European Journal of Therapeutics
pISSN: 2564-7784
eISSN: 2564-7040

Eur J Ther. 2024;30(6):797-807.
https://doi.org/10.58600/eurjther2363

Original Research

Evaluation of the Pons, Midbrain, Thalamus, Hippocampus, and Trigeminal Nerve with MRI in Patients with Cluster Headache

Mehmet Hamdi Şahan [1], Nuray Bayar Muluk [2,*], Fatih Koçtürk [3]

[1] Department of Radiology, Faculty of Medicine, Gaziantep University, Gaziantep, Türkiye
[2] Department of ENT, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye
[3] Department of Neurology, Faculty of Medicine, Gaziantep University, Gaziantep, Türkiye

Received: 2024-09-03 **Accepted:** 2024-12-18 **Published Online:** 2024-12-30

Corresponding Author
Nuray Bayar Muluk, MD
Address: Department of ENT, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye
E-mail: nuray.bayar@yahoo.com; nurayb@hotmail.com

ABSTRACT

Objectives: We investigated the volumetric changes of the brain structures and trigeminal nerve diameters in cluster headache (CH) by cranial MRI.

Methods: The cranial MRI images of 30 adult patients with CH and 30 adult subjects with normal cranial MRI results were included. In both groups, pons, midbrain, thalamus, and hippocampus volumes; and trigeminal nerve diameters were measured.

Results: There were no significant differences between pons (p=0.849), midbrain (p=0.855), bithalamic ($p=0.553^{Right}$, $p=0.523^{Left}$), and hippocampus volumes ($p=0.930^{Right}$, $p=0.698^{Left}$). In CH group, trigeminal nerve diameter (2.38±0.47 mm) was non-significantly higher than the control group (2.29±0.44 mm) (p=0.131). In the CH group, left thalamus and right hippocampus volumes were significantly higher than the contralateral side ($p<0.05$). In CH group, there were positive correlations between the pons and thalamus ($p=0.037^{Right}$ and $p=0.037^{Left}$) and hippocampus volumes ($p=0.002^{Right}$, $p=0.005^{Left}$); midbrain and bithalamic volumes ($p=0.001^{Right}$, $p=0.001^{Left}$); and right trigeminal nerve diameter (p=0.029); thalamus and pons($p=0.037^{Right}$, $p=0.037^{Left}$); and midbrain volumes ($p=0.001^{Right}$, $p=0.001^{Left}$); right and left hippocampus volumes (p=0.000); right and left trigeminal nerve diameters (p=0.000). In females, right hippocampus volumes were smaller than those in males (r= -0.374, p=0.042).

Conclusion: In CH patients, left thalamus volume was higher; and left hippocampus volume was lower. In CH patients, the limbic system and especially left hippocampus may be affected and get lower in volumetric analysis. Additionally, the right thalamus is affected showing lower volume in CH patients.

Keywords: cluster headache, pons, midbrain, thalamus, hippocampus, trigeminal nerve.

INTRODUCTION

Cluster headaches (CH) are primary headache disorders and are considered disorders of the brain [1,2]. In CH, ipsilateral hypothalamic gray area activation occurs, however in migraine without aura, the contralateral side of the brainstem activation was present [3-5]. There are other neurological symptoms, such as sensory, homeostatic, autonomic, cognitive and emotional processes that can be related to headaches. These symptoms are

related to the modulation of specific brainstem nuclei [1].

CH patients have severe or very severe and unilateral attacks of pain ("orbital, supraorbital or temporal "). Attacks last 15-180 minutes and occur from one to 8 times a day. İpsilateral conjunctival injection, nasal congestion, lacrimation, rhinorrhea, myosis, ptosis or eyelid edema, forehead and facial sweating are associated with the attacks; and one or more of these symptoms are seen [6]. CH may be episodic or chronic. In episodic form, "at least 2 cluster phases lasting 7 days to 1 year are separated by painless periods lasting at least 3 months"; and in chronic form, "clusters occur for a year or more without remission or occur with remission lasting less than 3 months" [6].

In the central and peripheral nervous system, various structures are involved in CH attack generation. These are "trigeminovascular system, parasympathetic nerve fibers (trigeminal autonomic) reflex and hypothalamus". When all of these structures are involved, CH attacks are initiated; and later, processing and perception of pain cortical areas of CNS will be activated [7]. Hypothalamus has an important role in the pathophysiology of the facial pain syndromes, including CH [8].

In the present study, we investigated the volumetric changes of the brain structures (pons, midbrain, thalamus, hippocampus) in CH patients; and the trigeminal nerve was also evaluated by cranial MRI

MATERIAL AND METHODS

This retrospective study was conducted at Gaziantep University, Medical Faculty, Radiology and Neurology Departments and Kırıkkale University, Medical Faculty, Department of Otolaryngology. This study was approved by "Gaziantep University Clinical Researches Ethics Committee" (Decision Number: 2022/303, Date:28.09.2022) and conducted according to the Declaration of Helsinki.

Main Points

- Hippocampus is located in the limbic system
- The left hippocampus may be affected and get lower in volumetric analysis in CH patients
- The right thalamus is affected showing lower volume in CH patients

Study Population and Exclusion Criteria

Patients diagnosed with cluster headache (CH) from our neurology clinic and a control group with similar demographic characteristics who underwent cranial MRI for any reason and met the study criteria were analyzed. A total of 60 cranial MRI sections were included, including 30 patients with cluster headaches and 30 control group subjects, taking into account similar studies in the literature [9,10]. Cluster headache patients were over 18 years of age, and diagnosed with a new episodes of cluster headache according to the criteria of the "International Classification of Headache Disorders (ICHD-3)" [11-13]. The mean ages of the CH group were 35.27±8.15 years (ranging from 19 to 53 years).

The control group consisted of subjects who had retrospective cranial MRI examinations for any reason, met the exclusion criteria, and matched the same demographic characteristics as the cluster headache group. Both groups included those who had complete and appropriate cranial MRI images based on measurement parameters. The mean ages of the control group were 35.20±7.51 years (ranging from 20 to 47 years).

Similar studies in the literature were evaluated [1,14]; and the minimum number of individuals required to determine the statistically significant volume change between the groups was found to be 52 in total, with 26 in each group (α=0.05, 1-β=0.80), to conduct statistical analysis using Gpower3.1 version.

