http://mnj.ub.ac.id/
DOI: 10.21776/ub.mnj.2025.011.01.07
eISSN: 2442-5001 **pISSN:** 2407-6724
Accredited by DIKTIRISTEK Decree No: 152/E/KPT/2023

MALANG NEUROLOGY JOURNAL MNJ

RESEARCH ARTICLE OPEN ACCESS

THE ASSESSMENT OF SERUM ADROPIN AND CATALASE LEVELS IN PATIENTS WITH ALZHEIMER'S DISEASE

Fatma Şimşek[1], Yunus Emre Aktaş[2], Ömer Lütfi Gündoğdu[3], Ahmet Kızıltunç[4]

Correspondence: *klamaks@hotmail.com*
[1]*Department of Neurology, Faculty of Medicine, Ataturk University Erzurum, Turkey.*
[2] *Department of Neurology, Erzurum Training and Research Hospital, Erzurum, Turkey.*
[3] *Department of Neurology, Faculty of Medicine, Recep Tayyip Erdogan University, Rize/Turkey.*
[4] *Department of Biochemistry, Faculty of Medicine, Ataturk University, Erzurum, Turkey.*

Article History:
Received: May 23, 2024
Accepted: December 16, 2024
Published: Jnauary 31, 2025

Cite this as:
Şimşek F, Aktaş YE, Gündoğdu OL, Kızıltunç A. The assessment of serum adropin and catalase levels in patients with alzheimer's disease. Malang Neurology Journal; 2025.11:32-38. DOI: http://dx.doi.org/10.21776/ub.mnj .2025.011.01.07

ABSTRACT

Background: Dementia is a disease that renders performing activities of daily living difficult and has a high cost of treatment.
Objective: In this context, this study was conducted to assess the adropin and catalase levels, the relationship between adropin and catalase levels, and the roles of adropin and catalase in treatment in patients diagnosed with Alzheimer's type dementia.
Methods: This observational analytical study's sample consisted of 30 patients with Alzheimer's disease (AD). Thirty individuals without dementia whose age and gender characteristics matched those with AD were included in the control group. The adropin and catalase levels in the serum samples collected from both patient and control groups were analyzed.
Results: Adropin and low-density lipoprotein cholesterol (LDLC) levels were notably elevated in patients with Alzheimer's disease (AD). In contrast, levels of vitamin D, albumin, and catalase were significantly reduced in these patients. Additionally, there was no meaningful correlation between the mini-mental state examination (MMSE) scores and the results of laboratory tests in individuals with AD. Additionally, it was determined that MMSE scores were positively correlated with adropin levels and negatively correlated with catalase levels. However, both correlations were statistically insignificant.
Conclusion: The low levels of catalase in patients with AD support the important role of oxidative stress in the disease. The high levels of adropin in these patients suggest that adropin acts as a defense mechanism for the body. Catalase and adropin can be used as biomarkers in the diagnosis of AD, but they are not suitable biomarkers for assessing cognitive functions.

Keywords: Alzheimer's disease, dementia, catalase, adropin

Introduction

Cognitive abilities typically decline with age. Mild cognitive impairment describes a situation where individuals experience noticeable difficulties in organizing and recalling daily tasks, yet these challenges are not severe enough to prevent them from acting independently.[1,2] In contrast, dementia is a syndrome marked by a progressive decline in two or more cognitive areas, leading to a loss of the ability to carry out everyday activities. Age is a significant risk factor for dementia, and as the population ages, the prevalence of this condition continues to rise. About 40% of Alzheimer's disease (AD) patients have modifiable risk factors, including low levels of education, hypertension, obesity, diabetes, hearing loss, depression, reduced physical activity, and social isolation.[3] Alzheimer's disease is the leading form of dementia, accounting for an impressive 80% of all cases.[4]

Adropin is a peptide produced by the energy homeostasis-associated (Enho) gene, which is predominantly found in the brain.[5-7] Research has indicated a correlation between Enho gene expression and genes linked to neurodegenerative disorders in both humans and animals.[6,7] Additionally, studies have revealed that the levels of adropin in plasma and its protein expression decline with age in the brains of rats, implying a connection between oxidative stress and the expression of certain protein markers.[8]

It is widely believed that oxidative stress plays an important role in the aging process. In parallel, oxidative stress has been implicated in the development of many metabolic diseases and neurodegenerative diseases such as AD. Our body has an antioxidant defense system against oxidative stress. This defense system is made up of various enzymes, proteins, and low-weight molecules. Catalase is one of the enzymes involved in this defense system. Many enzymes can neutralize hydrogen peroxide, with catalase being the most important. Catalase is an enzyme that breaks down hydrogen peroxide into water and oxygen molecules.[9,10]

It is important to detect the changes that occur in the brain structure with aging in patients with dementia and to

develop new treatment strategies targeting these changes. There is a need for novel medications that are effective in the treatment of dementia in order to reduce the economic burden for both the patient and the caregiver. In this context, this study was carried out to assess the adropin and catalase levels, the relationship between adropin and catalase levels, and the roles of adropin and catalase in treatment in patients diagnosed with Alzheimer's type dementia.

