American Journal of Biology and Natural Sciences
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Levels of Dopamine and Beta-Endorphin Hormones in Iraqi Children with Autism Spectrum Disorder

Hayder Atta Abdul-Jabbar Hasan, Muthana Ibrahim Maleek
Department of Biology, College of Science, University of Wasit, Iraq

Received: 2025, 15, Jun
Accepted: 2025, 21, Jul
Published: 2025, 20, Aug

Abstract: Autism is a neurodevelopmental disease that expresses itself in a variety of ways, most often within the first 3 years of a person's life. Difficulties in social communication and repetitive and stereotypical behaviors characterize it. The global prevalence of autism is estimated to be about 1 in 100 children, reaching up to 1 in 36 children in some high-income countries. This research focuses on studying the hormonal changes in children with Autism Spectrum Disorder (ASD) to improve scientific understanding of the biological changes associated with the disease. This study was conducted in Al-Zahra Teaching Hospital in Al-Kut / Iraq, on a sample of 50 children with autism (40 males and 10 females) aged 3 to 12 and a control group of 25 healthy children. Blood samples were collected from all participants. Dopamine and Beta-Endorphin were measured by using the ELISA technique. The mean dopamine level was significantly lower at a significance level of $P \leq 0.05$ in autistic children, 26.49 ng/L, compared to healthy controls, 44.5 ng/L. Conversely, beta-endorphin levels exhibited no statistically significant variations between the two groups, 22.85 pg/ml in autistic children and 21.1 pg/ml in healthy controls.

Keywords: Autism Spectrum Disorder (ASD); Beta-Endorphin; Dopamine.

Introduction

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by persistent deficits in social interaction and communication, alongside restricted and repetitive patterns of behavior, interests, or activities (1). It encompasses a wide range of clinical manifestations and severities, making its diagnosis and treatment particularly challenging. Increasing prevalence rates and the lack of a definitive biological marker have intensified research into the underlying neurobiological mechanisms contributing to ASD.

Among the critical neurochemical components implicated in ASD are the neurotransmitter dopamine and the neuropeptide beta-endorphin. Dopamine plays a key role in regulating motivation, reward processing, and social behavior (2), (3). Dysregulation of the dopaminergic system has been linked to the diminished reward value of social stimuli, a core feature observed in individuals with ASD (4). Similarly, beta-endorphin, a component of the endogenous opioid system, is involved in stress modulation, pain regulation, and emotional processing. Elevated levels of beta-endorphin in individuals with autism may contribute to altered affective and sensory responses (5), (6).

Material and Methods

Study Sample Description:

The study included a total of 75 children with age rang (3-12) comprising 50 patients diagnosed with Autism Spectrum Disorder and 25 healthy as control. The majority of ASD cases falling between the 5 to 8 years age range. The ASD group consisted of 40 males (80%) and 10 females (20%). All patients studded were from the Al-Zahra Teaching Hospital in Al-Kut / Iraq.

Diagnosis of ASD

All ASD diagnoses were confirmed based on clinical evaluation and standardized behavioral assessments specifically the Childhood Autism Rating Scale-Second Edition (CARS-2) and used to stratify symptom severity. The diagnosis was carried out by a consultant psychiatrist.

Methods

Venous blood sample (3 ml) was collected from each children of both healthy control group and patients . Blood sample was kept in plain plastic tube for Enzyme- linked Immunosorbent assays. The serum obtained by putting the blood samples in a plain plastic tube and allowed to clot at 37°C for 30 minutes before centrifugation. The tubes centrifuged at 5000 rpm for 5 minutes, serum was collected and kept in freezer until used (7),(8). Enzyme-linked immunosorbent assay (ELISA) technique was used to measure the Dopamine and Beta-Endorphin levels by using appropriates kits as below in Table (1).

Table (1): The Kits of Study Company and Sources.