Exclusion Criteria

Those with a history of cranial trauma and surgery, intracranial masses, diabetes or any metabolic disease, demyelinating or degenerative diseases affecting cerebral structures, "previous medical or neurological history", those taking any neurological drugs or substances, and those with "congenital and anatomical variations in the brain" were not included in the study.

MRI Technique and Measurements

MRI scans were conducted using a "3.0 Tesla MRI system" ("Ingenia, Philips Healthcare, Best, Netherlands") with a cranial coil. At Gaziantep University Hospital, the standard cranial MRI protocol for the 3.0-T MRI system included the following: T1-FFE (Fast Field Echo) sequences were performed in the "sagittal and axial planes" with parameters of TR ms/TE ms; 330/20, a field of view (FOV) of 230x130 mm, and a matrix of 256 × 139 mm. These scans had "a slice thickness of 4 mm and an intersection gap of 0.5 mm", resulting in 30-32 sagittal

and axial slices. T2-TSE ("Turbo Spin Echo") sequences were performed in the coronal plane with parameters of "TR ms/TE ms; 4040/80", a "FOV of 200x152 mm", and a matrix of 288 × 163 mm. These images had a "slice thickness of 4 mm" and "an intersection gap of 0.5 mm", resulting in 34 coronal slices.

Following image processing at the workstation, measurements were carried out by a radiologist manually (MHŞ).

Pons Volume (cm^3): The pons area was measured in each section from the axial T1-weighted images. The total volume was calculated by summing these areas and multiplying by the combined section thickness and intersection gap [7,15,16] (refer to Figure 1A, B).

Midbrain Volume (cm^3): Similarly, the midbrain area was measured from the axial T1-weighted images. The volume was determined by summing these areas and multiplying by the total section thickness and intersection gap [1,15] (refer to Figure 2A, B).

Bithalamic Volume (cm^3): For the bithalamic volume, the areas of the right and left thalami were measured from the axial T1-weighted images. The total volume was calculated by summing these areas and multiplying by the combined section thickness and intersection gap [1,15] (refer to Figure 3A, B).

-Hippocampus volumes (cm^3): After measuring the hippocampus areas in each section from coronal T2 weighted images, the sum of the areas was calculated. The volume was obtained by "multiplying this calculated value" by "the sum of the section thickness with the intersection gap" [1,14-18] (Figure 4A, B).

-Trigeminal nerve diameters (mm): The diameters of the trigeminal nerve was measured from the coronal T2 weighted images, in the cisternal region where the trigeminal nerve emerges from the pons, where it is most clearly seen [19-22] (Figure 5).

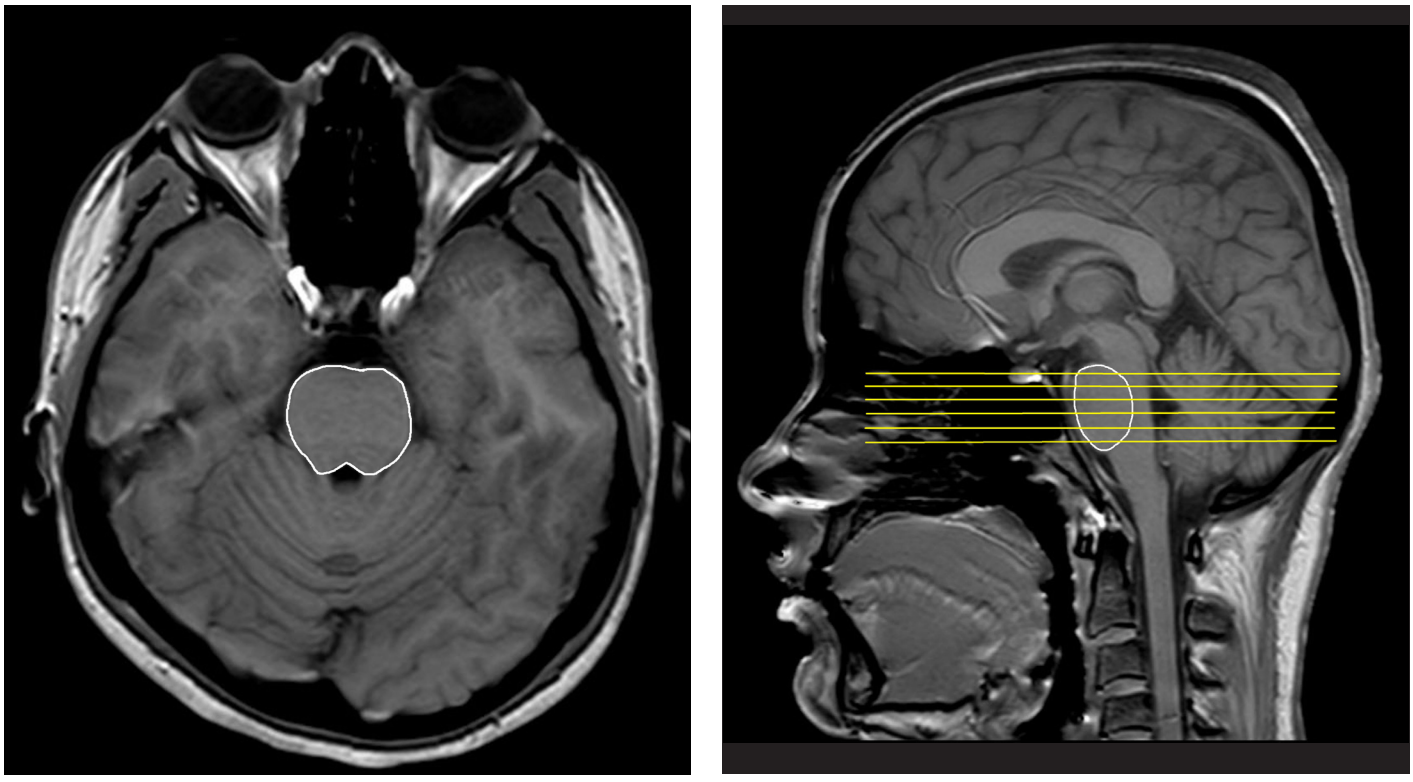
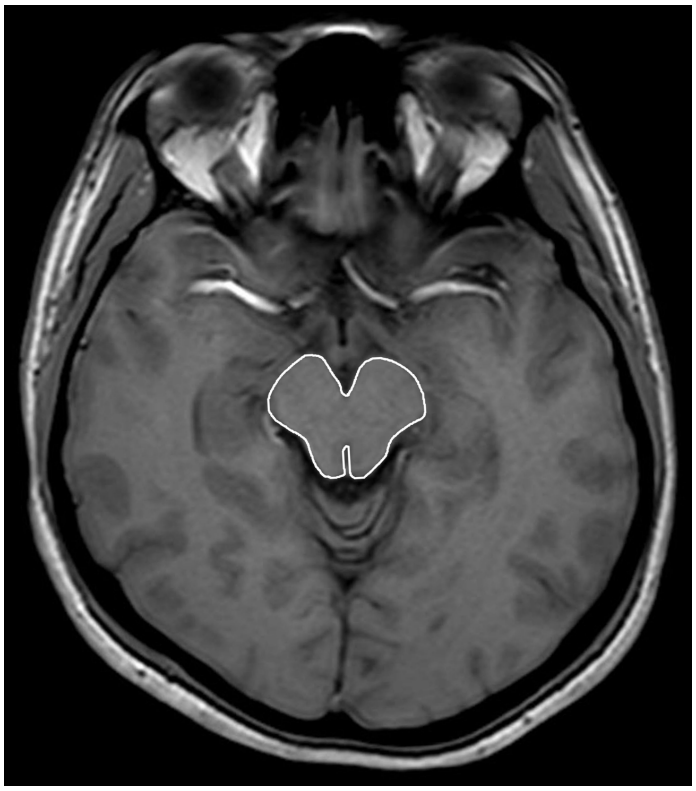


