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Effect of Serum Vitamin B12 Levels on Brain Volumes

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Abstract

Objective: To research the relationship between brain volumes and serum vitamin B12 markers.
Methods: To investigate the volume changes of serum vitamin B12 markers in brain magnetic resonance imaging measurements of 62 participants admitted to the clinic.
Results: Volumes were significantly higher in vitamin B12 users compared to non-users. Vitamin B12 and white matter volumes increase together with a strong relationship and significantly.
Conclusion: Levels of vitamin B12 can influence the brain using multiple mechanisms. Low vitamin B12 status increases the likelihood of brain atrophy and may even be a factor in cognitive decline.
Keywords: Vitamin B12, brain volumes, magnetic resonance imaging, white matter volumes, gray matter volumes, lobes volumes

INTRODUCTION

Vitamin B12 is an essential water-soluble vitamin and is involved in hematopoiesis, nervous system function, maintenance of gastrointestinal mucosal continuity and regulation of metabolic processes. A deficiency in vitamin B12 is linked to epithelial alterations in the gastrointestinal mucosa, neurological and psychiatric disorders, and hematopoietic disorders affecting erythrocyte formation.[1] The primary indicator in the diagnosis of vitamin B12 deficiency is changes in the hematopoietic system.[2] Furthermore, neurological disorders are often the earliest and in some cases the only clinical manifestations of a functional vitamin B12 deficiency.[3] Between 75% and 90% of people with clinically significant B12 deficiency have neurologic disorders, and in approximately 25% of cases these are the only clinical manifestations of B12 deficiency.[4-6] Vitamin B12's neurological importance is intimately associated with its regulatory mechanisms about brain development and function. Vitamin B12 deficiency can cause several neurological symptoms, including paresthesia, numbness on the skin, impaired coordination, and slowed nerve conduction velocity. Deficits in vitamin B12, particularly in older adults, can negatively affect on brain volume. Progressive brain atrophy in the elderly has been linked to vitamin B12 deficiency.[7] The relationship between brain volume and vitamin B12 has been studied, and significant findings have been made. Low levels of vitamin B12 were found to be significantly correlated with the rate at which brain volume was decreasing. A lower brain volume has been linked to lower levels of vitamin B12 and holotranscobalamin and higher levels of total homocysteine and methylmalonic acid.[8] Vitamin B12 and total homocysteine levels are said to be associated with accelerated brain aging in older adults. It highlights the need for randomized clinical trials to determine whether vitamin B12 supplementation is essential in slowing brain aging.[9] The possible correlation between brain volume and vitamin B12 may be crucial for preserving cognitive function in elderly individuals. However, it should be noted that there are different findings in the existing literature. In a different investigation, DTI revealed microstructural alterations in the white matter regions of patients who were vitamin B12 deficient, although conventional MR imaging revealed no abnormalities.[10] Our study's objective was to thoroughly investigate the connection between vitamin B12 levels and brain volume. The correlation between brain capacity and vitamin B12 levels is complicated and multidimensional. Low B12 levels may negatively affect brain volume, according to current studies; however, the precise mechanism and clinical implications of this effect are yet unclear.

Our study aims to fill the existing knowledge gap in this field by examining the relationship between vitamin B12 levels and brain volume in more detail. Our research holds particular significance in identifying the function of vitamin B12 in safeguarding brain health within the community. Our study's findings could have a significant impact on clinical procedures for the early detection and treatment of vitamin B12 deficiency and could help create new strategies to stop brain atrophy in the general population.

