Hu Y, J Forensic Leg Investig Sci 2023, 9: 077
DOI: 10.24966/FLIS-733X/100077

HSOA Journal of Forensic, Legal & Investigative Sciences

Research Article

The Association between Homocysteine Level and Balance Disorder among US Adults Varied In Different Sex Groups: A Cross-Sectional Study

Yang Hu[1], Duo Lin[2], Min Song[1], Dongmei Wu[1], Yuqing Zhang[1], Gongbo Li[1]* and Haiyan Luo[1]*

[1]Department of Neurology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

[2]Department of Neurology, Zhongshan Hospital of Traditional Chinese Medicine, Guangdong, China

Abstract

Background: High levels of homocysteine (Hcy) are associated with the occurrence of nervous system disorders. However, the relationship between Hcy and Balance Disorder has not been adequately studied. The aim of this study was to evaluate sex differences between them among US adults older than 40 years.

Method: We conducted a cross-sectional analysis of data from 1999-2004 National Health and Nutrition Examination Survey (NHANES). The study employs logistic regression models and interaction test.

Result: Of the 4,631 individuals (48.54% male), 1873 had Balance Disorder. Fully adjusted multivariate logistic regression models showed that for every 1 μmol/L increase in logarithm-transformed Hcy, the risk of Balance Disorder increased by 68%(OR=1.68, 95%CI: 1.19-2.37, p < 0.001). Subgroup analysis revealed the relationship between Hcy and balance disorders differs significantly by sex (p for interaction (0.05).

Conclusion: Among people older than 40 years in the United States, the relationship between Hcy levels and Balance Disorder varies according to sex. It is important to reduce exposure to risk factors in women to prevent possible deleterious effects of high levels of Hcy on Balance Disorder.

Keywords: Balance disorder; Homocysteine; NHANES; Sex

***Corresponding author:** Haiyan Luo, Department of Neurology, The Second Affiliated Hospital of Chongqing Medical University, No.74 Linjiang Road, Yuzhong District, Chongqing, 400010, China, Tel: +86 138 8386 1959; E-mail: haiyanl@hospital.cqmu.edu.cn

Gongbo Li, Department of Neurology, The Second Affiliated Hospital of Chongqing Medical University, No.74 Linjiang Road, Yuzhong District, Chongqing, 400010, China, Tel: +86 15803001109; E-mail: ligongbo@hospital.cqmu.edu.cn

Citation: Hu Y, Lin D, Song D, Wu D, Zhang Y, et al. (2023) The Association between Homocysteine Level and Balance Disorder among US Adults Varied In Different Sex Groups: A Cross-Sectional Study. Forensic Leg Investig Sci 9: 077.

Received: May 09, 2023; **Accepted:** June 01, 2023; **Published:** June 06, 2023

Introduction

Homocysteine (Hcy) is a sulfated amino acid derived from ingested methionine and is a component of the homocysteine-methionine cycle. High levels of Hcy can cause toxic effects and lead to neuron and neuronal cell death [1]. A growing body of evidence suggests that elevated levels of Hcy may be associated with an increased risk of cardiovascular, neurological, and psychiatric disorders in adults, including coronary artery disease, stroke, dementia, and depression [2,3]. However, there are few findings on balance disorder with Hcy levels in middle-aged and older adults. However, there is limited research on the association between Hcy levels and balance disorder in middle-aged and older adults.

Maintaining balance involves a complex series of sensorimotor control system [4], and a person's ability to maintain balance is crucial for almost all activities of daily living. The maintenance of human balance mainly relies on sensory input from the vestibular and visual systems, neural processing centers throughout the central nervous system, and motor output from the proprioceptive system. A decline in the functioning of any of these systems can lead to a balance deficit [5]. Imbalance leading to falls is the most common cause of serious injury in older adults and increases the risk of hospitalization [6]. While the prevalence of balance dysfunction in the U.S. is unknown, data from the National Health and Nutrition Examination Survey (NHANES) suggests that 35% of U.S. adults (69 million people) aged 40 years or older have objective evidence of vestibular dysfunction [7].