Figure 1. **A-** Measurement of the pons area in axial T1W images, **B-** Sections passing through the pons in sagittal T1W images.



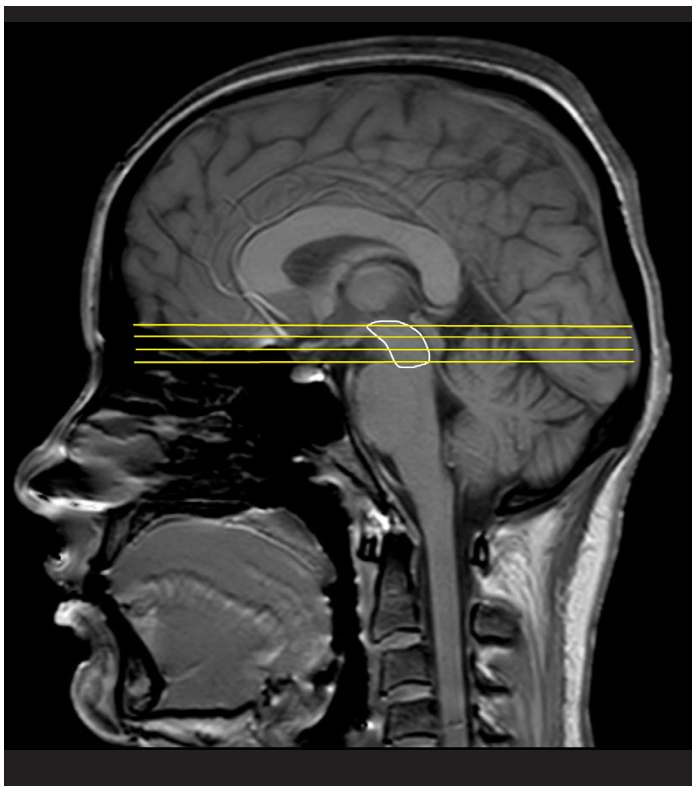
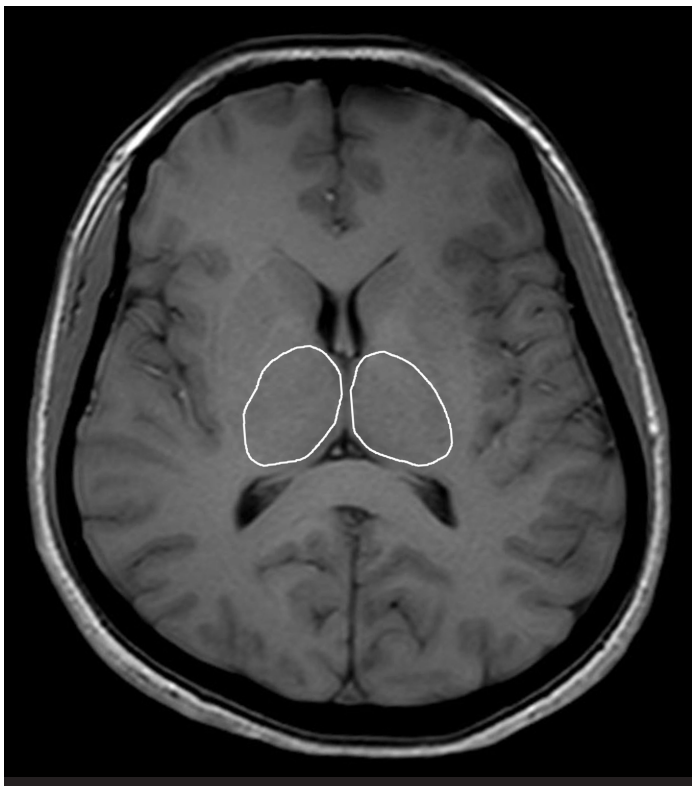