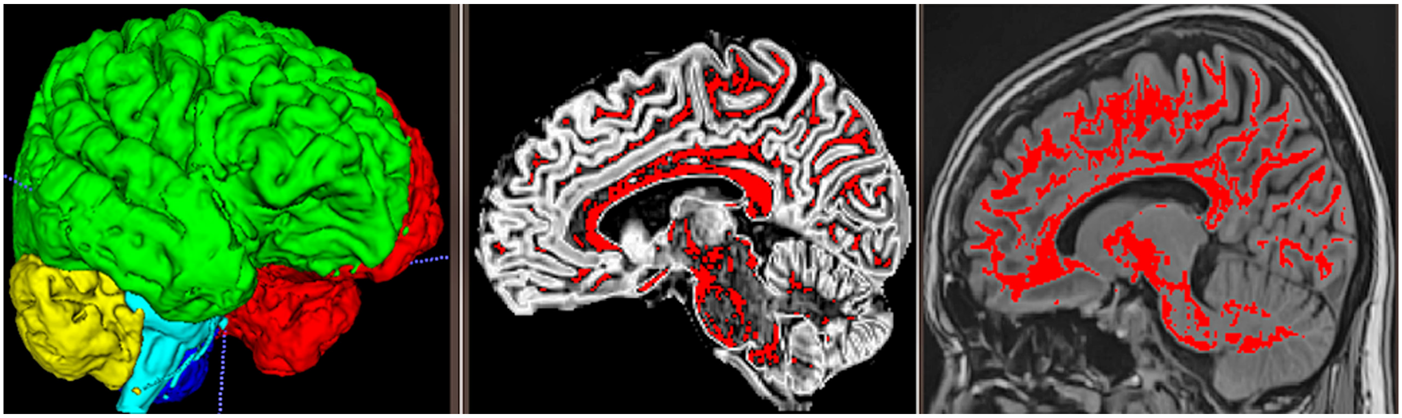

Figure 1. Fully-automated lobes, gray matter, white matter segmentation by volBrain.

MATERIAL AND METHODS

Participants

In our study, we retrospectively reviewed the images and serum vitamin B12 levels of 62 adult patients. All participants were informed in writing and informed consent was obtained. Approval for the study was obtained from Erzincan Binali Yıldırım University Clinical Research Ethics Committee (Ethics Committee decision date: November 30, 2023; Decision number: 2023-21/1) The study was conducted on human participants at Mengucek Gazi Training and Research Hospital. All procedures performed in this study complied with the ethical standards of the institution. The MRI used in the study is ethically and scientifically safe.

The study group consisted of healthy 24 volunteers who had used vitamin B12 within the last 1 year and healthy 38 volunteers who had not used vitamin B12 within the last 1 year, and were selected without a history of brain surgery or trauma, neurologic or psychiatric disease or substance abuse. Our study group consisted of 62 participants. There were 7 men and 55 women among the participants. The average age was 37.21 years (min-max 19-59 years).

Magnetic Resonance Imaging Protocol and Segmentation Method

The MRI used in the study was performed with a high-resolution magnetic resonance device (1.5 T Siemens Aera scanner, Germany). The measurements were performed as TR (repetition time) /TE (echo Time), 2200/2.67ms; flip angle 8; acquisition matrix, 256 × 246; FOV, 250X250 mm; acquisition time, 4 minutes 59 seconds; number of axial slices, 192; slice thickness = 1 mm (with no gap) in T1 weighted 3D Magnetization Prepared Rapid Gradient Echo sequence covering the whole brain.

Magnetic resonance imaging data processing and total brain, white matter, gray matter, thalamus, hippocampus, frontal lobe, temporal lobe, parietal lobe, occipital lobe, volumetric analyses were performed using volBrain (v.1.0, http://volbrain.upv.es), a free online MRI brain volumetry system. volBrain is a fully automated segmentation technique of which the algorithm is based on multi-atlas patch-based label fusion segmentation technology (Figure 1).[11]

MAIN POINTS

- Vitamin B12's neurological importance is intimately associated with its regulatory mechanisms about brain development and function.
- Low vitamin B12 status increases the likelihood of brain atrophy and may even be a factor in cognitive decline.
- Vitamin B12 and white matter volumes increase together with a strong relationship and significance.
- Brain volumes were significantly higher in vitamin B12 users compared to nonusers.

Statistical Analysis

IBM SPSS™ Version 22 (IBM SPSS Corp.; Armonk, NY, USA) program was used for statistical evaluation of the analyses. The normality of data distribution was assessed using the Kolmogorov–Smirnov test. One-way analysis of variance test and independent *t*-test were used to compare the age, gender, and brain volume variables between the group using vitamin B12 in the last year and the group not using vitamin B12 in the last year. Descriptive statistical methods (frequency, percentage, mean, standard deviation) were used to evaluate the study data. Partial correlation analysis was used to correlate volumetric measurements with vitamin B12 levels and brain volumes. A value of $p \leq .05$ was considered statistically significant for the results.

RESULTS

The median age of participants was 37.21 years (min-max 19-59 years) respectively. White matter, gray matter, total brain, thalamus, hippocampus, frontal lobe, temporal lobe, parietal lobe, occipital lobe volumes were significantly higher in vitamin B12 users compared to nonusers ($p < .05$ for all, Table 1). Correlation analysis was performed to determine the relationship between vitamin B12 and total brain volume, white matter volume, gray matter volume, thalamus volume,