Methods

Research Design

This research was structured as an observational analytical study. The study protocol received approval from our university's ethics committee (07/42/29.09.2022). All participants gave their informed consent prior to participating in the study.

Population and Sample

The study's population comprised a series of consecutive patients who presented to the Atatürk University Neurology Department with dementia of the Alzheimer type between November 2022 and April 2023. Thirty age-sex-matched volunteers with Alzheimer's type and 30 without dementia, who applied to our clinic consecutively and met the following criteria, participated in the study.

The criteria for including participants in the study were set at a minimum age of 60 years, having received a diagnosis of AD confirmed by two experienced neurologists based on clinical and neuroimaging assessment according to the diagnostic guidelines set by the National Institute on Aging and the Alzheimer's Association (NIA-AA), and having volunteered to participate in the study and signed the informed consent form.[11]

The study exclusion criteria were determined as being under 60 years old, having a history of head trauma, malignancy, mental retardation, psychiatric disease affecting cognitive functions, chronic neurological disease, including Parkinson's disease, epilepsy, multiple sclerosis, and ischemic-hemorrhagic stroke history, liver, kidney, and thyroid dysfunctions, a history of inflammatory disease in the last 1 month, diabetes mellitus, severe heart and lung disease, connective tissue disease, having been using anti-inflammatory medications, and not having volunteered to participate in the study.

Ultimately, the study included 30 patients with Alzheimer's disease as the patient group, and 30 individuals without dementia whose age and gender characteristics matched those with AD were included in the study as the control group.

Data Collection

Blood samples were drawn from the arm's antecubital area. after a 10-hour overnight fast and analyzed by the same experienced biochemist from the patient and control groups. Serum samples were centrifuged and placed in an Eppendorf tube and stored at -80 °C until a sufficient number of samples were collected for the study.

Biochemical analyses

Adropin levels were assessed using an enzyme-linked immunosorbent assay (ELISA) kit (SunRed Human AD ELISA kit, LOT: 202207, Cat. No: 201-12-3107).

Catalase activity was measured using the method of Beers et al.[12] The method is based on the steady increase in absorption by H_2O_2 in the ultraviolet range with decreasing wavelength. The absorbance difference (ΔA 240) is a measure of catalase activity per unit time. Accordingly, the decrease in absorption at 240 nm due to H_2O_2 consumption was measured.

The patients with AD and control subjects were asked to complete the mini-mental state examination (MMSE) with the help of two neurologists with comparable experience. Consequently, patients with AD scored 24 points or less on the MMSE, while control subjects scored 30 points. Participants' height (cm) and weight (kg) data, body mass index [BMI (kg/m^2)] values, educational levels, nighttime sleep durations (≤6 or >6 hours), smoking and alcohol use statuses (never, current, or old smoker or alcohol consumer), high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDLC), fasting blood glucose, insulin, vitamin D, C-reactive protein (CRP), and albumin levels were recorded.

Statistical Analysis

The analysis of the collected data was performed using SPSS version 20.0 software (Statistical Product and Service Solutions for Windows, IBM Corp., Armonk, NY, U.S., 2011). The Shapiro-Wilk test was utilized to assess whether the variables followed a normal distribution. Descriptive statistics for the data were reported as means with standard deviations for normally distributed continuous variables, while medians along with minimum and maximum values were used for those that did not follow a normal distribution. Categorical variables were expressed as counts and percentages. For the analysis, Student's t-test was used for variables exhibiting normal distribution, while the Mann-Whitney U test applied to those lacking normal distribution. Pearson's chi-squared test was employed for categorical variable analysis, and the a Spearman correlation analysis was conducted to evaluate the relationship between two numerical variables. that did not meet normal distribution assumptions. A probability value *(p)* of less than 0.05 was considered statistically significant.