Currently, the exact mechanism between Hcy and balance disorder remains unclear and requires further exploration. This study aimed to assess the relationship between Hcy and balance disorder in individuals over 40 years old in the United States using data from the 1999-2004 NHANES. The findings of this study may provide more accurate and effective methods for the prevention and treatment of this condition.

Method

Study population and design

NHANES is a population-based cross-sectional survey that collected nationally representative data on the health and nutrition of the U.S. household population using a complex, stratified, multistage probability design. The survey comprised of an interview portion that included demographic, socioeconomic, dietary, and health-related questions and a physical examination part that included physiological

measurements and laboratory examinations. The NHANES protocol was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board, and participants provided written informed consent.

For this study, we obtained data from the 1999-2004 NHANES database, including a total of 31,126 individuals over the age of 40. We excluded 25,599 individuals with missing balance disorder information, 162 individuals who did not have homocysteine measurements, and 734 individuals who did not have complete covariate information. Ultimately, our analysis included 4,631 participants (Figure1).

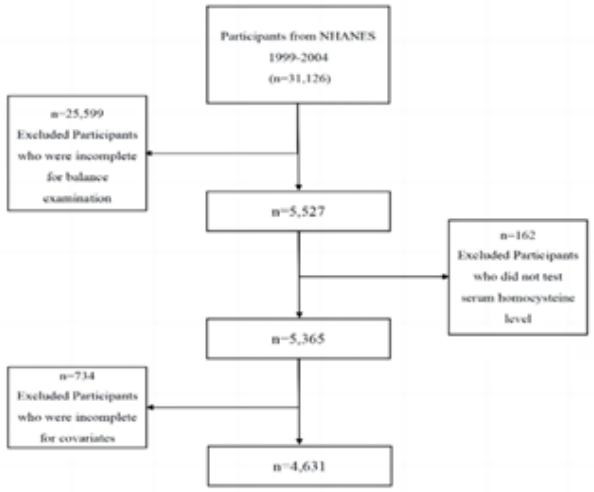

Figure 1: Flow chart of sample selection from the NHANES 1999–2004.

Variables

Balance examination

The Romberg Test of Standing Balance on Firm and Compliant Support Surfaces (CDC 2001b) was used to measure participants' ability to maintain balance under four test conditions that were ordered in increasing levels of difficulty [8]. Balance testing was scored on a pass/fail basis, with test failure defined as (a) the subject needing to open their eyes, (b) the subject moving their arms or feet to achieve stability, or (c) the subject beginning to fall or requiring operator intervention to maintain balance within a 30-second interval. As each successive test condition from 1 to 4 was progressively more difficult than the condition preceding it, the balance testing component was ended whenever a subject failed to pass a test condition (either during the initial test or in the re-test if the participant opted for one). For this study, we focused on test condition 4, which was designed to distinguish participants who could not stay standing when relying primarily on vestibular input. We categorized participants as having balance disorder if they did not pass test condition 4. The severity of vestibular balance disorder was defined by the time that condition 4 was unsuccessful (20 to < 30, 10 to < 20, and 0 to < 10 seconds). The time to failure, which was the duration until the loss of balance, was also recorded for test condition 4, with those who passed the test assigned the maximum value of 30 seconds.

Serum homocysteine and HHcy

To measure plasma homocysteine levels, a fasting blood sample was taken from each participant. The sample was collected in the morning after a fast of at least 8 hours but not more than 24 hours. The specimen collection and processing instructions followed the NHANES Laboratory/Medical Technologists Procedures Manual. The blood samples were then frozen and stored at a temperature of −20°C. The samples were transported to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for analysis. Hyperhomocysteinemia(HHcy) was defined as a plasma homocysteine level greater than 15 μmol/L [9].

Covariates

Demographic variables included age, race, educational level, marital status, Body Mass Index (BMI), smoking status, drinking status, and disease (hypertension, diabetes, stroke, and arthritis). Participants were categorized as "nonsmokers" (lifetime use of < 100 cigarettes), "former smokers" (previous history of smoking but no longer a smoker at the time of interview), or "current smokers" (lifetime use of ≥100 cigarettes and who currently smoke cigarettes) [10]. Body mass index (BMI) was calculated as a person's weight (mass) in kilograms divided by the square of height in meters. According to World Health Organization classification, participants were classified as underweight (<18.5), normal weight (18.5–24.99 kg/m2), overweight (25.00–29.99 kg/m2) or obese (≥30 kg/m2) [11].

