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Research Article

The Examination of Galectin-3 Levels in Children with Attention Deficit and Hyperactivity Disorder

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Abstract

Objectives: The etiopathogenesis of ADHD involves genetic, environmental, psychological, and brain structural variables. Inflammation is one ADHD etiology study field. Galectin-3 may enhance inflammation by inhibiting the anti-inflammatory cytokine interleukin-10 (IL-10). This study examined the link between blood galectin-3 concentrations and ADHD severity and levels in children with ADHD.

Methods: The clinic treated 34 first-time ADHD patients aged 5.2-14.1. Non-psychotropic first-time diagnoses were chosen. Patients were compared to 21 age- and gender-matched healthy controls. After a paediatrician exam, a psychiatrist screens healthy controls for mental illness using the Schedule for Mood Disorders and Schizophrenia in School-Age Children, Now and Lifetime Version-DSM-5 (K-SADS-PL-DSM-5). Conners' Parent Rating Scale (CPRS) and Conners' Teacher Rating Scale(CTRS) were used for diagnosis by a child and adolescent psychiatrist.

Results: Mean serum galectin-3 levels were compared between ADHD group and control groups. Serum galectin-3 level was 428.6 (SD±194.4) in the ADHD group and 183.7 ng/ml (SD±49.6) in the control group. ADHD group is found to have statistically significantly higher galectin-3 concentrations when compared to the control group (z=-5.15, p<.001).

Conclusion: In our study, it was found that serum galectin-3 levels were higher in children with ADHD and there was a significant correlation between ADHD severity and serum galectin-3 levels. Based on these findings, it is thought that galectin-3 may be associated with the etiopathogenesis of ADHD.

Keywords: ADHD, Galectin-3 Levels, Inflammation

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The neurodevelopmental condition Attention Deficit Hyperactivity Disorder (ADHD) is characterized by impulsivity, hyperactivity, and inattention.[1] With a frequency of 5.9–7.1%, ADHD is the most prevalent neurodevelopmental condition in children.[2] The frequency was determined to be 12.4% in a multicenter study done in Turkey.[3]

When examining the etiopathogenesis of ADHD, it is clear that a number of variables, including genetic, environmental, psychological, and structural alterations in the brain,[4] contribute to the disorder. Inflammation is one of the topics on which investigations on the aetiology of ADHD concentrate.[5] Numerous studies have demonstrated a connection between inflammation and ADHD.[6–8]

Galectins are a member of the lectin family, which has a preference for oligosaccharides and functions as the -galactosidase binding carbohydrate recognition domain.[9] A key player in cell proliferation, differentiation, migration, adhesion, apoptosis, and immune response is the galectin-3

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member of the galectin family.[10, 11] Numerous research have demonstrated the connection between mental illnesses and inflammation.[12, 13] Recently, there has been a striking rise in the number of scientific investigations looking at the connection between galectin-3 and psychiatric diseases. There are few studies that look at the connection between blood galectin-3 levels and schizophrenia, according to the literature.[14, 15] Kajitani et al.'s study is one of these investigations. They discovered that schizophrenia patients' blood galectin-3 levels were greater than those of healthy controls.[15] In the study by Borovcanin et al., it was discovered that galectin-3 levels are considerably greater during the remission phase and significantly lower during the attacks when patients with schizophrenia are compared to controls.[14] When human research investigating the connection between ADHD and galectin-3 are taken into account, it is clear that there are two studies on this topic, and the findings of these studies conflict or diverge.[16, 17] Işık et al.'s study is one of these studies. Galectin-3 levels have been discovered to be considerably greater in ADHD individuals.[16]

These two research that looked at the connection between ADHD and galectin-3 levels came up with different conclusions.[14, 16] Given the findings, it has been determined that more research is required to investigate the connection between galectin-3, which is known to be crucial in the etiopathogenesis of ADHD, and ADHD.

Methods

Samples

The Uşak Training and Research Hospital and the Kütahya Health Sciences University Evliya elebi Training and Research Hospital both participated in this study. The child and adolescent psychiatric outpatient clinic was used to find participants. 34 children and adolescents with ADHD who applied to the clinic for the first time and were diagnosed with the disorder range in age from 5.2-14.1 years. Patients who had never taken psychotropic medications previously and had just received a diagnosis were particularly chosen for the trial. The sick group was contrasted with 21 healthy controls who had the same age and gender as the patient group. The research excludes those with any significant psychiatric comorbidity, such as schizophrenia, bipolar illness, intellectual impairment, autism spectrum disorder, metabolic disorders, immunological diseases, endocrinological disorders, and abnormalities of the nervous system. The research does not accept participants who have used psychotropic medications during the last six months. Volunteers in the control group are in good health. The case group and healthy children both employ the same exclusion criteria. Age- and sex-matched healthy kids and teenagers who requested a regular checkup at the hospital's pediatric outpatient clinic from the same faculties as those stated above make up the control group. A psychiatrist will utilize the K-SADS-PL-DSM-5 (the Schedule for Mood Problems and Schizophrenia in School-Age Children, Now and Lifetime Version-DSM-5) to screen healthy controls for mental disorders following a physical examination by a pediatrician. The Non-Interventional Clinical Research Ethics Committee of the Kütahya Health Sciences University Presidency has examined and approved the study. The goal of the study has been explained to the study participants and their parents, and everyone has given their written agreement.