Results

The mean ages of the patient and control groups were 70.77±3.49 years and 69.77±2.45 years, respectively, showing no statistically significant difference in age between the two groups (p=0.205). Demographic and clinical characteristics, along with laboratory parameters for both groups, are detailed in Table 1. The levels of adropin and LDLC were notably higher in the patient group compared to the control group, while the levels of vitamin D, albumin, and catalase were significantly lower (p=0.001, p=0.012, p<0.001, p<0.001, and p<0.001, respectively). Figures 1 and 2 display the distribution of adropin and catalase levels among both the patient and control groups. There was no significant difference in adropin levels based on gender in either the patient or control groups (p=0.949 and p=0.525, respectively).

Table 1. Demographic, clinical, and laboratory data from both the patient and control groups.

Variables	Patient (n=30)	Control (n=30)	p
Age (year)	70.77±3.49	69.77±2.45	0.205[a]
Gender, n(%)			
Female	18(60)	18(60)	1
Male	12(40)	12(40)	1
Laboratory findings			
HDL-cholesterol (mg/dL)	49.97±12.75	46.20±10.86	0.223[*]
LDL-cholesterol (mg/dL)	138.90±41.35	113.80±33.21	**0.012**[*]
Vitamin D (ng/mL)	15.75±5.35	27.83±8.38	**<0.001**[*]
CRP (mg/L)	3.70(0.40-11.7)	2.70(0.20-9.80)	0.437[**]
Glucose (mg/dL)	88(74-180)	92(80-114)	0.437[**]
Insulin	6.10 (1.89-52)	8.35 (2.30-30.70)	0.209[**]
Albumin (g/dL)	3.80(2.80-4.40)	4.45(3.80-4.90)	**<0.001**[**]
Catalase (U/mL)	61.60(25.60-81.30)	125.30(67.30-194.10)	**<0.001**[**]
Adropin (pg/mL)	94.57(63.42-219.19)	76.51(21.68-116.88)	**0.001**[**]
BMI (kg/m^2)	28(22-35,6)	27(23-35)	0.847[**]
MMSE	19.50(11-25)	30	**<0.001**[**]
Smoking status, n (%)			
Never	22 (36.7)	15 (25)	
Current	0 (0)	4 (6.7)	0.06[***]
Former	8 (13.3)	11 (18.3)	
Cardiovasculer disease	15 (25)	16 (26.7)	1[***]
Hyperlypidemia, n(%)	13 (21.7)	7 (11.7)	0.171[***]
Drug			
Donepezil+memantine	7 (11.7)	-	
Ginkgo Biloba	2 (3.3)	-	**0.005**[***]
Drug-free	21 (35)	30 (50)	
Sleep duration, n(%)			
≤6 hour	15(25)	3(5)	**0.002**[***]
>6 hour	15(25)	27(45)	

Table 2. Correlation between MMSE and other parameters in dementia patients

Variables	MMSE	
	rho	p
Adropin	0.741	0.063
Catalase	-0.275	0.142
BMI	0.078	0.683
HDL-cholestrol	-0.046	0.809
LDL-cholestrol	0.039	0.837
Vitamin D	0.047	0.806
Glucose	0.005	0.978
Insulin	0.152	0.245
Albumin	0.146	0.440
CRP	0.205	0.277

HDL= High-density lipoprotein; LDL= Low-density lipoprotein; BMI= Body mass index; MMSE=Mini-mental state examination; CRP=C-reactive protein

Furthermore, no significant difference was found in adropin levels between Alzheimer's disease patients on disease-specific medication (n=9) and those who were not using any (n=21). There was also no significant correlation between MMSE scores and laboratory parameters in the AD patients (Table 2).

Additionally, a positive correlation was found between MMSE scores and adropin levels, while a negative correlation was observed with catalase levels. However, both correlations were statistically insignificant. There was no participant with alcohol use. There was no notable correlation between smoking status and Alzheimer's disease (AD) with a p-value of 0.06. Additionally, BMI values did not show a significant relationship with adropin levels (p=0.116, rho=0.205) or catalase levels (p=0.573, rho=0.074). Furthermore, when comparing adropin levels between AD patients and the control group based on sleep duration, there were no significant differences observed (p=0.548 and p=0.972, respectively). However, adropin level was significantly higher in those with ≤6 hours of sleep compared to those with >6 hours of sleep in the overall study group (p=0.047). There was also no significant relationship between adropin level and other laboratory parameters in patients with AD (Table 3).