ELISA kit	Company	Source
Human Dopamine ELISA Kit Cat. No. E1301Hu	BT LAB	China
Human Beta-Endorphin ELISA Kit Cat. No. SL0349Hu	Sun Long	China

Statistical Analysis:

Statistical analyses were conducted using SPSS 27 (2020). Data are presented as mean ± standard deviation. one-way ANOVA and independent T-test were used to assess significant differences among markers at $P \leq 0.05$.

Results:

The distribution of sex and age in autism patients and healthy controls was clearing in Table (2).

Table (2): Distribution of Sex and Age in Autism Patients and Healthy Controls.

Autism Patients			Healthy Controls		
Distribution of Sex					
Sex	Number	Percentage	Sex	Number	Percentage
Female	10	20%	Female	11	44%
Male	40	80%	Male	14	56%
Total	50	100%	Total	25	100%
Distribution of Age					
Age Group	Number	Percentage	Age Group	Number	Percentage
>5 year	8	16%	>5 year	6	24
5-8 year	29	58%	5-8 year	10	40
<8 year	13	26%	<8 year	9	36
Total	50	100%	Total	25	100%

In the current study, we analyzed the levels of neurochemical like dopamine and beta-endorphin in individuals diagnosed with Autism Spectrum Disorder (ASD) compared to healthy controls.

As detailed in Table (3) and Figure (1), dopamine levels were significantly reduced in ASD patients (26.49 ± 10.01 ng/L) compared to the control group (44.5 ± 13.07 ng/L), with a P-value of 0.000. This significant decrease suggests a possible disruption in dopaminergic signaling pathways, which have been widely implicated in the neurobiology of autism.

Although beta-endorphin levels were slightly higher in the ASD group (22.85 ± 7.96 pg/ml) compared to controls (21.1 ± 3.01 pg/ml), the difference was not statistically significant (P = 0.175), indicating that beta-endorphin may not play a major differential role in ASD pathogenesis.

Table (3): Dopamine and Beta-Endorphin Levels in Autism Patients and Healthy Controls.

Parameter	Group	N	Mean ± Standard Deviation	P-value
Dopamine (ng/L)	ASD Patients	50	26.49 ± 10.01	0.000 † S
	Control	25	44.5 ± 13.07	
Beta-Endorphin (pg/ml)	ASD Patients	50	22.85 ± 7.96	0.175 † NS
	Control	25	21.1±3.01	

N: Number; †: Independent Samples T-Test; NS: Not Significant at *P≤0.05*; S: Significant at *P≤0.05*.

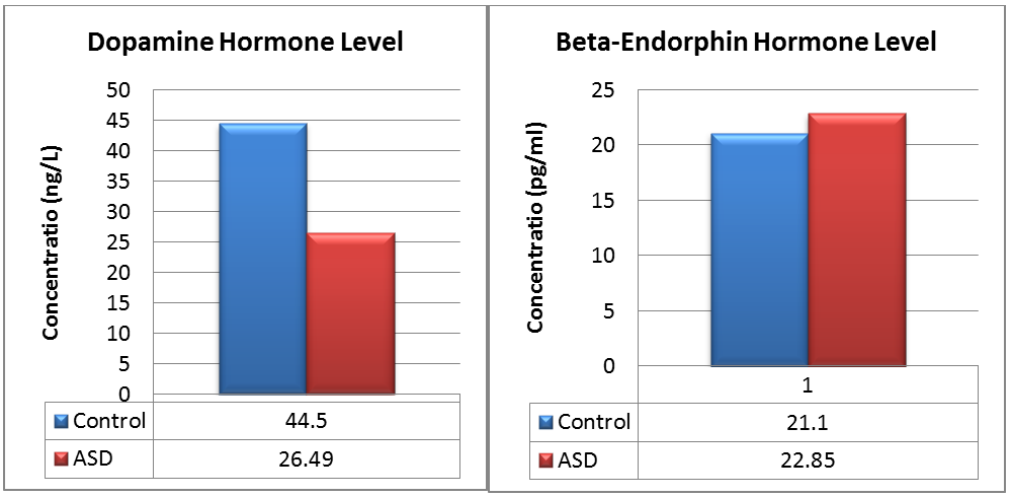

Figure (1): Levels of Dopamine (ng/L) and Beta-Endorphin (pg/ml) in Autism Patients and Healthy Controls.

