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RESEARCH ARTICLE

Evaluation of primary markers of inflammation and the systemic inflammation index in specific learning disabilities

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ABSTRACT

Aim: Specific learning disorder (SLD) is a term that refers to reading, writing and arithmetic difficulties. The neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and systemic inflammation index (SII) are affordable and accessible inflammatory biomarkers. This research aims to evaluate the relationship between NLR, PLR, SII and SLD to determine whether inflammation contributes to pathogenesis.

Methods: This study included 90 SLD-diagnosed patients and 90 age-, sex- and ethnicity-matched healthy controls. Blood cell counts and NLR, PLR and SII values were obtained from medical records and compared between the two groups.

Results: The NLR, PLR and SII were significantly higher ($p = 0.029$, $p = 0.033$ and $p = 0.018$ respectively) and lymphocyte counts were significantly lower ($p = 0.041$) in the SLD group. WISC-R total scores decreased with age in the SLD group (-1.988 coefficient, Beta = -0.247 ß, $p = 0.041$). Multivariate logistic regression analysis revealed that the SII was the only parameter independently associated with the diagnosis of SLD (Beta = 0.003, $p = 0.023$).

Conclusion: Inflammation might play a role in SLD etiopathogenesis. NLR, PLR and SII may be potential biomarkers for SLD in children. Further research may lead to early diagnosis and additional anti-inflammatory pharmacological therapies for SLDs.

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KEYWORDS
inflammation biomarkers; neurodevelopmental disorders; NLR; PLR; SII; specific learning disability

1. Introduction

In 1963, Samuel Kirk first used the term 'learning disability' to describe children with normal intellectual capacity who suffered from a brain-based disability that hindered their learning [1]. Reading impairment, or dyslexia, is poor reading proficiency despite average intelligence and education. Dyscalculia and dysgraphia, refer to difficulties in math and writing, respectively, and often coexist with other learning disabilities [2]. Although the etiology of specific learning disorders (SLD) remains unclear, scientific data indicate biologically based genetic and environmental factors [3,4].

The immune system affects brain and behavior via well-established molecular pathways. Patients treated with inflammatory cytokines for diseases such as hepatitis-C often experience symptoms of depression [5]. Similarly, anti-depressant effects of anti-inflammatory medicines have been demonstrated [6]. To date, several studies have shown a link between inflammation and neurodevelopmental disorders (NDDs) [7]. In 1977, the first report of immunological abnormalities in individuals with autism spectrum disorder (ASD) was published [8]. In the 1980s, Geschwind et al. proposed a relationship between dyslexia and immunological dysfunction during fetal development [9]. Although certain components of their theory are debatable, multiple studies support the theory that dyslexia is connected with a greater risk of immunological dysfunction in at least certain individuals [10–12].

Predicting inflammation with neutrophil-lymphocyte ratio (NLR) is a cost-effective and efficient method. Neutrophils produce cytokines and other inflammatory mediators that trigger oxidative stress and inflammation in the innate immune system, boosting infection response [13]. Lymphocytes are responsible for regulatory or protective functions in addition to their critical role in adaptive immunity. Frequently, decreased lymphocyte counts are indicative of general malhealth and compromised physiological stress [14]. The NLR was first created to establish an appropriate metric that accurately represents the level of stress and systemic inflammation in patients who are critically ill. However, further studies have shown that it has prognostic significance in predicting worse outcomes in several medical conditions, such as cardiovascular disorders and liver illnesses [15,16]. Psychiatric disorders, including schizophrenia, bipolar disorder (BD)

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and NDDs, have also been associated with elevated NLRs [17]. Cytokines and proinflammatory chemicals are also abundant in platelets. Therefore, the platelet count and the platelet-lymphocyte ratio (PLR) are other good predictors of the state of inflammation and have also been shown to be related to a variety of mental illnesses, such as schizophrenia, BD and obsessive-compulsive disorder (OCD) [18,19]. In 2014, Hu and colleagues introduced a novel prognostic indicator termed the systemic inflammation index (SII). This indicator was specifically designed to assess the prognosis of patients who underwent curative resection for hepatocellular cancer [20]. Various studies have used SII as a marker of subclinical inflammation and prognosis [21]. In addition, recent research has shown that the SII is higher in adults with mental disorders [22,23].