Statistical analysis

Categorical variables were presented as numbers and percentages calculated using sample weights, while continuous variables were presented as mean±SE. To examine group differences on all continuous measures, independent-samples t-tests were used. The distribution of the categorical variables between the balance disorder group and the normal vestibular function group was compared using Pearson chi-squared test. The suggested weighting method was used in the data analysis, considering significant differences. Since the distribution of the Hcy level is skewed, Hcy was included in the logistic regression model after logarithmic transformation [12]. Logistic regression analysis was performed to evaluate the association between homocysteine and balance dysfunction.

All statistical analyses were performed using Stata, and $P < 0.05$ was considered statistically significant.

Results

The characteristics of the subjects are presented in (Table 1). Of the 4631 participants, 2323 were male and 2308 were female. The mean homocysteine level was 8.95 ± 0.06 umol/L for those with normal balance function and 10.59 ± 0.15 umol/L for those with balance disorder. Participants with balance dysfunction were more likely to be older than 60 years old, female, have less than a high school education, be unmarried, smoke, have previously consumed alcohol, have a BMI indicating overweight (25.00-29.99kg/m^2), and have associated diseases such as diabetes, hypertension, stroke, and arthritis.

Characteristics	Total (N = 4,631)	Balance disorder		p value
		No (N = 2,758)	Yes (N =1,873)	
Age group, %				< 0.001
40-59 years	2485 (70.86)	1871 (80.84)	614 (49.79)	
≥ 60 years	2146 (29.14)	887 (19.16)	1259 (50.21)	
Gender, %				0.060
Male	2323 (48.54)	1413 (49.66)	910 (46.18)	
Female	2308 (51.46)	1345 (50.34)	963 (53.82)	
Race/ethnicity, %				0.460
Mexican American	937 (4.62)	554 (4.55)	383 (4.77)	
Other Hispanic	165 (4.75)	88 (4.43)	77 (5.44)	
Non-Hispanic White	2589 (78.37)	1525 (79.01)	1064 (77.01)	
Non-Hispanic Black	807 (8.62)	516 (8.66)	291 (8.53)	
Other races	133 (3.64)	75 (3.35)	58 (4.26)	
Educational levels, %				< 0.001
Below high school	1340 (17.90)	670 (14.45)	670 (25.21)	
High school	1118 (25.99)	639 (24.82)	479 (28.46)	
Above high school	2173 (56.10)	1449 (60.73)	724 (46.33)	
Marital status, %				< 0.001
Married	2979 (68.85)	1855 (71.75)	1124 (62.72)	
widowed	503 (6.75)	180 (4.33)	323 (11.86)	
Divorced	525 (11.62)	330 (11.38)	195 (12.11)	
separated	172 (3.28)	106 (3.31)	66 (3.21)	
Never married	273 (5.91)	164 (5.74)	109 (6.28)	
Living with partner	179 (3.60)	123 (3.49)	56 (3.82)	
Smoking status, %				0.273
Non-smokers	2181 (47.33)	1314 (48.47)	867 (44.93)	
Former smokers	1497 (31.23)	868 (30.35)	629 (33.09)	
Current smokers	953 (21.44)	576 (21.19)	377 (21.98)	
Drinking status, %				0.001
Never drinkers	692 (11.81)	345 (10.35)	347 (14.91)	
Former drinkers	614 (12.84)	354 (12.03)	260 (14.55)	
Current drinkers	3325 (75.35)	2059 (77.63)	1266 (70.54)	
Body mass index, %				0.004
Underweight	46 (1.06)	23 (0.87)	23 (1.46)	
Normal weight	1236 (28.73)	670 (28.02)	566 (30.22)	
Overweight	1897 (39.59)	1116 (38.26)	781 (42.40)	
Obese	1452 (30.62)	949 (32.85)	503 (25.92)	
Diabetes, %				
Yes	525 (7.56)	233 (5.77)	292 (11.34)	< 0.001
No	4014 (90.87)	2475 (92.77)	1539 (86.85)	
Borderline	92 (1.57)	50 (1.45)	42 (1.81)	
Hypertension, %				
Yes	1839 (34.29)	939 (29.69)	900 (44.03)	< 0.001
No	2792 (65.71)	1819 (70.31)	973 (55.97)	
Stroke, %				
Yes	145 (2.56)	48 (1.49)	97 (4.83)	< 0.001
No	4486 (97.44)	2710 (98.51)	1776 (95.17)	
Arthritis, %				
Yes	1537 (30.20)	765 (25.32)	772 (40.51)	< 0.001
No	3094 (69.80)	1993 (74.68)	1101 (59.49)	
Vitamin B12, serum (pmol/L)	462.00 (35.21)	486.38 (57.21)	426.12 (21.91)	0.401
Folate, serum (nmol/L)	34.88 (0.48)	33.33 (0.47)	37.17 (0.96)	< 0.001
Homocysteine (umol/L)	9.61 (0.07)	8.95 (0.06)	10.59 (0.15)	< 0.001