Figure 2. A- Measurement of the midbrain area in axial T1W images,

B- Sections passing through the midbrain in sagittal T1W images



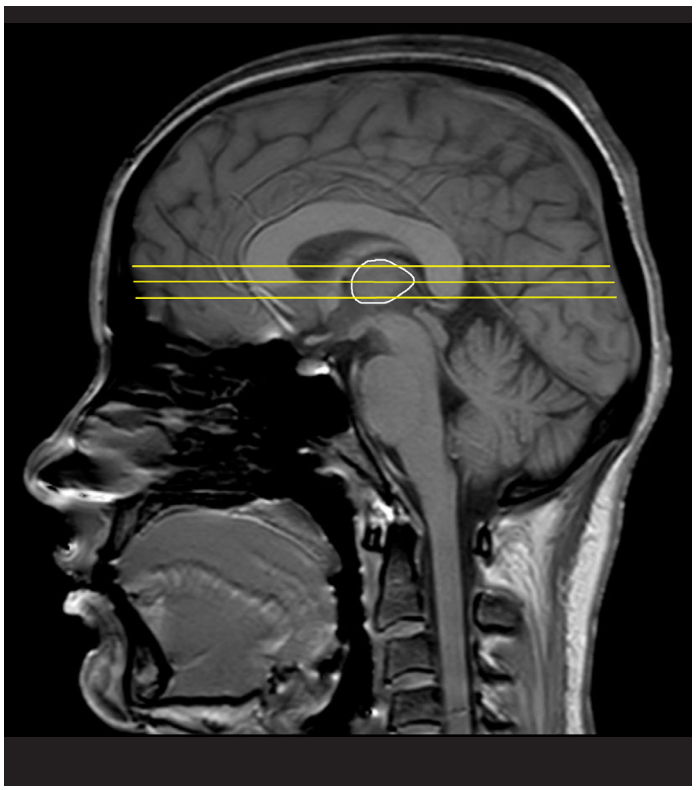
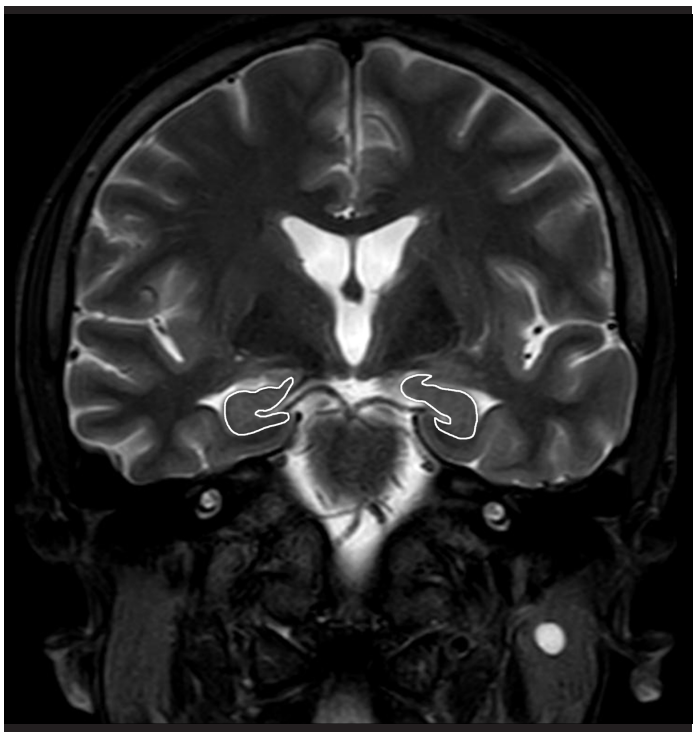


Figure 3. A- Measurement of bilateral thalamus area in axial T1W images,

B- Sections passing through the thalamus in sagittal T1W images.



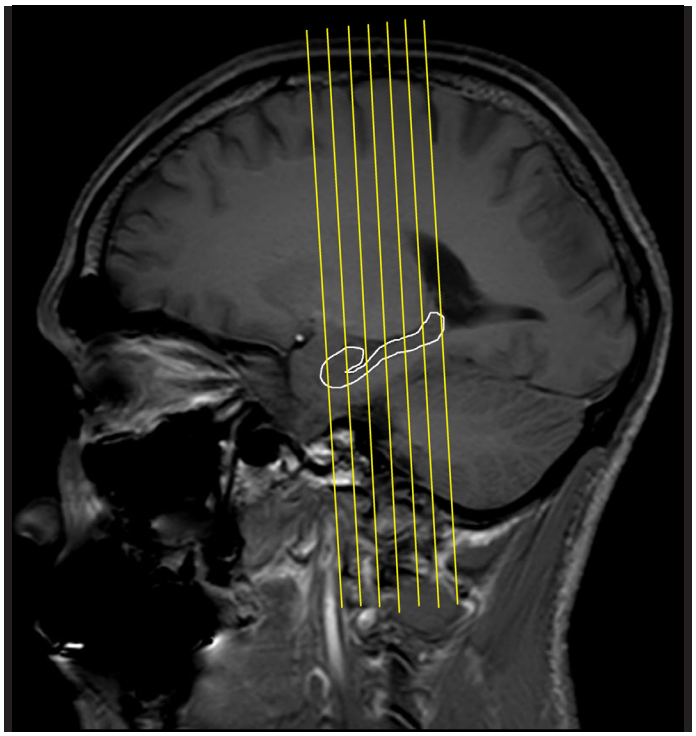


Figure 4.A-Measurement of bilateral hippocampus area in coronal T2W images,

B- Sections passing through the hippocampus in sagittal T1W images.

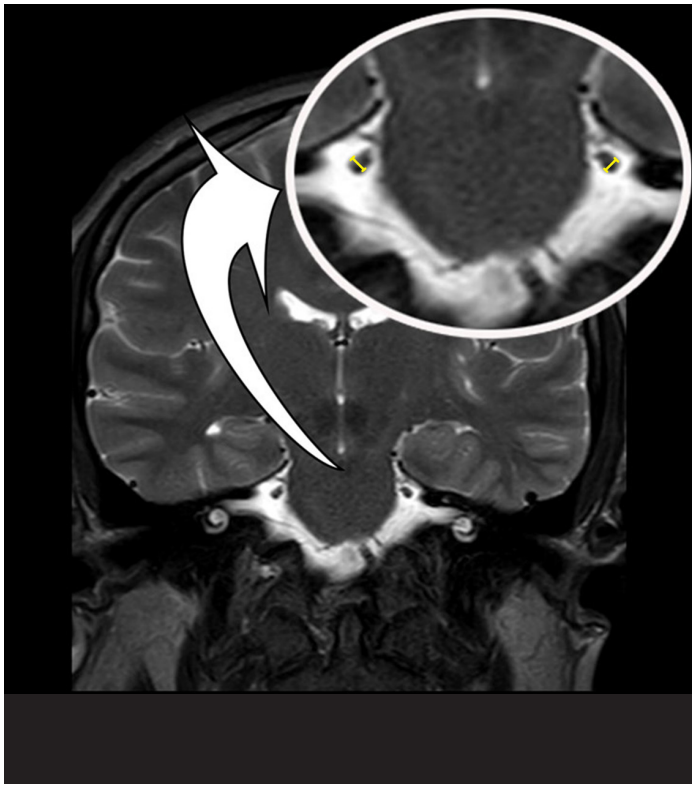


Figure 5. The appearance of both trigeminal nerve in coronal T2W images (white arrows), measurement technique in magnified images.

