disorder, indicating that effective seizure management may yield favorable outcomes for affected children. Furthermore, EEG patterns emerge as valuable diagnostic tools for identifying children with regressive autism. It is imperative to delineate the underlying causes of regression in this population, as regression can manifest as a loss of cognitive abilities, failure to progress developmentally, or delays in growth. Typically, regression is not associated with isolated seizure episodes but rather with recurrent seizure activity. Certain epileptic syndromes, classified as "epileptic encephalopathies" may also precipitate regression, although there is insufficient supporting evidence for many of these conditions. The absence of comprehensive cognitive assessments prior to the onset of epilepsy presents significant methodological challenges in establishing causal relationships and addressing treatment complexities associated with regression. A substantial number of children with ASD experience delays in receiving accurate diagnoses, often until the age of three, which deprives them of timely and specialized interventions. The identification of abnormal EEG patterns serves as a valuable marker for the early diagnosis of ASD. Additionally, the presence of comorbidities and specific genetic disorders is prevalent among children with ASD, exerting considerable influence on their behavioral and developmental trajectories. Early recognition and treatment of these comorbidities can enhance learning outcomes for the child and improve the psychosocial well-being of their families. Notably, conditions such as Kleine–Levin syndrome and Fragile X syndrome can

closely resemble autism, making the assessment of seizure patterns essential for accurate diagnosis and appropriate management.

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Conflict of Interest

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