The data presented in Table (4) and Figure (2) illustrates the frequency distribution of dopamine and beta-endorphin levels among control participants and individuals with Autism Spectrum Disorder (ASD), stratified by sex. The analysis aims to identify significant differences across groups using One-Way ANOVA, with a focus on gene folding or expression patterns. The Least Significant Difference (LSD) test was used to compare means, and significance was determined at $P \leq 0.05$.

Dopamine levels were significantly different across the three groups (P = 0.000). The control group exhibited the highest mean dopamine concentration (44.5 ± 13.07 ng/ml), followed by ASD males (27.86 ± 10.41 ng/ml), and ASD females (21.00 ± 5.84 ng/ml). The LSD value was 3.59, indicating significant variation. Different superscript letters (A, B, C) denote statistically significant differences among all groups.

There were no significant differences in beta-endorphin levels across groups (P = 0.553). The control group had a mean level of (21.1 ± 3.01 pg/ml), ASD males had (22.99 ± 8.74 pg/ml), and ASD females had (22.28 ± 3.67 pg/ml). All groups shared the same superscript letter (A), indicating no significant difference.

Table (4): Frequency Distribution of Dopamine and Beta-Endorphin Levels According to Sex.

Parameter	Group	N	Mean ± Standard Deviation	LSD	P-value
Dopamine (ng/L)	Control	25	^{A} 44.5±13.07	3.59	0.000 A S
	ASD Male	40	^{B} 27.86±10.41		
	ASD Female	10	^{C} 21.00±5.84		
Beta-Endorphin (pg/ml)	Control	25	^{A} 21.1±3.01	2.22	0.553 A NS
	ASD Male	40	^{A} 22.99±8.74		
	ASD Female	10	^{A} 22.28±3.67		

N: Number; LSD: Least Significant Difference; A: One Way ANOVA Test; NS: Not Significant at *P≤0.05*; S: Significant at *P≤0.05*.

Note: Different Letters within Gene Groups Denote to the Significant Differences at *P≤0.05*.

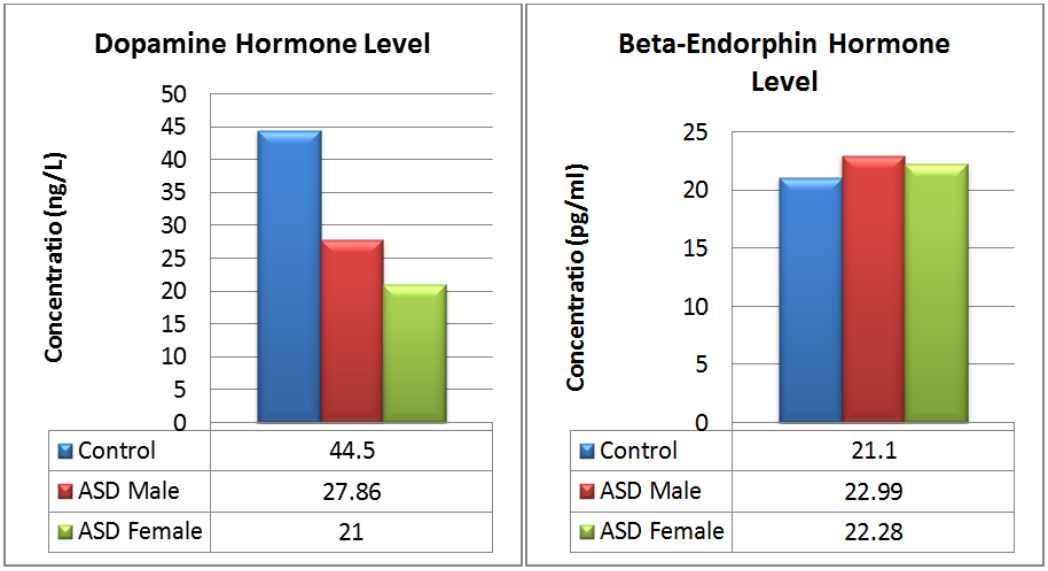

Figure (2): Frequency Distribution of Dopamine (ng/L) and Beta-Endorphin (pg/ml) Hormone Levels According to Sex.