Statistical Analysis

Data analysis for this study was performed using SPSS for Windows version 21.0 ("SPSS, INC, an IBM Company, Chicago, Illinois"). Initially, the Kolmogorov-Smirnov test was applied. Non-parametric tests were conducted if the p-value was < 0.05, while parametric tests were used if the p-value was > 0.05. The statistical methods employed included the "Chi-square test, independent samples t-test, paired samples t-test, Pearson correlation, and Spearman's rank correlation coefficient". A p-value of less than 0.05 was deemed statistically significant.

RESULTS

In the cluster headache (CH) group, there were 13 males (43.3%) and 17 females (56.7%). The control group comprised 12 males (40.0%) and 18 females (60.0%), with no significant gender distribution differences between the two groups ($p=0.793$, $\chi2=0.069$). Age differences between the groups were not significant ($p>0.05$) (Table 1).

Pons, Midbrain, Bithalamic, and Hippocampus Volumes

Measurements for pons, midbrain, bithalamic, and hippocampus volumes in both the CH and control groups are shown in Table 1 and Figure 6.

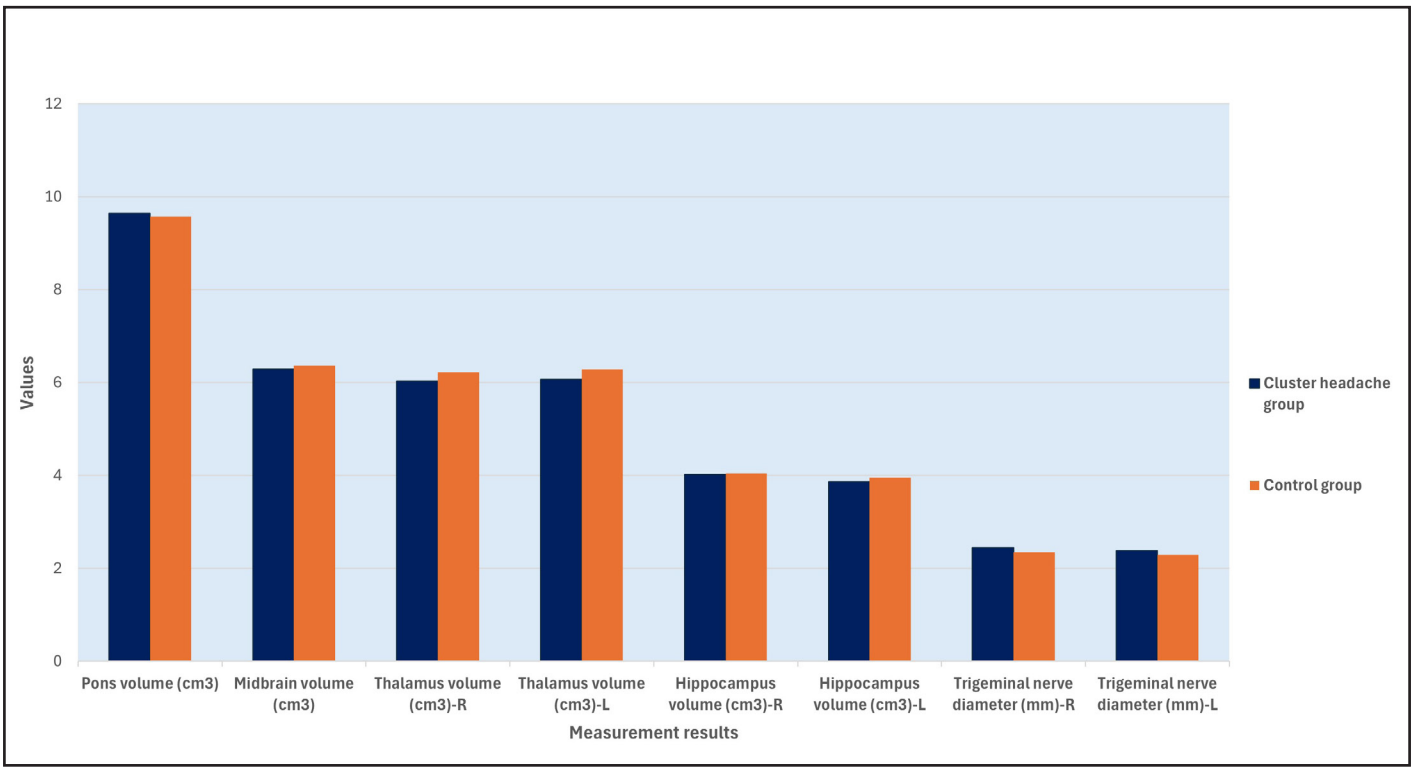


Figure 6. Measurement results for pons, midbrain, bithalamic, and hippocampus volumes in both the CH and control groups

Table 1. Measurement results in the cluster headache and control groups

		Group 1 (Cluster headache) (n=30)			Group 2 (Control group) (n=30)			P*
		Median	Std.Dev.	Mean	Median	Std.Dev.	Mean	
Age		35.27	37.00	8.15	35.20	36.00	7.51	0.974
Measurement results								
Pons volume (cm^3)		9.64	9.70	1.64	9.57	9.20	1.46	0.849
Midbrain volume (cm^3)		6.29	6.27	1.40	6.36	6.05	1.39	0.855
Thalamus volume (cm^3)	R	6.03	5.63	1.33	6.22	5.93	1.07	0.553
	L	6.07	5.70	1.35	6.28	6.12	1.11	0.523
	P**	0.027			0.124			
Hippocampus volume (cm^3)	R	4.02	3.97	0.68	4.04	4.25	0.88	0.930
	L	3.87	3.75	0.66	3.95	4.15	0.86	0.698
	P**	0.019			0.045			
Trigeminal nerve diameter (mm)	R	2.45	2.45	0.54	2.34	2.30	0.46	0.407
	L	2.38	2.42	0.47	2.29	2.31	0.44	0.447
	P**	0.131			0.273			