Table 1. Comparison of Volumes of Different Brain Regions According to Groups

	Not Using B12 Group (n = 38)		Using B12 Group (n = 24)		
	Mean (cm^3)	SD (cm^3)	Mean (cm^3)	SD (cm^3)	*p*
White matter	420.10	27,74	*497.20*	*45.56*	<.001**
Gray water	613.91	41.97	*681.46*	*51.02*	<.001**
Total brain	1034.01	59.54	*1178.66*	*87.97*	<.001**
Thalamus	10.51	0.78	*11.85*	*0.90*	<.001**
Hippocampus	7.44	0.60	*8.00*	*0.61*	.001*
Frontal lobe	151.80	14.95	*169.24*	*16.18*	<.001**
Temporal lobe	102.55	9.41	*115.20*	*8.48*	<.001**
Parietal lobe	91.94	7.49	*104.04*	*9.81*	<.001**
Occipital lobe	67.59	6.29	*74.30*	*7.32*	.001*

SD, standard deviation.
**P*-value < .05 significant.
***P*-value < .001 highly significant.

Table 2. Association of Different Brain Regions with Vitamin B12

		Correlations									
		B12	White Matter	Graywater	Brain	Thalamus	Hippocampus	Frontal lobe	Temporal Lobe	Parietal Lobe	Occipital Lobe
B12	*r*	1									
	p										
White matter	*r*	.287*	1								
	p	.024									
Graywater	*r*	.177	.736	1							
	p	.169	.000								
Brain	*r*	.247	.926	.937	1						
	p	.053	.000	.000							
Thalamus	*r*	.207	.716	.839	.837	1					
	p	.107	.000	.000	.000						
Hippocampus	*r*	.125	.530	.664	.643	.493	1				
	p	.333	.000	.000	.000	.000					
Frontal lobe	*r*	.174	.640	.901	.833	.782	.599	1			
	p	.177	.000	.000	.000	.000	.000				
Temporal lobe	*r*	.150	.707	.845	.836	.683	.478	.705	1		
	p	.243	.000	.000	.000	.000	.000	.000			
Parietal lobe	*r*	.181	.752	.935	.909	.815	.645	.826	.788	1	
	p	.158	.000	.000	.000	.000	.000	.000	.000		
Occipital lobe	*r*	.113	.614	.805	.765	.608	.582	.664	.615	.791	1
	p	.383	.000	.000	.000	.000	.000	.000	.000	.000	

*Correlation is significant at the 0.05 level (2-tailed).

hippocampus volume, frontal lobe volume, temporal lobe volume, parietal lobe volume, occipital lobe volume. As a result of the statistics; a strong positive and significant relationship was found between vitamin B12 and white matter volumes. In other words, vitamin B12 and white matter volumes increase together with a strong relationship and significantly ($p < .05$, Table 2).

DISCUSSION

Our study showed that brain volumes were larger in the group that had used vitamin B12 in the last 1 year compared to the group that had not used vitamin B12 in the last 1 year. Brain volumetric measurements were positively correlated with serum vitamin B12 supplementation. However, there was also a correlation found between increased brain volume and higher vitamin B12 levels. Our study suggests a beneficial effect of vitamin B12 supplementation for brain volumes; in contrast to the group that did not get vitamin B12 supplements, the group that took vitamin B12 supplements in our research had larger brain volumes. An investigation revealed correlations between different markers of vitamin B12, white matter lesions, and cognitive performance.[12] In our study, a strong positive and significant correlation was found between vitamin B12 and white matter volumes. Patients with vitamin B12 deficiency or disease affecting vitamin B12 metabolism have been shown to demonstrate areas of demyelination on brain MRI.[13,14] Consequently, our results provide credence to the idea that low vitamin B12 status increases the likelihood of brain atrophy and may even be a factor in cognitive decline.

This study elucidates the relationship between vitamin B12 supplementation and brain volume, indicating a positive influence, particularly on white matter volume. However, the connection between B12 deficiency and brain health is multifaceted and intricate. While our results suggest a potential link between brain volume variations and B12 levels, they underscore the need for more in-depth exploration of the underlying mechanisms.

In conclusion, our study suggests a beneficial effect of vitamin B12 supplementation on brain volume. However, comprehensive studies involving larger, demographically diverse cohorts are essential for a clearer understanding of the relationship between vitamin B12 supplementation and brain health, potentially solidifying the benefits of B12 supplementation for brain health in the broader population.

Study Limitations

The study is constrained by a limited participant number, an imbalance in gender distribution, and its execution in a single hospital, which may limit the applicability of findings to the general population. These limitations should be taken into consideration when interpreting the results. Future research, conducted with larger and more diverse populations across various locations, would enhance the generalizability of our findings.

Ethics Committee Approval: Erzincan Binali Yıldırım University Clinical Research Ethics Committee (Ethics Committee decision date: November 30, 2023; decision number: 2023-21/1).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflict of interest to declare.

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