Table 1: Weighted characteristics of participants by Balance Disorder from NHANES 1999–2004 (n = 4631).

N (Weighted %): Categorical variables are presented as number and percentage (calculated using sample weights). Continuous variables are presented as mean±SE. Independent-samples t tests were used to examine group differences on all continuous measures. Pearson chi-squared test was performed to compare the distribution of the categorical variables between the vestibular dysfunction group and the normal vestibular function group. $p < 0.05$ indicates a statistically significant difference.

The results of the multiple regression analysis are presented in (Table 2). In the unadjusted model, there was a positive association between log Hcy and balance disorder (OR=2.69, 95% CI: 1.95-3.72, $p < 0.001$). This association remained significant after adjusting for confounders in model 2 (OR=2.01, 95% CI: 1.41-2.84, $p < 0.001$) and model 3 (OR=1.68, 95% CI: 1.19-2.37, $p < 0.001$). To further analyze the relationship, we transformed the continuous variable (log Hcy) into categorical variables. The results showed that the risk of balance disorder in patients with HHcy was 68% higher than the risk in patients with normal Hcy levels (OR=1.68, 95% CI: 1.18-2.38, $p < 0.05$).

In further examining the relationship between log Hcy and balance disorder, we investigated potential interaction effects while adjusting for confounding factors. Our findings revealed a significant difference in the relationship between log Hcy and balance disorder based on sex stratification (P for interaction <0.05). As presented in (Table 3), after adjusting for confounders, we found that log Hcy (OR=1.73, 95%CI: 1.15-2.60, $p < 0.05$) and HHcy (OR=1.74, 95%CI: 1.10-2.73, $p < 0.05$) were positively associated with balance disorder in women, resulting in a 74% increased risk. However, among men, the risk increase was 63%, and the positive correlation was not statistically significant ($p > 0.05$). Nevertheless, the interaction test indicated a significant difference between the risk increases in women and men, indicating that gender significantly impacted the relationship between Hcy and vestibular function.

Discussion

In this cross-sectional study, we investigated the relationship between Hcy levels and balance disorders in individuals over the age of 40. Our results indicate a positive correlation between Hcy levels and the risk of balance disorders, with a stronger correlation observed in women based on subgroup analysis.

While few studies have examined the association between Hcy and balance disorder, previous research has produced mixed results. One prospective study of 41 patients with various vestibular disorders found no relationship between Hcy levels and Peripheral balance Disorder (PVD) [13]. Similarly, a Chinese case-control study of 240 individuals with Benign Paroxysmal Positional Vertigo (BPPV) found no significant difference in Hcy levels between BPPV patients and control groups [14]. However, a retrospective analysis of 90 patients with vestibular neuritis found that elevated Hcy may