*p value shows the results of independent samples t-test

**p value shows the results of paired samples t-test

Table 2. Correlation test results in the cluster headache group

			Pons Volume (cm^3)	Midbrain volume (cm^3)	Thalamus volume (cm^3)		Hippocampus volume (cm^3)		Trigeminal nerve diameter (mm)	
			R	L	R	L	R	L		
Pons volume (cm^3)		r		0.124	0.382	0.383	0.549	0.501	0.064	0.132
		P*		0.515	0.037	0.037	0.002	0.005	0.735	0.487
Midbrain volume (cm^3)		r	0.124		0.582	0.588	-0.016	-0.022	0.399	0.355
		P*	0.515		0.001	0.001	0.933	0.909	0.029	0.054
Thalamus volume (cm^3)	R	r	0.382	0.582		0.998	0.266	0.212	0.246	0.273
		P*	0.037	0.001		0.000	0.155	0.260	0.191	0.144
	L	r	0.383	0.588	0.998		0.277	0.217	0.258	0.277
		P*	0.037	0.001	0.000		0.138	0.249	0.168	0.138
Hippocampus volume (cm^3)	R	r	0.549	-0.016	0.266	0.277		0.878	0.190	0.176
		P*	0.002	0.933	0.155	0.138		0.000	0.316	0.352
	L	r	0.501	-0.022	0.212	0.217	0.878		0.168	0.191
		P*	0.005	0.909	0.260	0.249	0.000		0.375	0.312
Trigeminal nerve diameter (mm)	R	r	0.064	0.399	0.246	0.258	0.190	0.168		0.879
		P*	0.735	0.029	0.191	0.168	0.316	0.375		0.000
	L	r	0.132	0.355	0.273	0.277	0.176	0.191	0.879	
		P*	0.487	0.054	0.144	0.138	0.352	0.312	0.000	
Age		r	0.061	0.196	0.018	0.032	-0.096	-0.203	-0.025	-0.066
		P*	0.747	0.299	0.924	0.866	0.613	0.281	0.896	0.730
Gender (Code 1: Male, Code 2: Female)		r	-0.058	-0.214	-0.222	-0.229	-0.374	-0.265	-0.238	-0.070
		P**	0.759	0.256	0.238	0.223	0.042	0.158	0.206	0.713

* p value shows the results of Pearson correlation test

** p value shows the results of Spearman's correlation rho efficient test

No significant differences were found between the pons (p=0.849), midbrain (p=0.855), bithalamic ($p=0.553^{Right}$, $p=0.523^{Left}$), and hippocampus volumes ($p=0.930^{Right}$, $p=0.698^{Left}$) of the CH and control groups. Within the CH group, the volume of the left thalamus was notably greater than that of the right thalamus (p=0.027) (see Table 1). In both the CH (p=0.019) and control (p=0.045) groups, the right hippocampus volume was significantly larger compared to the left hippocampus volume (Table 1).

Trigeminal Nerve Diameters

Trigeminal nerve diameters did not show significant differences between the CH and control groups ($p=0.407^{Right}$, $p=0.447^{Left}$). Moreover, there were no significant differences in the diameters of the right and left trigeminal nerves within either group (Table 1).

Correlation Test Results in CH Group

Correlation analysis results for the CH group are provided in Table 2.

In the CH group, left thalamus and right hippocampus volumes were significantly higher than the contralateral side ($p<0.05$). In CH group, there were positive correlations between the pons and thalamus ($p=0.037^{Right}$ and $p=0.037^{Left}$) and hippocampus

volumes ($p=0.002^{Right}$, $p=0.005^{Left}$); midbrain and bithalamic volumes ($p=0.001^{Right}$, $p=0.001^{Left}$); and right trigeminal nerve diameter (p=0.029); thalamus and pons($p=0.037^{Right}$, $p=0.037^{Left}$); and midbrain volumes ($p=0.001^{Right}$, $p=0.001^{Left}$); right and left hippocampus volumes (p=0.000); right and left trigeminal nerve diameters (p=0.000). In females, right hippocampus volumes were smaller than those in males (r= -0.374, p=0.042) (Table 2).

DISCUSSION

CH is a primary headache disorder marked by intense, unilateral pain and accompanying "ipsilateral autonomic symptoms", falling under the category of trigeminal autonomic cephalalgias. It includes conditions such as "paroxysmal hemicrania, acute unilateral neuralgic headaches, and hemicranial continua", all contributing to the "trigeminal autonomic cephalalgia spectrum" [23]. CH affects less than 1% of the population and is more commonly observed in men [24,25]. The onset typically occurs between the ages of 20 and 40 years [24,25].

Several factors can trigger CH attacks. For instance, "subcutaneous histamine injections" induce attacks in 69% of patients. Other potential triggers include "seasonal changes, allergens, stress, or nitroglycerin". Alcohol may provoke attacks during a cluster period but not during remission. Approximately 50% of patients consume alcohol, and "80%" are heavy smokers [6]. Vascular changes, such as "extracranial temporal artery dilation" following the onset of pain, may be secondary to primary neuronal discharge [6].

Our findings indicated no significant differences in the volumes of the "pons, midbrain, bithalamic regions, or hippocampus" between the CH and control groups. Although there were no significant differences in trigeminal nerve diameters between the CH and control groups, the CH group exhibited a slightly larger average diameter (2.38±0.47 mm) compared to the control group (2.29±0.44 mm). A larger sample size might reveal more significant differences. In the CH group, female subjects had smaller right hippocampus volumes compared to males.

The exact pathophysiology of CH remains unclear (26,27). The cyclical nature of attacks suggests a disruption in biological rhythms, potentially involving central disinhibition of "nociceptive and autonomic pathways", especially within the trigeminal system controlled by the hypothalamus [28]. Our study's observation of a slightly increased trigeminal nerve diameter in CH patients may indicate an influence on the trigeminal pathways.

Cluster headaches typically follow a circadian and seasonal pattern, with frequent night-time attacks. This pattern suggests a significant role of the hypothalamus in the condition's pathophysiology. The daily attack cycle tends to last about an hour in men, indicating possible "gender-specific functional differences" in the hypothalamus [7,29].