Discussion

The results of this research indicated that patients with Alzheimer's disease (AD) had notably lower catalase levels and significantly higher adropin levels compared to control subjects. Additionally, there was no significant correlation found between MMSE scores and the levels of adropin and catalase in individuals with AD. The Enho gene, which encodes adropin, is linked to energy balance and fat metabolism. Research has also shown that blood adropin levels are reduced in individuals with obesity compared to those without.[13,14]

Other studies demonstrated a positive or insignificant relationship between obesity and adropin levels.[15–17] In sum, the relationship between adropin levels and obesity is not clear. It is known that AD patients have problems with appetite and eating, and these cause weight changes and metabolic problems in patients.[18,19] Therefore, it is possible that adipocytokines play a role in the pathogenesis of

neurodegenerative diseases that cause metabolic disorders such as dementia and AD.

Table 3. Correlation between age and other laboratory parameters of adropin in dementia patients

		Catalase	HDL	LDL	VitaminD	Insulin	Glucose	CRP	Albumin	Age
Adropin	**rho**	0.046	0	-0.095	-0.127	0.232	-0.042	0.215	0.131	0.126
	p	0.810	1	0.617	0.502	0.217	0.826	0.254	0.489	0.507

HDL= High-density lipoprotein; LDL= Low-density lipoprotein; CRP=C-reactive protein

In this study, there was a positive but insignificant relationship between BMI and adropin level. A study demonstrated a clear observational relationship between low BMI value and the risk of developing AD but did not find any relationship between genetically determined BMI and AD risk.[20] This finding may be attributed to the decrease in BMI in the advanced stages of AD. In this study, the fact that the albumin levels were significantly lower in patients with AD compared to control subjects seems to be due to the decrease in BMI in the prodromal stages of AD. Studies did not find any significant relationship between AD and LDLC.[21,22] In comparison, in this study, LDLC levels are significantly higher in patients with AD compared to control subjects; however, there is no significant relationship between LDLC and adropin levels.

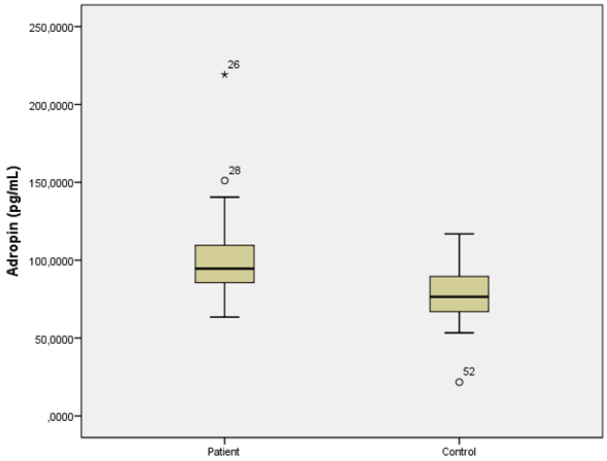


Figure 1. The distribution of adropin levels among participants in both the patient and control groups is given.

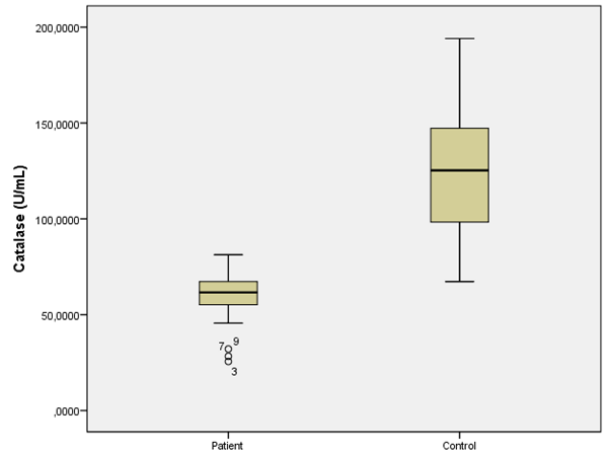


Figure 2. The distribution of catalase levels among participants in both the patient and control groups is given.