Diagnosis and Symptom Assessment

Sociodemographic and clinical data have been presented for the study in a format created by the researchers. Using the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Now and Lifetime Version-DSM-5 (K-SADS-PL-DSM-5), each patient had a thorough diagnostic examination.[18] Conners' Parent Rating Scale (CPRS) and Conners' Teacher Rating Scale (CTRS) have both been applied throughout the diagnosing process.

Revised/Long Form of Conners' Parent Rating Scale: This measure is broken down into various subscales, including ones for psychosomatic symptoms, opposition, hyperactivity, anxiety-shyness, perfectionism, and cognitive problems/inattention. The subscales of cognitive issues/inattention and hyperactivity are employed in this investigation. For contribution, DSM-IV indices, the ADHD index, and the Global Index according to DSM-IV diagnostic criteria are employed. Parents are being asked to respond to questions that take the last month into account. Each question has four possible responses: not at all true (sometimes), slightly true (occasionally), pretty true (often), and fully true (nearly often).[19] The scale will soon be referred to in the text as CPRS.

Revisions to Conners' Teacher Rating Scale (Long Form): 38 questions make up this scale, which also has 6 subscales and 3 additional subscales based on DSM-IV symptoms for ADHD, including the ADHD index, Conners' Global Index, and DSM-IV Symptoms Index. Teachers are expected to assess student behavior by looking over the previous month's behavior. Each question has four possible responses: not at all true (sometimes), slightly true (occasionally), pretty true (often), and totally true (nearly often).[19] The scale will soon be referred to in the text as CTRS.

Biochemical Analysis

Participant venous blood samples were collected between 8.00-10.30 hours after fasting overnight. After that, blood

samples were centrifuged at 4000 rpm at 4 °C for 5 minutes and the separated serum was stored at -80 °C until the time of the assay. Serum galectin-3 levels were measured by using commercial enzyme-linked immunosorbent assay kits following the manufacturers' protocols (Human galectin-3 Elisa Kit, bioassay technology laboratory, China; Cat. No E1951Hu). The results of these analyses are presented in ng/dl. The intra-assay and inter-assay coefficients of variation of the galectin-3 kit were both CV <10%.

Statistical Analysis

Statistical analysis has been performed by using SPSS 22. The Shapiro-Wilkinson test has been used to determine whether the distribution of the variables is normal. Relationships between binary variables have been evaluated with the χ^2 test. Scale scores and biochemical parameters of the patient and control groups are compared according to their distribution characteristics by using Student's t test or Mann-Whitney U test. The correlation between serum galectin-3 levels and psychological test scores has been evaluated with Spearmen's rho correlation coefficient. A p value less than 0.05 is considered to be statistically significant.

Results

This study includes 34 ADHD patients (26 boys and 8 girls) and 21 healthy controls (11 boys and 10 girls). There is no statistically significant difference between the groups in terms of gender (χ^2 (1, n=55) =3,15, p=.07). The mean age of the ADHD group is 8.92 (SD±2.78), and the mean age of the control group is 7.69 (SD±3.17) years. There is no significant age difference between ADHD and control groups (t=-1.50, p=.13). In addition, the mean body mass index (BMI) of the ADHD group is 22.14 (SD±2.40), and 21.91 (SD±2.48) of the control group, and no statistically significant difference has been detected between the groups in terms of BMI (t=0.34, p=.73). Demographic variables are presented in Table I.

When the CTRS total scale scores (z= -2.54, p= .01) and CPRS total scale scores (z= -4.86, p<.01) of the ADHD and control groups are compared, it is seen that there have been statistically significant differences between the ADHD and control groups. Besides, it has been examined whether there is a difference between the CTRS subscale tests. Cognitive problems/inattention, hyperactivity, ADHD index and impulsivity sub-dimensions are compared with the Mann-Whitney U test.

As a result of this evaluation, it has been detected that there is a statistically significant difference in cognitive problems/inattention (z= -2.07, p<.05), ADHD index (z=-2.65, p<.01) and impulsivity (z=-2.27, p<.05) subscales in CTRS subscales. There is also a statistically significant difference in all subscales in CPRS subscales (p<.05). The data related to the comparison of Conners' scores are shown in Table 1.