NDDs are pervasive, lifelong disorders for which pharmacological interventions are not readily available. The substantial increases in the prevalence of NDDs over a relatively short period may not be attributed solely to genetic factors and/or improved diagnostic criteria [24]. There is widespread consensus that environmental risk factors and genetic predispositions during key neurodevelopment, particularly inflammation, affect NDD susceptibility and severity [25]. Identifying NDDs at an early stage may result in prompt actions that have the potential to decrease their social and economic consequences.

The NLR, PLR and SII are currently being extensively investigated by medical disciplines as indicators of systemic inflammation [26]. This is due to their accessibility through standard blood counts, which eliminates the necessity for costly immunoassays. This research aims to compare the NLR, PLR and SII of SLD individuals to healthy controls to determine if inflammation underlies SLD. To the best of our knowledge, no studies have investigated the SII in childhood mental disorders or NDDs, including SLD.

2. Materials & methods

2.1. Participants

In this cross-sectional/retrospective study, we performed a retrospective analysis of a database of complete blood counts (CBC) for 180 individuals from their medical records. The SLD group consisted of 90 children aged between 7 and 12 (30 girls and 60 boys) who applied to the child and adolescent psychiatry outpatient clinic at an education and research hospital and received a SLD diagnosis between June 2023 and January 2024. The control group consisted of 90 age-, ethnicity- and gender-matched healthy, randomly selected children (34 girls and 56 boys) who applied to the pediatric outpatient clinic for regular care in the same period to obtain a health license, such as for participating in sports. Blood cell counts were obtained from the CBC panel and used to calculate the NLR, PLR and SII. The exclusion criteria for both groups included the following: a chronic medical condition; comorbid psychiatric disorders (including other NDDs); neurologic or genetic disorders; obesity (body mass index (BMI) >30 kg/m^2); and the existence of an active infectious disease at the time of blood sample collection that could influence the CBC panel.

The Alaaddin Keykubat University Faculty of Medicine Clinical Trials Ethical Committee (ALKÜ-KAEK) (10354421-2023/10-03) approved this study, and all procedures adhered to local laws and regulations as well as the Helsinki Declaration. We obtained written informed consent from the parents and verbal consent from the children.

2.2. Psychiatric examination

We used clinical interviews based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), family interviews, teacher information forms and psychiatric examinations, including evaluation of age and grade level reading, writing and arithmetic abilities, to make the diagnosis of SLD. The researchers documented sociodemographic and clinical information using a questionnaire. Every participant in the study underwent a diagnostic evaluation by a child/adolescent psychiatrist using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime Version (K-SADS-PL). Licensed psychologists administered the Wechsler Intelligence Scale for Children-Revised (WISC-R) to the SLD group participants to determine intelligence quotient (IQ) scores.

2.3. Statistical analysis

The data were analyzed using SPSS version 26.0 software. The normality of the distribution of variables was tested using the Kolmogorov-Smirnov test. An independent *t*-test was used to compare the mean values of normally distributed continuous variables between groups, and the Mann-Whitney U test was used to compare the median values of nonnormally distributed continuous variables between groups. The chi-square test was used to compare the frequencies of categorical variables between groups. The correlation between laboratory parameters and WISC-R scores was assessed using the Pearson correlation coefficient, depending on the normality of the variables. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic performance of the SII for distinguishing the SLD group from the control group. Logistic regression analysis was

performed for the SLD group only to investigate the parameters that might influence SLD diagnosis. A *p*-value less than 0.05 was considered to indicate statistical significance, and the *p*-value was calculated bidirectionally.

3. Results

Table 1 shows the sociodemographic data of the research participants. The SLD group consisted of 90 subjects (30 females and 60 males), and the control group consisted of 90 subjects (36 females and 54 males). The gender distribution was also similar: 34.2% of females were in the SLD group, and 40.9% of females were in the control group ($p = 0.353$). The SLD group had a mean age of 9.06 ± 1.59 years, while the control group had a mean age of 9.46 ± 1.75 years. There was no significant difference in age between the two groups ($p = 0.116$). The parental demographics of both cohorts were comparable in terms of age, occupation and level of education ($p > 0.05$). The sole observable difference in family composition was the statistically greater percentage of single-parent households within the SLD group ($p = 0.047$). The two groups did not significantly differ in terms of the number of siblings, the number of children, the presence of mental disorders in the family, or the income level. The mean scores for the WISC-R verbal and performance subtests and the WISC-R total scores were 77.3 ± 14.2, 100.0 ± 14.4 and 88.1 ± 12.7, respectively, for the SLD group (Table 1).