	OR (95% CI)	*p* value
Model 1		
Hyperhomocysteinemia		
No	reference	
Yes	2.61 (1.79, 3.82)	< 0.001**
Homocysteine (umol/L)[a]	2.69 (1.95, 3.72)	< 0.001**
p for interaction: log homocysteine (umol/L) × gender	1.23 (1.14, 1.32)	< 0.001**
Model 2		
Hyperhomocysteinemia		
No	reference	
Yes	1.99 (1.42, 2.79)	< 0.001**
Homocysteine (umol/L)[a]	2.01 (1.41, 2.84)	< 0.001**
p for interaction: log homocysteine (umol/L) × gender	1.13 (1.05, 1.22)	0.002*
Model 3		
Hyperhomocysteinemia		
No	reference	
Yes	1.85 (1.31, 2.62)	0.001*
Homocysteine (umol/L)[a]	1.89 (1.34, 2.66)	< 0.001**
p for interaction: log homocysteine (umol/L) × gender	1.12 (1.04, 1.21)	0.006
Model 4		
Hyperhomocysteinemia		
No	reference	
Yes	1.68 (1.18, 2.38)	0.005*
Homocysteine (umol/L)[a]	1.68 (1.19, 2.37)	0.004*
p for interaction: log homocysteine (umol/L) × gender	1.09 (1.01, 1.19)	0.036*

Table 2: Association of homocysteine with Balance Disorder from 1999 to 2004 National.

Health and Nutrition Examination Survey (N = 4,631).

Logistics regression analyses were conducted using sample weights, with significance set at p < 0.05. p < 0.05*, p < 0.001**.

a log transformed

Model 1: unadjusted for any potential confounders;

Model 2 adjusted for age, gender, and race;

Model 3 adjusted for age, gender, race, educational level, marital status, body mass index (BMI), smoking status, drinking status, vitamin B12 (pmol/L), and folate (nmol/L).

Model 4 adjusted for age, gender, race, educational level, marital status, body mass index (BMI), smoking status, drinking status, vitamin B12 (pmol/L), folate (nmol/L) and disease (hypertension, diabetes, stroke, and arthritis).

	Man (n=2,323)		Woman (n=2,308)	
	OR (95% CI)	*p value*	OR (95% CI)	*p value*
Model 1				
Hyperhomocysteinemia				
No	reference		reference	
Yes	2.75 (1.69, 4.46)	< 0.001**	2.53 (1.40, 4.56)	0.003
Homocysteine (umol/L)a	2.92 (1.75, 4.86)	< 0.001**	3.18 (2.03, 4.97)	< 0.001**
Model 2				
Hyperhomocysteinemia				
No	reference		reference	
Yes	2.06 (1.28, 3.34)	0.004	1.93 (1.17, 3.16)	0.011
Homocysteine (umol/L)a	2.11 (1.25, 3.56)	0.006	1.92 (1.26, 2.93)	0.003
Model 3				
Hyperhomocysteinemia				
No	reference		reference	
Yes	1.92 (1.15, 3.23)	0.014	1.82 (1.16, 2.86)	0.010
Homocysteine (umol/L)a	1.98 (1.17, 3.34)	0.012	1.87 (1.23, 2.84)	0.004
Model 4				
Hyperhomocysteinemia				
No	reference		reference	
Yes	1.60 (0.92, 2.79)	0.095	1.74 (1.10, 2.73)	0.018
Homocysteine (umol/L)a	1.63 (0.95, 2.82)	0.078	1.73 (1.15, 2.60)	0.009

Table 3: Association of homocysteine with Balance Disorder by gender difference from 1999 to 2004 National Health and Nutrition Examination Survey (N = 4,631).

Logistics regression analyses were conducted using sample weights, with significance set at p < 0.05. p < 0.05*, p < 0.001**.

a log transformed

Model 1: unadjusted for any potential confounders;

Model 2: adjusted for age, gender, and race;

Model 3: adjusted for age, gender, race, educational level, marital status, body mass index (BMI), smoking status, drinking status, vitamin B12 (pmol/L), and folate (nmol/L).

Model 4: adjusted for age, gender, race, educational level, marital status, body mass index (BMI), smoking status, drinking status, vitamin B12 (pmol/L), folate (nmol/L) and disease (hypertension, diabetes, stroke, and arthritis).

play a role in preventing recovery after a recent vestibular neuritis [15]. Additionally, a case report describes a 68-year-old woman with severe symptoms of Ménière's syndrome and increased fasting serum homocysteine [16]. The inconsistent results among these studies could be due to differences in the populations investigated and the presence of confounding factors. Further research is needed to better understand the relationship between Hcy and balance disorder and to determine if Hcy levels could be a potential biomarker or therapeutic target for balance disorders.