Sleep disorder is common in patients with AD. Sleep is an important factor in consolidating memory.[23] It has been speculated that sleep disorder provokes AD and AD provokes sleep disorder. There are studies indicate that sleep disorders may elevate the risk of Alzheimer's disease (AD) by increasing the accumulation of amyloid beta.[24] The key characteristics of Alzheimer's disease consist of extracellular amyloid beta plaques, intracellular neurofibrillary tangles comprised of hyperphosphorylated tau protein, and the degeneration of synapses and neurons.[25] In AD, the clearance of amyloid beta is compromised due to a reduced capacity of microglia to phagocytize, which stems from elevated cytokine levels and decreased expression of amyloid beta phagocytosis receptors.[26] Additionally, amyloid beta aggregates interact with receptors on microglial cells, triggering inflammatory activation that leads to the release of proinflammatory cytokines, such as tumor necrosis factor alpha (TNF-α) and interleukin (IL) 1β.[26] Cytokines like IL-1, IL-6, and TNF are involved in initiating a rapid immune response and also contribute to inflammatory changes.[27] In a study conducted with patients with obstructive sleep apnea, a disease in which inflammatory processes play a role, it was shown that adropin, IL-1 and TNF-α levels increase in proportion to the severity of the sleep disorder.[28] Another study showed that adropin levels decreased and proinflammatory cytokines increased in correlation with the severity of obstructive sleep apnea.[29] The relationship between sleep and adropin levels remains unclear. This study found that adropin levels were significantly higher in individuals who slept for six hours or less. These results support the existence of a relationship between adropin levels and sleep. However, the answer to the question of whether it is the sleep duration that affects adropin levels or other causes in the etiology of sleep disorders is not clear. Sleep apnea syndrome was not questioned in the patients included in the study; only the sleep duration was considered. This may have affected our study results. The lack of a positive but significant relationship between MMSE score and adropin level in this study suggests that adropin is not very effective in cognition. In a study conducted in rats with myocardial infarction, it was shown that increased adropin expression in the cardiac organ could create a compensatory response by maintaining glucose homeostasis and glycogen storage.[30] In an experimental study with mice, adropin was shown to support brain function during aging.[31] In this study, the positive correlation between adropin expression and protein markers of tau pathology supports our findings.[31] Recent studies indicate that adropin affects the cerebral vasculature, helping to preserve neurological functions during cerebral ischemia.[32,33] Considering the results of other studies, the high adropin level in patients with AD in our study was considered as a protective mechanism, like the body's defense mechanism.

Oxidative stress is implicated in various metabolic and neurodegenerative disorders. There is a connection between oxidative stress, aging, and neurodegenerative diseases. Our body has mechanisms to defend against oxidative stress, and catalase—an important antioxidant enzyme—plays a crucial role in inhibiting apoptosis linked to oxidative stress and inflammation.[34,35] Research indicates that in Alzheimer's disease (AD), there is an increase in amyloid beta levels. An experimental study demonstrated that

amyloid beta can directly interact with catalase, leading to reduced enzyme activity and elevated hydrogen peroxide levels in neuroblastoma cell cultures.[36] This heightened amyloid beta presence in AD can ultimately result in cellular toxicity. In our investigation, we found that catalase levels were significantly lower in patients with AD, which is consistent with these findings. Additionally, another experimental study observed an increase in catalase levels after treatment with adropin in animals suffering from Parkinson's disease and ulcers, suggesting that adropin has neuroprotective and gastroprotective benefits.[37] Furthermore, research has indicated that adropin enhances the expression of nuclear factor erythroid 2 (Nrf2).[38] Nrf2 has a protective effect on cells against oxidative stress.[39] In the study conducted by Demirdöğen et al. on multiple sclerosis patients, adropin levels were found to be low and no correlation was found between adropin levels and hypothalamic atrophy.[40] All of these studies support a strong relationship between oxidative stress and adropin. However, the fact that adropin levels increase in some neurodegenerative diseases and decrease in others suggests that different mechanisms are effective.

Vitamins are important organic substances that support basic cellular functions. However, given that they are synthesized at a low rate in the human body, they must be taken regularly with the diet. Many studies have investigated the effect of vitamins on cognitive functions.[41,42] There are studies showing that vitamin D supplementation causes improvement in MMSE scores and cognitive functions [43]. This study found that vitamin D levels were significantly lower in patients with Alzheimer's disease (AD) compared to control subjects. Additionally, there was a positive correlation—though not statistically significant—between vitamin D levels and the Mini-Mental State Examination (MMSE) scores. These findings suggest that vitamin D supplementation may be important for supporting cognitive functions.

Limitations of the Study

Our study has definitive limitations, such as the inclusion of patients with a history of cardiovascular issues and the absence of cerebrospinal fluid measurements. These factors may impact the robustness of our findings. There is limited information regarding adropin's ability to penetrate the blood-brain barrier. It is believed that adropin has difficulty moving from the bloodstream into the central nervous system because of its lipophilic nature and size. As a result, it is likely that the effects observed in the brain originate from adropin produced locally. Thus, not measuring spinal fluid was not considered to affect our findings.