The mean hemoglobin levels and red blood cell (RBC), white blood cell (WBC), neutrophil, eosinophil, basophil, monocyte and platelet counts were not significantly different between the two groups ($p > 0.05$). However, the mean lymphocyte count was significantly lower in the SLD group (2.90 ± 0.85) than in the control group (3.15 ± 0.77) ($p = 0.041$). The SLD group also had a significantly higher NLR (1.80 ± 1.14 vs. 1.47 ± 0.80, $p = 0.029$), PLR (121.82 ± 47.93 vs. 108.70 ± 32.52, $p = 0.033$) and SII (531.33 vs. 440.97, $p = 0.018$) than did the control group (Table 2 & Figure 1).

Age was negatively correlated with the WISC-R verbal ($r = -0.254$, $p = 0.017$), WISC-R performance ($r = -0.238$, $p = 0.026$) and WISC-R total ($r = -0.260$, $p = 0.014$) scores, suggesting that older children in the SLD group had lower cognitive abilities. Furthermore, the results of the logistic regression analysis demonstrated that age had a statistically significant impact on the WISC-R total score. As age increased, the analysis revealed a statistically significant decrease in WISC-R total scores (-1.988 coefficient, -0.247 ß, $p = 0.041$). The NLR, PLR and SII were positively correlated with each other ($p < 0.001$), suggesting that they reflect similar aspects of systemic inflammation. The NLR, PLR and SII were not significantly correlated with any of the WISC-R subscales ($p > 0.05$) (Figure 2).

We used receiver operating characteristic (ROC) curve analysis to identify the best cut-off value for the SII, which we found to be 535.67, to predict SLD. The cut-off point was established using Youden's index, with a maximum value of 0.222. The sensitivity and specificity of the test were computed to be 72.22 and 50%, respectively, for this cut-off value. The positive predictive value (PPV) was 64.29%, while the negative predictive value (NPV) was 59.09%. In addition, the area under the curve (AUC) was 0.602 ($p = 0.018$). The results show that the test used is a proficient instrument for identifying SLD, and the cut-off value accurately predicts the presence or absence of the disease with considerable precision. These findings have the potential to aid in clinical practice, as well as diagnosis and follow-up procedures (Figure 3).

The R^2, McFadden R^2 and Cox & Snell R^2 values of the logistic regression model were 0.0689, 0.0911 and 0.122, respectively, indicating a modest level of predictive accuracy. Logistic regression analysis was used to examine the effect of various predictors on the likelihood of SLD. The results presented in Table 3 reveal that most of the predictors did not have a statistically significant effect ($p > 0.05$). However, the systemic inflammation index (SII) was found to be a significant predictor of SLD, with an odds ratio of 1.003 (95% CI: 1.0–1.006) ($B = 0.003$, $p = 0.023$). This suggests that higher SII values are associated with a slightly increased likelihood of SLD. Overall, the SII showed a significant association with the likelihood of SLD, while other variables in the model, including age, maternal and paternal age, number of siblings, sex, PLR and NLR, did not show significant predictive power (Table 3).

4. Discussion

Increasing evidence suggests that inflammation and immune activation contribute to central nervous system dysfunction, which is associated with mental disorders [27,28]. Previous research examining cytokine levels in cerebral fluid revealed that children diagnosed with OCD, schizophrenia and attention-deficit hyperactivity disorder (ADHD) had impairments in both their cell-mediated and humoral immune responses [29]. According to Buske-Kirschbaum et al., psychological stress and allergic inflammation activate inflammatory cytokines that affect the prefrontal cortex and neurotransmitter systems implicated in ADHD pathogenesis [30]. de Theije and colleagues reported autistic-like repetitive behaviors and decreased social communication in a mouse model of food allergy. They suggested that neuroimmune interactions have an impact on brain circuits that are

Table 1. Comparison of sociodemographic data between the specific learning disorder group and the control group.