Discussion

Pavăl, D. proposed his "dopamine hypothesis of ASD" in 2017. This hypothesis postulated that autistic behavior is caused by dysfunctions in the dopaminergic system of the midbrain. To be more specific, a malfunction of the mesocorticolimbic circuit is associated with social deficiencies, while a dysfunction of the nigrostriatal circuit is associated with stereotypical behaviors (2).

A study by Schalbroeck *et al.* (2021) investigated whether individuals with autism spectrum disorder (ASD) exhibit increased striatal dopamine synthesis capacity and whether this is associated with social defeat, measured as unwanted loneliness. Using [18F]-FDOPA PET/CT scans, the researchers compared 44 unmedicated, non-psychotic adults with ASD to 22 matched controls, aged 18–30. Results showed no significant difference in striatal dopamine synthesis capacity between the two groups (p= 0.87), nor was there a significant association between dopamine synthesis and loneliness within the ASD group (p= 0.96). Sub-regional analyses (associative, limbic, and sensorimotor striatum) and adjusted models yielded similar findings. The study concludes that in this sample, dopaminergic function is not elevated in ASD and is not linked to social defeat, challenging some assumptions about dopamine dysregulation and psychosis risk in ASD (9).

Researchers investigated dopamine (DA) neurotransmission in an autism spectrum disorder (ASD) mouse model with elevated expression of eukaryotic initiation factor 4E (eIF4E). Using an integrative approach that combined genetic manipulation, behavioral testing, synaptic physiology, and imaging techniques, they found that increased eIF4E expression leads to behavioral inflexibility and impaired striatal DA release. The impairment in DA signaling was linked to dysfunctional nicotinic acetylcholine receptor activity, which disrupts calcium dynamics in dopaminergic axons. These findings highlight a mechanistic pathway through which translational dysregulation affects DA neurotransmission and contributes to core behavioral symptoms of ASD (10).

Transgenic mice serve as valuable models for investigating the effects of autism spectrum disorder (ASD) risk genes on neuronal function, particularly within the dopamine system. Individuals with ASD may possess de novo missense mutations in the *SLC6A3* gene, which encodes the dopamine transporter, but such occurrences are few (11). Research on mouse models with ASD-associated mutations has shown compromised dopamine transmission in the striatum and modified social behaviors typical of ASD (12).

In a study of the effect of bee pollen and probiotics on the levels of some neuropeptides, including beta-endorphin, in an animal model of autism induced by giving it propionic acid, the results found that the level of beta-endorphin decreased significantly in the autism group compared to the control group (13).

Research on beta-endorphin values in Autism Spectrum Disorder (ASD) patients has yielded interesting results. One study published in the journal PLOS ONE found that plasma beta-endorphin levels were significantly higher in individuals with autism compared to controls. This study, which involved 73 children and adolescents with autism and 115 matched controls, also discovered that beta-endorphin levels were positively associated with autism severity and heart rate responses to pain (14).

Another study published in the European Neuropsychopharmacology journal found that beta-endorphin levels in peripheral blood mononuclear cells were higher in autistic children than in healthy controls. This study suggested that long-term naltrexone treatment may reduce beta-endorphin levels and improve symptoms in autistic children (15).

A study published in *The British Journal of Psychiatry* titled "Plasma Beta-Endorphin Concentrations in People with Learning Disability and Self-Injurious and/or Autistic Behaviour" measured plasma beta-endorphin levels in 33 individuals with intellectual disabilities who exhibited self-injurious and/or autistic behaviors. The results showed that individuals with severe self-injurious behavior had lower beta-endorphin levels compared to those with autistic behaviors but without severe self-injury. These findings support the hypothesis that severe self-injurious behavior may be linked to dysfunctions in the endogenous opioid system (16).