Conclusion

The finding that catalase levels were notably reduced in Alzheimer's disease (AD) patients compared to control subjects highlights the significant influence of oxidative stress in AD. Conversely, the discovery that adropin levels were considerably elevated in AD patients indicates that adropin may serve as a protective mechanism within the body. In addition, the fact that adropin levels are significantly higher in those with more pronounced sleep disorders suggests that sleep is effective in adropin release. The lack of a meaningful positive correlation between MMSE scores and adropin levels indicates that adropin might not be a viable treatment option for Alzheimer's disease. Nevertheless, further large-scale research is necessary to substantiate the conclusions of this study. Considering that adropin is a peptide secreted from many organs, it is likely that selecting more specific patient groups will contribute to obtaining more meaningful results when selecting patients in future studies.

Acknowledgement

Our manuscript is not supported by any sponsoring agency or person.

Conflict of Interest

There is neither an actual nor a possible conflict of interest with the organization funding the research.

References

1. Petersen RC. Mild cognitive impairment as a diagnostic entity. J Intern Med; 2004. 256(3):183-194. DOI: 10.1111/J.1365-2796.2004.01388.X
2. Bennett DA, Wilson RS, Schneider JA, et al. Natural history of mild cognitive impairment in older persons. Neurology; 2002. 59(2):198-205. DOI: 10.1212/WNL.59.2.198
3. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet; 2020. 396(10248):413-446. DOI: 10.1016/S0140-6736(20)30367-6/ATTACHMENT/CEE43A30-904B-4A45-A4E5-AFE48804398D/MMC1.PDF
4. Crous-Bou M, Minguillón C, Gramunt N, Molinuevo JL. Alzheimer's disease prevention: From risk factors to early intervention. Alzheimer's Res Ther; 2017. 9(1):1-9. DOI: 10.1186/S13195-017-0297-Z/TABLES/2
5. Wong CM, Wang Y, Lee JTH, et al. Adropin is a brain membrane-bound protein regulating physical activity via the NB-3/notch signaling pathway in mice. J Biol Chem; 2014. 289(37):25976-25986. DOI: 10.1074/jbc.M114.576058
6. Butler AA, Zhang J, Price CA, et al. Low plasma adropin concentrations increase risks of weight gain and metabolic dysregulation in response to a high-sugar diet in male nonhuman primates. J Biol Chem; 2019. 294(25):9706-9719. DOI:10.1074/JBC.RA119.007528/ATTACHMENT/ADD6A30F-CAEB-4F79-B614-523DE43BD9E8/MMC1.PDF
7. Banerjee S, Ghoshal S, Girardet C, et al. Adropin correlates with aging-related neuropathology in humans and improves cognitive function in aging mice. npj Aging Mech Dis; 2021. 7(1):1-17. DOI: 10.1038/s41514-021-00076-5
8. Yang C, DeMars KM, Candelario-Jalil E. Age-Dependent Decrease in Adropin is Associated with Reduced Levels of Endothelial Nitric Oxide Synthase and Increased Oxidative Stress in the Rat Brain. Aging Dis; 2018. 9(2):322-330. DOI: 10.14336/AD.2017.0523