Parameter		SLD group (n = 90)	Control group (n = 90)	*p*-value
Age		9.06 ± 1.59	9.46 ± 1.75	0.116[a]
Gender	Female	30 (34.2%)	36 (40.9%)	0.353[c]
	Male	60 (65.8%)	54 (59.1%)	
Maternal age		38.22 ± 6.11	38.93 ± 6.65	0.457[a]
Maternal employment status	Housewife	68 (75.6%)	62 (68.9%)	0.597[c]
	Free	12 (13.3%)	16 (17.8%)	
	Institutional	10 (11.1%)	12 (13.3%)	
Maternal education	Primary education	58 (64.4%)	55 (61.1%)	0.825[c]
	High school	26 (28.9%)	27 (30.0%)	
	Above high school	6 (6.7%)	8 (8.9%)	
Paternal age		41.77 ± 6.09	42.10 ± 6.65	0.735[a]
Paternal employment status	Unemployed	9 (10.0%)	8 (8.9%)	0.240[c]
	Free	56 (62.2%)	66 (73.3%)	
	Institutional	25 (27.8%)	16 (17.8%)	
Paternal education	Primary education	55 (61.1%)	45 (50.0%)	0.248[c]
	High school	23 (25.6%)	33 (36.7%)	
	Above high school	12 (13.3%)	12 (13.3%)	
Family structure	Nuclear family	78 (86.7%)	88 (97.8%)	0.047[c]
	Single parent	10 (11.1%)	2 (2.2%)	
	Extended family	2 (2.1%)	0 (0%)	
Number of children		2 (1–4)	2 (1–4)	0.137[b]
Number of siblings		2 (1–5)	2 (1–4)	0.057[b]
Psychiatric illness in the family		8 (7.0%)	1 (1.5%)	0.103[c]
Income level	1–2 MW	32 (36.0%)	22 (24.4%)	0.139[c]
	2–3 MW	45 (50.6%)	48 (53.3%)	
	4 and above MW	12 (13.5%)	20 (22.2%)	
WISC-R verbal (n = 88)		77.3 ± 14.2		
WISC-R performance (n = 88)		100.0 ± 14.4		
WISC-R total (n = 88)		88.1 ± 12.7		

[a]Independent *t*-test (mean ± SD).
[b]Mann-Whitney U test [median (min-max).
[c]Chi-Square test (n%)].

Table 2. Comparison of laboratory parameters between the specific learning disorder group and the control group.

Parameter	SLD group (n = 90)	Control group (n = 90)	*p*-value
Hemoglobin	12.79 ± 1.15	12.67 ± 1.29	0.509[a]
RBC	4.80 ± 0.46	4.66 ± 0.58	0.087[a]
WBC	8.58 ± 3.04	8.81 ± 3.02	0.620[a]
Nötrofil	4.48 ± 1.87	4.29 ± 1.64	0.473[a]
Lenfosit	2.90 ± 0.85	3.15 ± 0.77	**0.041**[a]
Eozonofil	0.21 (0.00–7.30)	0.19 (0.00–5.00)	0.686[b]
Bazofil	0.04 (0.00–0.50)	0.03 (0.00–0.30)	0.754[b]
Monosit	0.54 (0.24–10.10)	0.58 (0.20–1.73)	0.795[b]
Platelet	325.43 ± 82.80	327.47 ± 80.59	0.930[a]
NLR	1.80 ± 1.14	1.47 ± 0.80	**0.029**[a]
PLR	121.82 ± 47.93	108.70 ± 32.52	**0.033**[a]
SII	531.33 (111.78–2188.00)	440.97 (125.87–1302.40)	**0.018**[a]

[a]Independent *t*-test (mean ± SD).
[b]Mann-Whitney u test [median (min-max).