Lee, et al [30] compared the "limbic structures" and covariance network in CH patients and healthy controls. Volumetric analysis of the "subcortical limbic structures" ("the hippocampus, amygdala, thalamus, mammillary body, hypothalamus, basal forebrain, septal nuclei, fornix, and nucleus accumbens") was performed. Patients with cluster headaches showed significant alterations in the "limbic covariance network". They found that the left hippocampus volume of the CH patients was lower than the control group [30]. In the present study, no significant differences were detected between hippocampus volumes of the CH and control group. However, in the CH group, the left hippocampus volume was significantly lower than the right hippocampus volume.

"Functional imaging with PET" shows ipsilateral hypothalamus activation during CH attacks [23]. Long-term "high-frequency electrical stimulation of the posterior hypothalamus with an implanted electrode" may relieve the symptoms of this disorder [4,31,32].

In the MRI-diffusion study of Király et al. [33], the size of subcortical structures ("caudate, putamen, and thalamus") and diffusion parameters were normal in controls. However "right amygdala's mean fractional anisotropy, right caudate nucleus' mean axial diffusivity parallel (AD) and diffusion values, and right pallidum's radial diffusion (RD) were higher in CH patients. The mean anisotropy of the right pallidum was lower in the CH group. Positive correlations were observed between left and right hippocampus volumes, as well as negative correlations between headache days and certain brain metrics such as AD values of the thalamus and mean diffusivity and RD values of the left hippocampus [33]. In the present study, the volume of the left thalamus was significantly greater compared to the right, while the volume of the left hippocampus was notably smaller than the right. Additionally, positive correlations were observed between the volumes of the pons, thalamus, and hippocampus; between the midbrain, bithalamic volumes, and the right

trigeminal nerve diameter; and between the volumes of the right and left hippocampus. These findings are consistent with those reported by Király et al. [33].

PET studies [3] have shown activation in the "ipsilateral inferior hypothalamic gray matter" during CH attacks, with "voxel-based morphometry" revealing structural abnormalities in this area [34]. Other research suggests that trigeminal nerve stimulation does not directly activate the hypothalamus [35], which supports the hypothesis that the hypothalamus plays a causative role in CH [7]. Dysfunctional interactions between pain matrix brain regions may lead to disinhibition of the "hypothalamic-trigeminal pathway", triggering CH attacks. Ipsilateral parasympathetic symptoms might be due to direct hypothalamic effects or peripheral stimulation via "the superior salivatory nucleus (SSN) parasympathetic efferents" [36,37].

Limitations

The limitations of our work are listed as the followings: (1) The most important limitation in our study is that we have performed manual volumetric analysis; and did not evaluate inter/intra-observer variability. To reduce this limitation, extensive studies have been conducted using empirical guidelines for determining anatomical boundaries. Automated volumetric analysis tools can be used in the future studies. (2) Lack of standardization in the measurements and the absence of normative data that would allow the physician to interpret bio-benchmark values in patient care. (3) Since the study is retrospective, the MRI sections include routine cranial MRI slices. It does not include sections with different MRI sequences specific to measurements.

CONCLUSION

As a conclusion, in CH patients left thalamus volume was higher; and left hippocampus volume was lower compared to the other side. No differences were found compared to the control group. There were positive correlations between pons, thalamus, midbrain and hippocampus volumes; and trigeminal nerve diameters. In CH patients, the limbic system and especially the left hippocampus may be affected and get lower in volumetric analysis. Additionally, the right thalamus is affected showing lower volume in CH patients.

Funding: None

Conflict of interest: The authors declare that there is no conflict of interest.

Informed Consent: There is no need to take informed consent because the data were evaluated retrospectively.

Ethical Approval: This study is retrospective. Ethics committee approval was obtained from Gaziantep University Clinical Researches Ethics Committee Decision Number: 2022/303, Date:28.09.2022).

Author Contributions: Conception: M.H.Ş.; N.B.M.; F.K. - Design: M.H.Ş.; N.B.M.; F.K. Data Collection and/or Processing: M.H.Ş.; F.K. - Analysis and/or Interpretation: N.B.M. - Literature: M.H.Ş.; N.B.M.; F.K. - Review: M.H.Ş.; N.B.M.; F.K. - Writing: N.B.M.; F.K.

REFERENCES

[1] Vila-Pueyo M, Hoffmann J, Romero-Reyes M, Akerman S (2019) Brain structure and function related to headache: Brainstem structure and function in headache. Cephalalgia. 39(13):1635-1660. https://doi.org/10.1177/0333102418784698

[2] San-Juan D, Velez-Jimenez K, Hoffmann J, Martínez-Mayorga AP, Melo-Carrillo A, Rodríguez-Leyva I, García S, Collado-Ortiz MÁ, Chiquete E, Gudiño-Castelazo M, Juárez-Jimenez H, Martínez-Gurrola M, Marfil A, Nader-Kawachi JA, Uribe-Jaimes PD, Darío-Vargas R, Villareal-Careaga J (2024) Cluster headache: an update on clinical features, epidemiology, pathophysiology, diagnosis, and treatment. Frontiers in Pain Research. 5:1373528. https://doi.org/10.3389/fpain.2024.1373528

[3] May A, Bahra A, Büchel C, Frackowiak RS, Goadsby PJ (1998) Hypothalamic activation in cluster headache attacks. Lancet. 352(9124): 275–278. https://doi.org/10.1016/S0140-6736(98)02470-2

[4] Russell, MB. (2004) Epidemiology and genetics of cluster headache. The Lancet Neurology. 3(5): 279-283. https://doi.org/10.1016/S1474-4422(04)00735-5

[5] Weiller C, May A, Limmroth V, Jüptner M, Kaube H, Schayck RV, Coenen HH, Diener HC (1995) Brain stem activation in spontaneous human migraine attacks. Nat Med. 1(7):658–660. https://doi.org/10.1038/nm0795-658

[6] Blanda M (2021) Cluster Headache. In: Singh NN (Ed). Medscape. Available from https://emedicine.medscape.com/article/1142459-overview#a2 Accessed online at 25

August 2022

[7] Hoffmann J, May A (2018) Diagnosis, pathophysiology, and management of cluster headache. Lancet Neurol. 17(1):75-83. https://doi.org/10.1016/S1474-4422(17)30405-2