9. Deisseroth A, Dounce AL. Catalase: Physical and chemical properties, mechanism of catalysis, and physiological role; 1970. 50(3):319-375. DOI: 10.1152/PHYSREV.1970.50.3.319
10. von Ossowski I, Hausner G, Loewen PC. Molecular evolutionary analysis based on the amino acid sequence of catalase. J Mol Evol; 1993. 37(1):71-76. DOI: 10.1007/BF00170464/METRICS
11. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement; 2011. 7(3):263-269. DOI: 10.1016/J.JALZ.2011.03.005
12. BEERS RF, SIZER IW. A spectrophotometric method for measuring the breakdown of hydrogen peroxide by catalase. J Biol Chem; 1952. 195(1):133-140. DOI: 10.1016/s0021-9258(19)50881-x
13. Soltani S, Kolahdouz-Mohammadi R, Aydin S, Yosaee S, Clark CCT, Abdollahi S. Circulating levels of adropin and overweight/obesity: a systematic review and meta-analysis of observational studies. Hormones; 2022. 21(1):15-22. DOI: 10.1007/S42000-021-00331-0/TABLES/3
14. Thapa D, Xie B, Manning JR, et al. Adropin reduces blood glucose levels in mice by limiting hepatic glucose production. Physiol Rep; 2019. 7(8):e14043. DOI: 10.14814/PHY2.14043
15. Inal ZO, Erdem S, Gederet Y, et al. The impact of serum adropin and ischemia modified albumin levels based on BMI in PCOS. Endokrynol Pol; 2018. 69(2):135-141. DOI: 10.5603/EP.A2018.0002
16. Topuz M, Celik A, Aslantas T, Demir AK, Aydin S, Aydin S. Plasma Adropin Levels Predict Endothelial Dysfunction like Flow-Mediated Dilatation in Patients with type 2 Diabetes Mellitus; 2013. 61(8):1161-1164. DOI: 10.2310/JIM.0000000000000003
17. Bousmpoula A, Kouskouni E, Benidis E, et al. Adropin levels in women with polycystic ovaries undergoing ovarian stimulation: correlation with lipoprotein lipid profiles; 2017. 34(2):153-156. DOI: 10.1080/09513590.2017.1379498
18. Luchsinger JA, Gustafson DR. Adiposity and Alzheimer's disease. Curr Opin Clin Nutr Metab Care; 2009. 12(1):15-21. DOI: 10.1097/MCO.0B013E32831C8C71
19. Aziz NA, Van Der Marck MA, Pijl H, Olde Rikkert MGM, Bloem BR, Roos RAC. Weight loss in neurodegenerative disorders. J Neurol; 2008. 255(12):1872-1880. DOI: 10.1007/S00415-009-0062-8/METRICS
20. Nordestgaard LT, Tybjærg-Hansen A, Nordestgaard BG, Frikke-Schmidt R. Body Mass Index and Risk of Alzheimer's Disease: A Mendelian Randomization Study of 399,536 Individuals. J Clin Endocrinol Metab; 2017. 102(7):2310-2320. DOI: 10.1210/JC.2017-00195
21. Reitz C, Tang MX, Luchsinger J, Mayeux R. Relation of Plasma Lipids to Alzheimer Disease and Vascular Dementia. Arch Neurol; 2004. 61(5):705-714. DOI: 10.1001/ARCHNEUR.61.5.705
22. Launer LJ, White LR, Petrovitch H, Ross GW, Curb JD. Cholesterol and neuropathologic markers of AD. Neurology; 2001. 57(8):1447-1452. DOI: 10.1212/WNL.57.8.1447
23. Westermann J, Lange T, Textor J, Born J. System Consolidation During Sleep – A Common Principle Underlying Psychological and Immunological Memory Formation. Trends Neurosci; 2015. 38(10):585-597. DOI: 10.1016/J.TINS.2015.07.007
24. Mander BA, Winer JR, Jagust WJ, Walker MP. Sleep: A Novel Mechanistic Pathway, Biomarker, and Treatment Target in the Pathology of Alzheimer's Disease? Trends Neurosci; 2016. 39(8):552-566. DOI: 10.1016/J.TINS.2016.05.002
25. Lin L, Zheng LJ, Zhang LJ. Neuroinflammation, Gut Microbiome, and Alzheimer's Disease. Mol Neurobiol; 2018. 55(11):8243-8250. DOI: 10.1007/S12035-018-0983-2/METRICS
26. Heneka MT, Carson MJ, Khoury J El, et al. Neuroinflammation in Alzheimer's disease. Lancet Neurol; 2015. 14(4):388-405. DOI: 10.1016/S1474-4422(15)70016-5
27. Mantovani A, Dinarello CA, Molgora M, Garlanda C. IL-1 and related cytokines in innate and adaptive immunity in health and disease. Immunity; 2019. 50(4):778. DOI: 10.1016/J.IMMUNI.2019.03.012
28. Celikhisar H, Ilkhan GD. Alterations in Serum Adropin, Adiponectin, and Proinflammatory Cytokine Levels in OSAS. Can Respir J; 2020. 2020:2571283. DOI: 10.1155/2020/2571283
29. Kong Z, Liu Y. Soluble Vascular Adhesion Protein-1 Level Correlates With Adropin and Inflammatory Biomarkers in Patients With Obstructive Sleep Apnea. Ear, Nose Throat J; Published online March 9, 2022. DOI: 10.1177/01455613221074147/ASSET/IMAGES/LARGE/10.1177_01455613221074147-FIG3.JPEG
30. Aydin S, Aydin S, Kuloglu T, et al. Elevated adropin: A candidate diagnostic marker for myocardial infarction in conjunction with troponin-I. Peptides; 2014. 58:91-97. DOI: 10.1016/J.PEPTIDES.2014.06.001
31. Banerjee S, Ghoshal S, Girardet C, et al. Adropin correlates with aging-related neuropathology in humans and improves cognitive function in aging mice. npj Aging Mech Dis 2021 71; 2021. 7(1):1-17. DOI: 10.1038/s41514-021-00076-5
32. Yang C, Lavayen BP, Liu L, et al. Neurovascular protection by adropin in experimental ischemic stroke through an endothelial nitric oxide synthase-dependent mechanism. Redox Biol; 2021. 48:102197. DOI: 10.1016/J.REDOX.2021.102197
33. Yang C, Liu L, Lavayen BP, et al. Therapeutic Benefits of Adropin in Aged Mice After Transient Ischemic Stroke via Reduction of Blood-Brain Barrier Damage. Stroke; 2023. 54(1):234-244. DOI: 10.1161/STROKEAHA.122.039628
34. Islam KN, Kayanoki Y, Kaneto H, et al. TGF-β1 Triggers Oxidative Modifications and Enhances Apoptosis in Hit Cells Through Accumulation of Reactive Oxygen Species by Suppression of Catalase and Glutathione Peroxidase. Free Radic Biol Med;