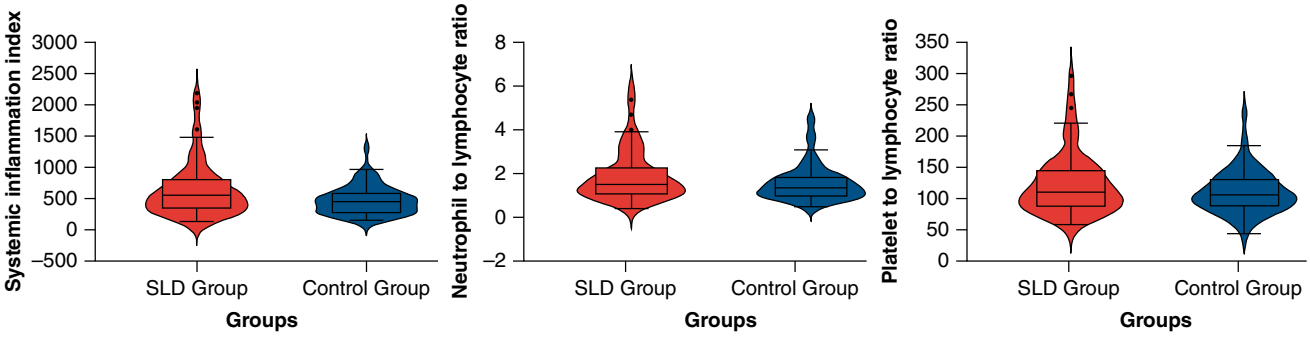

Figure 1. Box plots representing the distributions of the SII, neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in the specific learning disorder group and controls.