Our cross-sectional study conducted from 1999 to 2004 revealed a significant positive correlation between Hcy levels and balance disorder, with a stronger association in women. After adjusting for confounding factors, including disease, our multiple logistic regression model found no significant interaction between Hcy and gender. However, the impact of disease on balance function was greater in men. We further analyzed the reason for the gender difference and found that the decrease in estradiol during menopause may lead to an increase in Hcy and cysteine, resulting in endothelial dysfunction in postmenopausal women [17]. Previous studies have reported that the concentration of Hcy increases in postmenopausal women, and estrogen levels are negatively correlated with Hcy levels in women [18,19]. Hence, sex hormones may play a role in the relationship between balance disorders and Hcy. Additionally, Hcy levels can increase due to inadequate intake of folic acid (vitamin B9), vitamin B12, and vitamin B6, which are essential cofactors for enzymes involved in Hcy metabolism. To account for this, we adjusted for the effects of folic acid and vitamin B12 on Hcy levels.

Hcy is a sulfur-containing amino acid found in the human body, and it serves as an important intermediate in the metabolism of methionine and cysteine. One key function of homocysteine is its involvement in the methylation cycle, during which methyl is transferred to various substrates [20]. Homocysteine can be utilized in two ways: 1) it can be methylated to methionine through the catalytic activity of N5 force n10-methylenetetrahydrofolate reductase, and 2) it can be converted to cysteine through the catalysis of Cystine β Synthase (CBS) [21]. HHcy, or an abnormally high level of homocysteine in the blood, can result from an imbalance of processes and factors involved in homocysteine metabolism.

HHcy is a condition characterized by elevated levels of homocysteine in the blood, typically defined as homocysteine levels exceeding 15umol/l. Homocysteine is known to damage blood vessels through several mechanisms. For instance, high levels of homocysteine can induce hypermethylation of DNA promoter regions, which increases the expression of p66shc in endothelial cells and results in oxidative stress [22].This, in turn, can reduce the availability of nitric oxide, a potent vasodilator [23], leading to endothelial cell damage and increased lipid peroxidation and oxidation [24]. Consequently, HHcy is linked to a prothrombotic state characterized by increased platelet aggregation, production of Tissue Factor (TF) [25], and activation of coagulation factors such as VMagneX and XII, as well as decreased activation of protein C and cell surface thrombomodulin [26-28]. Taken together, these findings suggest that HHcy may contribute to vascular inflammation, hypercoagulability, and the development of atherosclerosis and associated thrombotic events [29].

The common causes of peripheral vertigo are known to be BPPV, vestibular neuritis, and Meniere's disease. However, the pathophysiological mechanism underlying peripheral vertigo remains unclear. The link between homocysteine and balance disorder can be explained through various mechanisms. Firstly, the blood-labyrinth barrier protects the inner ear from abnormalities in the circulating blood, but metabolic disorders can still affect vestibular function [30]. Additionally, labyrinthine branches receive less collateral flow from the internal carotid artery, making them vulnerable to the effects of atherosclerosis [31]. Thus, vascular endothelial injury caused by homocysteine may lead to balance disorder. Secondly, homocysteine can lead to oxidative stress and the accumulation of free radicals and other oxidizing substances. These oxygen free radicals can cause vestibular-cochlear poisoning and result in permanent damage to sensory hair cells and neurons [32]. Homocysteine may also affect the function of the vestibular system by regulating the level of neurotransmitters. For example, Acetylcholine (ACh) has long been identified as the primary neurotransmitter of the efferent vestibular system in most animals [33]. Studies have shown that an increase in homocysteine level is related to a decrease in acetylcholine sensitivity [34]. However, the specific molecular mechanisms of this regulation are currently unknown.

In summary, the association between Hcy and balance disorder appears to be multifactorial, involving vascular endothelial injury, oxidative stress, and regulation of neurotransmitters. Further investigation into these mechanisms can enhance our understanding of the link between homocysteine and balance disorder, leading to the development of more effective strategies for prevention and treatment.