1997. 22(6):1007-1017. DOI: 10.1016/S0891-5849(96)00493-5
35. Yabuki M, Kariya S, Ishisaka R, et al. Resistance to nitric oxide-mediated apoptosis in HL-60 variant cells is associated with increased activities of Cu,Zn-superoxide dismutase and catalase. Free Radic Biol Med; 1999. 26(3-4):325-332. DOI: 10.1016/S0891-5849(98)00203-2
36. Habib LK, Lee MTC, Yang J. Inhibitors of catalase-amyloid interactions protect cells from β-amyloid-induced oxidative stress and toxicity. J Biol Chem; 2010. 285(50):38933-38943. DOI: 10.1074/JBC.M110.132860/ATTACHMENT/76EDBCCA-1D8A-416E-9534-51D825029B29/MMC1.PDF
37. Abo El Gheit RE, Atef MM, El Deeb OS, et al. Unique novel role of adropin in a gastric ulcer in a rotenone-induced rat model of Parkinson's disease. ACS Chem Neurosci; 2020. 11(19):3077-3088. DOI: 10.1021/ACSCHEMNEURO.0C00424/ASSET/IMAGES/LARGE/CN0C00424_0005.JPEG
38. Chen X, Xue H, Fang W, et al. Adropin protects against liver injury in nonalcoholic steatohepatitis via the Nrf2 mediated antioxidant capacity. Redox Biol; 2019. 21:101068. DOI: 10.1016/J.REDOX.2018.101068
39. Gupte AA, Lyon CJ, Hsueh WA. Nuclear factor (erythroid-derived 2)-like-2 factor (Nrf2), a key regulator of the antioxidant response to protect against atherosclerosis and nonalcoholic steatohepatitis. Curr Diab Rep; 2013. 13(3):362-371. DOI: 10.1007/S11892-013-0372-1/FIGURES/1
40. DEMİRDÖĞEN F, AKDAĞ T, GÜNDÜZ ZB, ODABAŞ FÖ. Investigation of serum adropin levels and its relationship with hypothalamic atrophy in patients with multiple sclerosis. Mult Scler Relat Disord; 2022. 66:103948. DOI: 10.1016/J.MSARD.2022.103948
41. Forbes SC, Holroyd-Leduc JM, Poulin PhD MJ, Hogan DB. Effect of Nutrients, Dietary Supplements and Vitamins on Cognition: a Systematic Review and Meta-Analysis of Randomized Controlled Trials. Can Geriatr J; 2015. 18(4):231. DOI: 10.5770/CGJ.18.189
42. Suh SW, Kim HS, Han JH, et al. Efficacy of Vitamins on Cognitive Function of Non-Demented People: A Systematic Review and Meta-Analysis. Nutr; 2020. 12(4):1168. DOI: 10.3390/NU12041168
43. Annweiler C, Fantino B, Gautier J, Beaudenon M, Thiery S, Beauchet O. Cognitive Effects of Vitamin D Supplementation in Older Outpatients Visiting a Memory Clinic: A Pre–Post Study. J Am Geriatr Soc; 2012. 60(4):793-795. DOI: 10.1111/J.1532-5415.2011.03877.X