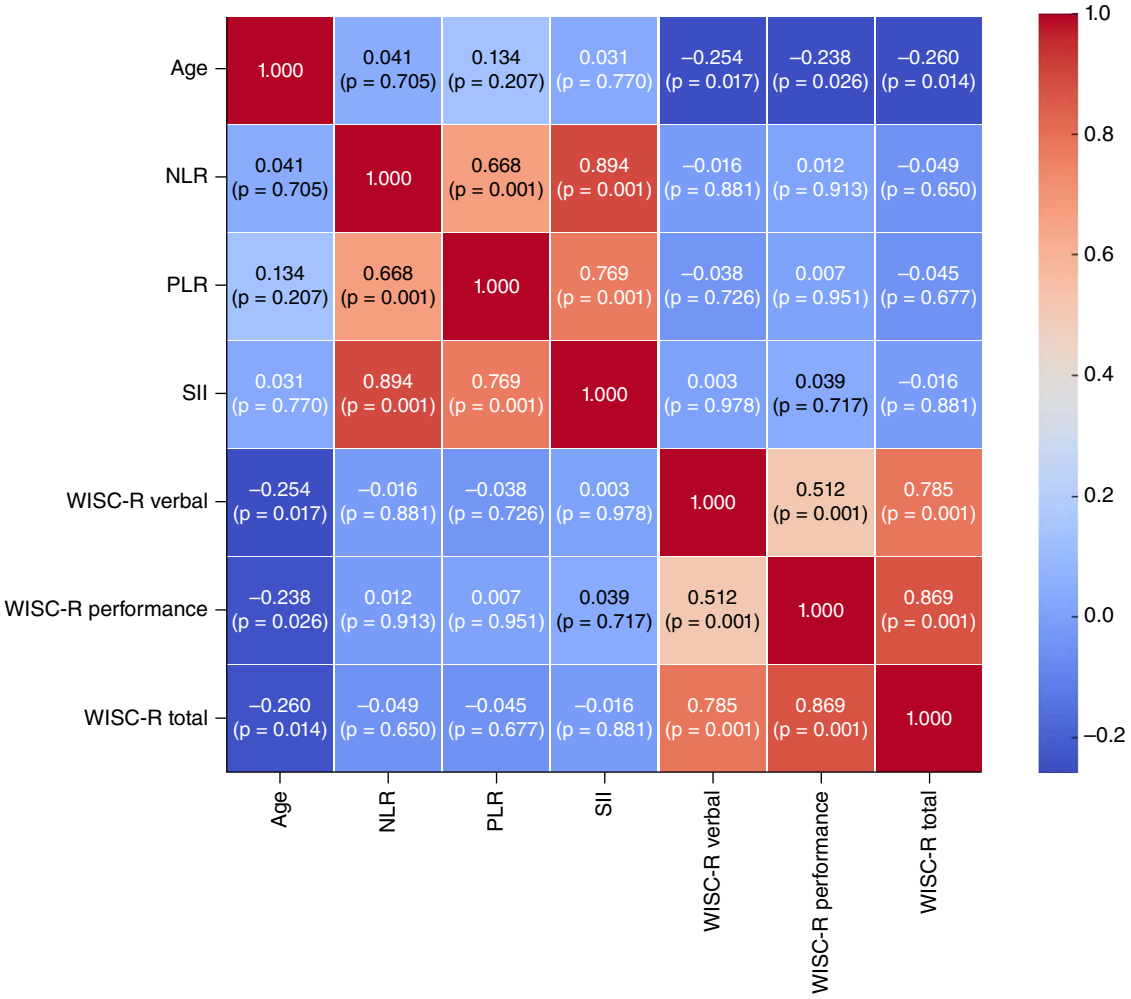

Figure 2. Correlations of age, systemic inflammatory parameters and WISC-R subscales.

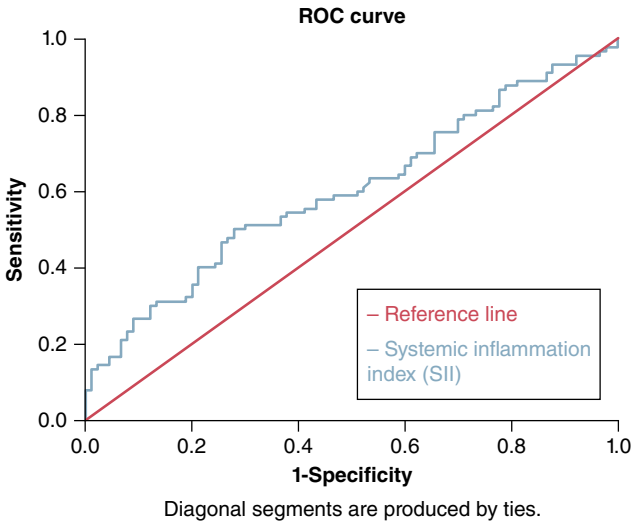

Figure 3. ROC analysis of the relationship between the SII and specific learning disorder.

involved in cognition and social interaction due to a genetic predisposition [31].

Blood biomarkers are often utilized to analyze inflammatory processes, but many of them are expensive or difficult to use for regular exams. Thus, less expensive, simpler approaches are needed. The NLR is a cost-effective, highly sensitive and reliable inflammatory parameter. Its original purpose was to measure stress and systemic inflammation in critically ill patients, but it has since been shown to predict poor outcomes in pancreatitis and cardiovascular and liver diseases [32]. Research has shown a correlation between high NLRs and elevated C-reactive protein (CRP) and cytokine levels [33]. As a consequence, the NLR is increasingly used to evaluate systemic inflammation. PLR is yet another low-cost, dependable and readily accessible inflammatory parameter [34]. Additionally, a low lymphocyte count is common during the systemic inflammatory response and is reportedly associated with mortality [35,36]. The NLR and PLR have been studied in adult patients with a variety

Table 3. The impact of predictors on the specific learning disorder as determined by logistic regression analysis.

Variable	B	S.E.	Wald	Sig.	Exp(B)	95% CI for EXP(B) Lower	95% CI for EXP(B) Upper
Constant	1.686	1.601	1.109	0.292	5.396		
Age	-0.14	0.106	1.737	0.188	0.869	0.706	1.071
Maternal age	-0.015	0.043	0.12	0.729	0.985	0.905	1.072
Paternal age	-0.007	0.044	0.026	0.872	0.993	0.911	1.082
Number of siblings	0.258	0.217	1.41	0.235	1.294	0.845	1.982
Gender	-0.395	0.36	1.208	0.272	0.674	0.333	1.363
SII	0.003	0.001	5.154	**0.023**	1.003	1.0	1.006
PLR	-0.001	0.006	0.009	0.923	0.999	0.988	1.013
NLR	-0.008	0.006	1.109	0.093	0.992	0.98	1.004

Bold values denote statistical significance.

of neuropsychiatric illnesses, such as mood disorders, schizophrenia and Parkinson's disease [17,37]. A meta-analysis revealed that the NLR was significantly elevated in patients with nonaffective psychosis, whereas the PLR remained unchanged [38]. Another study reported elevated NLRs and PLRs and lower lymphocyte counts in both first-episode schizophrenia patients and manic-episode BD patients [23]. Additionally, newly diagnosed depressive patients were reported to have a higher NLR and lower lymphocyte count, which improved after 3 months of antidepressant treatment [39].