A study found that children with autism have lower plasma beta-endorphin levels compared to non-autistic children, suggesting a potential link between the endogenous opioid system and autism-related behaviors (17).

The study by Nagamitsu, (1994) investigates the levels of beta-endorphin in cerebrospinal fluid (CSF) in children with neurological disorders. The research focuses on the variation of beta-endorphin levels across different pediatric neurological conditions. It finds that there is a significant fluctuation in these levels, which might reflect the neurological and pain responses associated with various disorders. This study suggests that the measurement of beta-endorphin in CSF could provide valuable insights into the pathophysiology of neurological conditions in children, although the levels may either increase or decrease depending on the specific disorder (18).

In the study conducted by Tarnowska *et al.*, (2023) elevated levels of beta-endorphin are suggested as a potential factor in autism spectrum disorders (ASD), with some research showing higher concentrations in individuals with ASD. However, the evidence remains inconclusive, and additional research is required to verify the function of beta-endorphin in the development of ASD (19).

Conclusions:

Dopamine levels are significantly reduced in children with ASD. Beta-endorphin level showed no statistically significant changes. These biomarkers may offer insight into ASD mechanisms and potential therapeutic targets.

References

1. American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders: DSM-5™*, 5th ed. Arlington, VA: American Psychiatric Publishing, 2013. https://www.psychiatry.org/psychiatrists/practice/dsm
2. D. Pavăl, "A dopamine hypothesis of autism spectrum disorder," *Developmental Neuroscience*, vol. 39, no. 5, pp. 355–360, 2017. https://doi.org/10.1159/000478725
3. E. Bowton, C. Saunders, I. A. Reddy, N. G. Campbell, P. J. Hamilton, L. K. Henry *et al.*, "SLC6A3 coding variant Ala559Val found in two autism probands alters dopamine transporter function and trafficking," *Translational Psychiatry*, vol. 4, no. 10, pp. e464–e464, 2014. https://doi.org/10.1038/tp.2014.90
4. C. C. Clements, A. R. Zoltowski, L. D. Yankowitz, B. E. Yerys, R. T. Schultz, and J. D. Herrington, "Evaluation of the social motivation hypothesis of autism: a systematic review and meta-analysis," *JAMA Psychiatry*, vol. 75, no. 8, pp. 797–808, 2018. https://doi.org/10.1001/jamapsychiatry.2018.1100
5. S. Tordjman, P. A. McBride, M. E. Hertzig, M. E. Snow, G. M. Anderson, L. M. Hall *et al.*, "Plasma β-endorphin, adrenocorticotropin hormone, and cortisol in autism," *Journal of Child Psychology and Psychiatry*, vol. 38, no. 6, pp. 705–715, 1997. https://doi.org/10.1111/j.1469-7610.1997.tb01697.x
6. I. Roth-Deri, T. Green-Sadan, and G. Yadid, "β-Endorphin and drug-induced reward and reinforcement," *Progress in Neurobiology*, vol. 86, no. 1, pp. 1–21, 2008. https://doi.org/10.1016/j.pneurobio.2008.06.003
7. N. H. H. Hamdan, "Evaluation of the level of alkaline phosphatase, calcium, and vitamin D3 in patients with celiac disease," *Wasit Journal for Pure Sciences*, vol. 3, no. 3, pp. 192–196, 2024. https://doi.org/10.31185/wjps.445
8. Al-Zaidi, E. A., & Maleek, M. I. (2025). Levels of EPOR Protein and Gene Expression of SLC11A2, SLC40A1 in Children with Iron Deficiency Anemia. *International Journal of Environmental Sciences*, *11*(3s), 850-856. https://theaspd.com/index.php/ijes/article/view/344/315
9. R. Schalbroeck, F. H. van Velden, L. F. de Geus-Oei, M. Yaqub, T. van Amelsvoort, J. Booij, and J. P. Selten, "Striatal dopamine synthesis capacity in autism spectrum disorder and its

relation with social defeat: an [18F]-FDOPA PET/CT study," *Translational Psychiatry*, vol. 11, no. 1, p. 47, 2021. https://doi.org/10.1038/s41398-020-01174-w