Our study has several strengths, including the use of a nationally representative sample and a large sample size that allowed for subgroup analysis. We believe that our findings are highly relevant to the population as a whole, especially as this is the first study to investigate the relationship between homocysteine and balance disorder in individuals over 40. However, we must also acknowledge the limitations of our study. First, our study is cross-sectional, and thus we cannot establish a causal relationship between homocysteine and balance disorder. Further research is needed to determine the exact nature of this relationship. Second, we cannot rule out the possibility of biases from unmeasured confounding factors.

Conclusion

In summary, our study suggests that there is a significant association between elevated Hcy levels and an increased risk of balance disorder in Americans over the age of 40, particularly in women. This highlights the importance of promoting a healthy lifestyle that includes a well-balanced diet rich in vitamins and antioxidants to reduce Hcy levels and decrease the risk of developing balance disorders. Future studies should aim to explore the underlying mechanisms and establish a causal relationship between Hcy and balance disorder, which can further inform effective prevention and treatment strategies.

Statement of Ethics

This study was approved by the ethics review board of the National Center for Health Statistics and written informed consents were obtained from each participant.

Author's Contribution

Y Hu, G Li and H Luo conceived and designed the study. Y Hu, M Song, D Wu and Y Zhang conducted the formal analysis and developed the methodology. Y Hu and D Lin wrote the initial drafts. D Wu and Y Zhang helped draft the manuscript. G Li and H Luo are the corresponding authors of this work and supervised work on the entire manuscript. All the authors read and approved the final manuscript.

Acknowledgement

We would like to thank our colleagues from the Department of Neurology, The Second Affiliated Hospital of Chongqing Medical University, who provided valuable advice regarding the manuscript.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding was received for this study.

Data Availability Statement

The survey data are publicly available on the internet for data users and researchers throughout the world (www.cdc.gov/nchs/nhanes/).