However, there is not as much research examining inflammatory biomarkers in mental health problems in childhood as in adults. Adolescents with major depressive disorder are reported to have higher NLRs and PLRs than healthy controls, which were positively correlated with Beck Depression Inventory scores [40]. Ozyurt et al. found that adolescents with OCD and AD had higher NLRs and PLRs than the control group and those with just OCD [18]. Inflammation biomarkers derived from CBC except for SII have also been investigated in NDDs in childhood. In comparison to healthy controls, children with ADHD exhibited higher NLRs and PLRs and lower lymphocyte counts [41,42]. Kutlu et al. reported increased NLR but a similar PLR and lower lymphocyte counts in the ASD group than in the healthy controls [43]. According to another study, higher Childhood Autism Rating Scale (CARS) scores were associated with greater NLRs in children with ASD [44]. Based on the findings presented above, inflammatory processes may affect the development of synaptogenesis and neural connections in the early stages of life and may play a role in the development of many NDDs as well as SLDs. A review of the literature revealed little research examining the role of inflammation in SLD. Tønnessen et al. reported a significant association between dyslexia, handedness and immune disorders [11]. Dyslexic children were reported to exhibit significant variations in the amounts of IgA antibodies to dietary proteins [45]. SLD has been reported in 40 percent of male children born to mothers with systemic lupus erythematosus (SLE) [46]. Additionally, we found two studies that examined the NLR and PLR in SLDs. The first study compared 31 SLD patients without comorbidities to 33 healthy controls. Although there was no difference in the PLR between the two groups, the SLD group had higher NLRs and lower lymphocyte counts [47]. The second study compared 70 SLD patients with 69 healthy controls, and the NLR and PLR did not differ between the two groups [48]. In our research, we found that the NLR and PLR were significantly higher in patients with SLD, and the mean lymphocyte count was significantly lower in the SLD group than in the healthy controls, in line with the literature.

SII, a novel biomarker of systemic inflammation can be easily calculated from formula using measurements of platelets (P), neutrophils (N) and lymphocytes (L) per liter of peripheral blood: SII = P × N/L [20]. It has been used to predict the prognosis of many neurological and cardiac illnesses [49]. Evidence indicating that inflammation is involved in the etiology of psychiatric diseases has led researchers to investigate SII in mental disorders. Recent research indicated that schizophrenia, BD, anxiety and methamphetamine and cannabis use disorder patients have a significantly higher SII than healthy individuals in the adult population [23,50,51]. However, we were unable to locate any study that examined SII in childhood mental disorders. In our research, we found that SII was higher in patients with SLD than in the healthy controls. Additionally, a multivariate logistic regression analysis revealed that only higher SII values were associated with SLD diagnosis. The results of our study indicate that inflammation may contribute to the etiology of SLDs.

In terms of the overall disease burden that children and adolescents experience, psychiatric disorders play a significant role. They are the primary cause of impairment among young people worldwide. Indeed, several mental diseases begin during childhood or adolescence [52]. Modern psychiatric disorder treatment programs target at-risk individuals and treat them early to modify their illness trajectory and reduce developmental delays. Stud-

ies have indicated that increased inflammatory markers in childhood are associated with NDDs, including SLDs [53,54]. In this framework, the evidence linking inflammation to SLD during its early clinical manifestations could significantly impact treatment, especially for individuals with elevated inflammatory markers. Identifying a particular group of individuals who have higher inflammatory activity may allow for the use of anti-inflammatory therapy approaches that reduce disease burden. Our study's results and literature both show a link between an inflammatory state and SLD, suggesting that inflammatory markers, such as those in other medical fields, may be useful as biomarkers for SLD diagnosis, severity and progression. Unfavorable school results, limited vocational options, decreased employment rates, low self-esteem and poor mental and physical health are all associated with SLDs [55]. Early identification of SLDs is crucial for ensuring that children with SLDs can fully achieve their educational potential. However, early identification alone is insufficient because difficulties associated with SLDs may not become apparent until a child begins school. This "waiting for failure" attitude is problematic. Prolonged inability to read and inadequate school performance may result in social isolation and externalized and internalized behavioral problems [56]. Furthermore, the earliest stages of a child's education, such as kindergarten, are the most successful for implementing interventions [57]. Therefore, it is essential to have additional tools for early diagnosis, and inflammatory markers may serve as one such tool.