Besides, in this study, mean serum galectin-3 levels are also compared between ADHD group and healthy control groups. Serum galectin-3 level is found to be 428.6 (SD±194.4) in the ADHD group and 183.7 ng/ml (SD±49.6) in the control group. ADHD group is found to have statistically significantly higher galectin-3 concentrations when compared to the control group (z=-5.15, p<.001) (Table 2).

Table 1. Demographic and clinical features of children with ADHD and healthy controls. The comparison of CTRS and CPRS subscales

	ADHD Group (n=34)	Healthy Control Group (n=21)	t/z/ χ^2	p
Gender (male/female)	26/8	11/10	3.15**	0.7
Age	8.92±2.78	7.69±3.17	-1.50*	0.13
BMI	22.14±2.40	21.91±2.48	0.34*	0.73
CTRS				
Cognitive problems/Inattention	8.06±5.71	4.28±2.05	-2.07ɪ	0.03
Hyperactivity	7.00±5.84	3.38±1.98	-1.56ɪ	0.11
ADHD Index	15.81±10.45	7.80±3.34	-2.65ɪ	<0.01
Impulsivity	8.00±5.71	4.09±2.73	-2.27ɪ	0.02
CTRS Total Score	56.12±32.63	31.23±9.71	-2.54ɪ	0.01
CPRS				
Cognitive problems/Inattention	16.84±9.95	5.38±2.97	-4.44ɪ	<0.01
Hyperactivity	12.36±7.89	4.09±2.86	-3.80ɪ	<0.01
ADHD Index	19.18±11.29	5.61±2.24	-4.88ɪ	<0.01
Impulsivity	10.03±6.53	3.85±1.49	-2.92ɪ	0.03
CPRS Total Score	94.84±47.63	34.80±8.89	-4.86ɪ	<0.01

* Student t test, ɪMann-Whitney U test; **Chi-square test. ADHD: attention deficit hyperactivity disorder. BMI: body mass index. CTRS-R/L: Conners' Teacher Rating Scale Revised/Long Form. CPRS-R/L: Conners' Parent Rating Scale Revised/Long Form. p<0.05 values are in bold.

Table 2. The comparison of serum galectin-3 levels between ADHD and healthy control groups

	ADHD Group	Healthy Control Group	Mann-Whitney U test	
			z	p
Human galectin-3 levels (ng/ml)	428.6 (SD±194.4)	183.7 (SD±49.6)	-5.15	<0.001

Mann-Whitney u test is applied due to the fact that the galectin-3 data has not shown a normal distribution.

Discussion

This study examines the relationship between serum galectin-3 levels and the severity of ADHD in children. This study found that serum galectin-3 levels and the severity of ADHD are significantly correlated, and that serum galectin-3 levels are higher in children with ADHD. According to these findings, galectin-3 might be involved in the etiopathogenesis of ADHD.

Galectin-3 and mental illnesses have only been the subject of a small number of investigations to far.[14, 16, 20] Only two research have looked at the connection between galectin-3 and ADHD as far as we are aware. Wu et al.'s study is one of these investigations. Galectin-3 levels were shown in their research to be lower in people with ADHD than in healthy controls, and it has been proposed that this is because people with ADHD have lower levels of the tyrosine hydroxylase enzyme, micro mRNA let7, and galectin-3.[17, 21] In a different research by Işk et al., it was shown that those with ADHD had greater blood levels of galectin-3 than healthy controls.[16] In this investigation, it was discovered that the levels of galectin-3 were considerably higher in the ADHD group than in the healthy controls. This results suggests that, as a result of the higher blood levels of the protein found in the ADHD group, galectin-3 may have a role in the etiopathogenesis of ADHD.

Inflammation affects the levels of cytokines in ADHD. Numerous investigations have demonstrated that IL-6, IL-2, IL-10, IL-13, 1L-16, and INF-alpha levels in peripheral blood are elevated in ADHD.[21]

The inclusion of newly diagnosed and untreated paediatric patients is one of the benefits of this study. However, the study contains significant deficiencies. The first is the small sample size, which necessitates additional research with larger sample sizes. Second, because the study was cross-sectional, it was not possible to establish a temporal and causal relationship between galectin-3 and ADHD. Prospective investigations are required to determine whether ADHD and galectin-3 are causally related. Lastly, because the participants of the study were young children, the findings cannot be generalised to all persons with ADHD.

Disclosures

Ethics Committee Approval: Kütahya Health Science University Non-Interventional Clinical Research Ethics Committee. Date: 02/03/2022. Number: (2022/03-17).

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