References

1. Li XA, Ho YS, Chen L, Hsiao WL (2016) The Protective Effects of Icariin against the Homocysteine-Induced Neurotoxicity in the Primary Embryonic Cultures of Rat Cortical Neurons. Molecules 21: 11.
2. Homocysteine and risk of ischemic heart disease and stroke: A meta-analysis (2002) JAMA 288: 2015-2022.
3. Kamath AF, Chauhan AK, Kisucka J, Dole VS, Loscalzo J et al. (2006) Elevated levels of homocysteine compromise blood-brain barrier integrity in mice. Blood 107: 591-593.
4. Djukic T, Filipovic N (2017) Numerical modeling of the cupular displacement and motion of otoconia particles in a semicircular canal. Biomech Model Mechanobiol 16: 1669-1680.
5. Horak FB (2006) Postural orientation and equilibrium: What do we need to know about neural control of balance to prevent falls? Age Ageing 35 Suppl 2.
6. Bergen G, Stevens MR, Burns ER (2016) Falls and Fall Injuries Among Adults Aged ≥65 Years - United States, 2014. MMWR Morb Mortal Wkly Rep 65: 993-998.
7. Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB (2009) Disorders of balance and vestibular function in US adults: data from the National Health and Nutrition Examination Survey, 2001-2004. Arch Intern Med 169: 938-944.
8. Min KB, Lee KJ, Park JB, Min JY (2012) Lead and cadmium levels and balance and vestibular dysfunction among adult participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2004. Environ Health Perspect 120: 413-417.
9. Li M, Hu L, Zhou W, Wang T, Zhu L, et al. (2020) Nonlinear association between blood lead and hyperhomocysteinemia among adults in the United States. Sci Rep 10:17166.
10. Noh H-M, Park YS (2020) Handgrip strength, dynapenia, and mental health in older Koreans. Sci Rep 10: 4004.
11. WHO (2000) Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 894.
12. Shi Y, Wu Z, Wu J, Chen Z, Li P (2022) Serum Homocysteine Level Is Positively Correlated With Serum Uric Acid Level in U.S. Adolescents: A Cross Sectional Study. Front Nutr 9: 818836.
13. Aydın E, Babakurban ST, Ozgirgin ON, Ozlüoğlu LN (2012) The relationship of homocysteine, vitamin B12, folic acid levels with vertigo. Kulak Burun Bogaz Ihtis Derg 22: 214-218.
14. Yuan J, Dai J, Li WA, Hu W (2017) Factors Associated with Benign Paroxysmal Positional Vertigo: A Chinese Case-Control Study. Med Sci Monit 23: 3885-3889.
15. Raponi G, Teggi R, Gatti O, Giordano L, Bussi M (2013) Postural control in patients after a recent vestibular neuritis with hyperhomocysteinemia. Indian J Otolaryngol Head Neck Surg. 65: 146-50.
16. Scaramella JG (2003) Hyperhomocysteinemia and left internal jugular vein thrombosis with Ménière's symptom complex. Ear Nose Throat J 82: 859-60.
17. Keller AC, Klawitter J, Hildreth KL, Christians U, Putnam K, et al. (2019) Elevated plasma homocysteine and cysteine are associated with endothelial dysfunction across menopausal stages in healthy women. J Appl Physiol 126: 1533-1540.
18. Fernández-Miranda C, de la Calle M, Manuel Bris J, Muelas M, Gómez P, et al. (2001) [Influence of menopausal status in homocysteine plasma levels]. Med Clin (Barc) 116: 206-208.
19. Wouters MG, Moorrees MT, van der Mooren MJ, Blom HJ, Boers GH, et al. (1995) Plasma homocysteine and menopausal status. Eur J Clin Invest 25: 801-805.
20. Fernández-Arroyo S, Cuyàs E, Bosch-Barrera J, Alarcón T, Joven J, et al. (2015) Activation of the methylation cycle in cells reprogrammed into a stem cell-like state. Oncoscience 2: 958-967.
21. Ganguly P, Alam SF (2015) Role of homocysteine in the development of cardiovascular disease. Nutr J 14: 6.
22. Loscalzo J, Handy DE (2014) Epigenetic modifications: basic mechanisms and role in cardiovascular disease (2013 Grover Conference series). Pulm Circ 4: 169-174.
23. Zhang S, Bai YY, Luo LM, Xiao WK, Wu HM, et al. (2014) Association between serum homocysteine and arterial stiffness in elderly: A community-based study. J Geriatr Cardiol 11: 32-8.
24. Hirano K, Ogihara T, Miki M, Yasuda H, Tamai H, et al. (1994) Homocysteine induces iron-catalyzed lipid peroxidation of low-density lipoprotein that is prevented by alpha-tocopherol. Free Radic Res 21: 267-276.
25. Durand P, Lussier-Cacan S, Blache D (1997) Acute methionine load-induced hyperhomocysteinemia enhances platelet aggregation, thromboxane biosynthesis, and macrophage-derived tissue factor activity in rats. FASEB 11: 1157-1168.
26. Rodgers GM, Kane WH (1986) Activation of endogenous factor V by a homocysteine-induced vascular endothelial cell activator. J Clin Invest 77: 1909-1916.
27. Rodgers GM, Conn MT (1990) Homocysteine, an atherogenic stimulus, reduces protein C activation by arterial and venous endothelial cells. Blood 75: 895-901.
28. Lentz SR, Sadler JE (1991) Inhibition of thrombomodulin surface expression and protein C activation by the thrombogenic agent homocysteine. J Clin Invest 88: 1906-1914.
29. Mangge H, Becker K, Fuchs D, Gostner JM (2014) Antioxidants, inflammation and cardiovascular disease. World J Cardiol 6: 462-77.
30. Rybak LP (1995) Metabolic disorders of the vestibular system. Otolaryngol Head Neck Surg 112: 128-132.
31. Gomez CR, Cruz-Flores S, Malkoff MD, Sauer CM, Burch CM (1996) Isolated vertigo as a manifestation of vertebrobasilar ischemia. Neurology 47: 94-97.
32. Kim J-B, Jung JY, Ahn J-C, Rhee CK, Hwang H-J (2009) Antioxidant and anti-apoptotic effect of melatonin on the vestibular hair cells of rat utricles. Clin Exp Otorhinolaryngol 2: 6-12.
33. Guo C-K (2018) Existence of nicotinic receptors in a subset of type I vestibular hair cells of guinea pigs. Brain Res 1681: 85-90.
34. Bhalodia YS, Sheth NR, Vaghasiya JD, Jivani NP (2011) Homocysteine-dependent endothelial dysfunction induced by renal ischemia/reperfusion injury. J Nephrol 24: 631-635.

HERALD

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752