IQ scores are variable; numerous IQ examinations administered since childhood reveal considerable individual variation [58]. Empirical evidence suggests that specific NDDs may be associated with a progressive decline in IQ with age [59]. A longitudinal study of cognitive aging revealed that 23% of individuals with ASD showed signs of cognitive loss. Our research revealed a statistically significant decrease in WISC-R total scores as age increased in SLD patients, supporting the data on cognitive decline in NDDs.

This research has several strengths and limitations. Although a few studies have examined the SII in adult patients with neuropsychiatric diseases, we have not identified any research examining the SII in children with mental disorders. To our knowledge, our study is the first to examine the SII in children with an NDD. Higher values of the SII further demonstrate that individuals with SLDs have elevated levels of inflammation. The present study, despite using a relatively larger sample size of 90 SLD patients and 90 healthy controls, requires consideration of the following limitations. First and foremost, this was a cross-sectional retrospective study, which made it impossible to assess other proinflammatory markers, such as cytokine levels. Furthermore, our research's limited scope at a single site and small sample size may limit its applicability to a larger population. Additional prospective longitudinal studies with larger sample sizes and multicenter research may provide more accurate findings.

5. Conclusion

The etiology of SLD is unknown; however, this research suggested that inflammatory pathways may be involved. Individuals with immune abnormalities may be associated with a wider range of age groups, subtypes of SLD and even distinct immune endophenotypes. To determine whether immunity influences SLD pathogenesis, follow-up studies should examine the NLR, PLR, SII and other immunological markers, such as interleukins and cytokines. At present, no universally accepted threshold for the NLR, PLR, or SII that can definitively determine whether the values are within the normal range. In the future, standardizing "normal" and "elevated" levels would be helpful if they are to serve as reliable and consistent markers of increased inflammatory processes. This would make it easier to compare studies and diseases. The NLR, PLR and SII may be beneficial for identifying SLD patients early to reduce the burden of the disorder, as well as for those who might benefit from further anti-inflammatory pharmaceutical treatment.

Article highlights

Introduction
- Learning disability is a broad term that includes a range of heterogeneous disorders characterized by a delay or impairment in learning and use abilities such as reading, writing, or arithmetic despite average intelligence and education.
- In recent years, researchers have studied the role of inflammatory biomarkers, such as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), lymphocyte count and systemic inflammation index (SII), in various mental disorders for diagnosis and prognosis.
- SII has never been studied in childhood mental disorders, including specific learning disabilities (SLD).

Results
- The present study found that children with SLDs have higher NLRs, PLRs and SII, as well as lower lymphocyte counts than controls.
- We also discovered that in children with SLDs, IQ decreases as age increases.

Discussion
- The results of our study (higher NLR, PLR and SII and lower lymphocyte counts) suggest elevated levels of inflammation in children with SLDs.
- Our study demonstrated that SII is independently associated with SLD diagnosis.

Conclusion & future perspective
- Identifying biomarkers in SLDs for early diagnosis, monitoring and prognosis is important to reduce disease burden and economic costs.
- The use of SII (an inexpensive, easily accessible and reproducible biomarker) can be beneficial in SLD patients.

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Author contributions

PA Avşar: conceptualization, methodology, data curation, writing-original draft preparation, reviewing and editing. T Kara: conceptualization, methodology, data curation. O Kocaman: visualization, investigation, data curation. M Akkuş: formal analysis, supervision, software, validation, reviewing and editing.

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The authors have no financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, stock ownership or options and expert testimony.

Writing disclosure

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval (Alaaddin Keykubat University Faculty of Medicine Clinical Trials Ethical Committee (ALKÜ-KAEK) (10354421-2023/10-03)) and/or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Data availability statement

Research data are stored in an institutional repository and will be shared with the corresponding author upon request.

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