10. J. Carbonell-Roig, A. Aaltonen, K. Wilson, M. Molinari, V. Cartocci, A. McGuirt *et al.*, "Dysregulated acetylcholine-mediated dopamine neurotransmission in the eIF4E Tg mouse model of autism spectrum disorders," *Cell Reports*, vol. 43, no. 12, 2024. https://doi.org/10.1016/j.celrep.2024.114997
11. P. J. Hamilton, N. G. Campbell, S. Sharma, K. Erreger, F. H. Hansen, C. Saunders *et al.*, "De novo mutation in the dopamine transporter gene associates dopamine dysfunction with autism spectrum disorder," *Molecular Psychiatry*, vol. 18, no. 12, pp. 1315–1323, 2013. https://doi.org/10.1038/mp.2013.102
12. G. E. DiCarlo, J. I. Aguilar, H. J. Matthies, F. E. Harrison, K. E. Bundschuh, A. West *et al.*, "Autism-linked dopamine transporter mutation alters striatal dopamine neurotransmission and dopamine-dependent behaviors," *The Journal of Clinical Investigation*, vol. 129, no. 8, pp. 3407–3419, 2020. https://doi.org/10.1172/JCI127411
13. M. A. Alghamdi, L. Al-Ayadhi, W. M. Hassan, R. S. Bhat, M. A. Alonazi, and A. El-Ansary, "Bee pollen and probiotics may alter brain neuropeptide levels in a rodent model of autism spectrum disorders," *Metabolites*, vol. 12, no. 6, p. 562, 2022. https://doi.org/10.3390/metabo12060562
14. S. Tordjman, G. M. Anderson, M. Botbol, S. Brailly-Tabard, F. Perez-Diaz, R. Graignic *et al.*, "Pain reactivity and plasma β-endorphin in children and adolescents with autistic disorder," *PloS One*, vol. 4, no. 8, p. e5289, 2009. https://doi.org/10.1371/journal.pone.0005289
15. A. G. Cazzullo, M. C. Musetti, L. Musetti, S. Bajo, P. Sacerdote, and A. Panerai, "β-Endorphin levels in peripheral blood mononuclear cells and long-term naltrexone treatment in autistic children," *European Neuropsychopharmacology*, vol. 9, no. 4, pp. 361–366, 1999. https://doi.org/10.1016/S0924-977X(99)00010-3
16. S. H. Willemsen-Swinkels, J. K. Buitelaar, F. G. Weijnen, J. H. Thijssen, and H. Van Engeland, "Plasma beta-endorphin concentrations in people with learning disability and self-injurious and/or autistic behaviour," *The British Journal of Psychiatry*, vol. 168, no. 1, pp. 105–109, 1996. https://doi.org/10.1192/bjp.168.1.105
17. R. Weizman, I. Gil-ad, J. Dick, S. Tyano, G. A. Szekely, and Z. Laron, "Low plasma immunoreactive β-endorphin levels in autism," *Journal of the American Academy of Child & Adolescent Psychiatry*, vol. 27, no. 4, pp. 430–433, 1988. https://doi.org/10.1097/00004583-198807000-00009
18. S. Nagamitsu, "CSF beta-endorphin levels in pediatric neurologic disorders," *The Kurume Medical Journal*, vol. 40, no. 4, pp. 233–241, 1994. https://doi.org/10.2739/kurumemedj.40.233
19. K. Tarnowska, E. Gruczyńska–Sękowska, D. Kowalska, E. Majewska, M. Kozłowska, and R. Winkler, "The opioid excess theory in autism spectrum disorders - is it worth investigating further?," *Critical Reviews in Food Science and Nutrition*, vol. 63, no. 19, pp. 3980–3993, 2023. https://doi.org/10.1080/10408398.2021.1996329