[8] Islam J, Rahman MT, Ali M, Kc E, Park YS (2024) Potential hypothalamic mechanisms in trigeminal neuropathic pain: a comparative analysis with migraine and cluster headache. J Headache Pain. 25(1):205. https://doi.org/10.3389/fpain.2024.1373528

[9] Lee DA, Lee J, Lee H-J, Park KM (2022) Alterations of limbic structure volumes and limbic covariance network in patients with cluster headache. Journal of Clinical Neuroscience. 103:72-77. https://doi.org/10.1016/j.jocn.2022.07.003

[10] Liu H-Y, Chou K-H, Lee P-L, Fuh JL, Niddam DM, Lai KL, Hsiao FJ, Lin YY, Chen WT, Wang SJ, Lin CP (2017) Hippocampus and amygdala volume in relation to migraine frequency and prognosis. Cephalalgia. 37(14):1329-1336. https://doi.org/10.1177/0333102416678624

[11] Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition (2018) Cephalalgia. 38(1):1-211. https://doi.org/10.1177/0333102417738202

[12] Wei DY, Yuan Ong JJ, Goadsby PJ (2018) Cluster Headache: Epidemiology, Pathophysiology, Clinical Features, and Diagnosis. Annals of Indian Academy of Neurology. 21(Suppl 1):S3-S8. https://doi.org/10.4103/aian.AIAN_349_17

[13] May A, Swanson JW, Dashe JF (2014) Cluster headache: Epidemiology, clinical features, and diagnosis. J W Swanson (Ed), UpToDate, Retrieved from.

[14] Headache Classification Committee of the International Headache Society (1988) Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia. 8 (suppl 7): 1–96. PMID: 3048700.

[15] Giorgio A, De Stefano N (2013) Clinical use of brain volumetry. Journal of Magnetic Resonance Imaging. 37(1):1-14. https://doi.org/10.1002/jmri.23671

[16] Mrzilková J, Zach P, Bartoš A, Tintěra J, Řípová D (2012) Volumetric analysis of the pons, cerebellum and hippocampi in patients with Alzheimer's disease. Dementia and geriatric cognitive disorders. 34(3-4):224-234. https://doi.org/10.1159/000343445

[17] Hardcastle C, O'Shea A, Kraft JN, Albizu A, Evangelista ND, Hausman HK, Boutzoukas EM, Van Etten EJ, Bharadwaj PK, Song H, Smith SG, Porges EC, Dekosky S, Hishaw GA, Wu SS, Marsiske M, Cohen R, Alexander GE, Woods AJ (2020) Contributions of hippocampal volume to cognition in healthy older adults. Frontiers in Aging Neuroscience. 12:593833. https://doi.org/10.3389/fnagi.2020.593833

[18] Özdemir M, Soysal H, Eraslan Ö, Dilli A (2019) Normative hippocampal volumetric measurements using magnetic resonance imaging. Turkish Journal of Medical Sciences. 49(5):1464-1470. https://doi.org/10.3906/sag-1903-233

[19] Bathla G, Hegde A (2013) The trigeminal nerve: an illustrated review of its imaging anatomy and pathology. Clinical Radiology. 68(2):203-213. https://doi.org/10.1016/j.crad.2012.05.019

[20] Sen S, Bilgin SS, Atasever A (2020) Morphometric evaluation of trigeminal nerve and Meckel cave with 3.0 magnetic resonance imaging. Journal of The Anatomical Society of India. 69(1):31-36. https://doi.org/10.4103/JASI.JASI_38_19

[21] Tian P, Yang J, Deng S, Guo L, Qian H, Li F (2018) Magnetic resonance imaging study of morphological and microstructural changes in the trigeminal nerve in trigeminal neuralgia due to neurovascular compression. Int J Clin Exp Med. 11(3):2471-2476.

[22] Gunes A, Bulut E, Akgoz A, Mocan B, Gocmen R, Oguz KK (2018) Trigeminal nerve and pathologies in magnetic resonance imaging–a pictorial review. Polish Journal of Radiology. 83:e289-e296. https://doi.org/10.5114/pjr.2018.76921

[23] Khawaja SN, Scrivani SJ (2019) Trigeminal autonomic cephalalgia and facial pain: areview and case presentation. J Oral Facial Pain Headache. 33(1):e1–7. https://doi.org/10.11607/ofph.2143

[24] Bjørn Russell M (2004) Epidemiology and genetics of cluster headache. Lancet Neurol. 3(5):279–283. https://doi.org/10.1016/S1474-4422(04)00735-5

[25] Fischera M, Marziniak M, Gralow I, Evers S (2008) The incidence and prevalence of cluster headache: a meta-analysis of population-based studies. Cephalalgia. 28(6):614–618. https://doi.org/10.1111/j.1468-2982.2008.0159 2.x

[26] Holle D, Obermann M, Katsarava Z (2009) The electrophysiology of cluster headache. Curr Pain Headache Rep. 13(2):155-159. https://doi.org/10.1007/s11916-009-0026-9

[27] Mendizabal JE, Umana E, Zweifler RM (1998) Cluster headache: Horton's cephalalgia revisited. South Med J. 91(7): 606-617. https://doi.org/10.1097/00007611-199807000-00002

[28] Goadsby PJ (2002) Pathophysiology of cluster headache: a trigeminal autonomic cephalgia. Lancet Neurol. 1(4):251-257. https://doi.org/10.1016/s1474-4422(02)00104-7

[29] Lund N, Barloese M, Petersen A, Haddock B, Jensen R (2017) Chronobiology differs between men and women with cluster headache, clinical phenotype does not. Neurology. 88(11): 1069–1076. https://doi.org/10.1212/WNL.0000000000003715

[30] Lee DA, Lee J, Lee HJ, Park KM (2022) Alterations of limbic structure volumes and limbic covariance network in patients with cluster headache. J Clin Neurosci. 103:72-77. https://doi.org/10.1016/j.jocn.2022.07.003.

[31] Leone M, Franzini A, Bussone G (2001) Stereotactic stimulation of posterior hypothalamic gray matter in a patient with intractable cluster headache. N Engl J Med. 345(19):1428–1429. https://doi.org/10.1056/NEJM200111083451915

[32] Franzini A, Ferroli P, Leone M, Broggi G (2003) Stimulation of the posterior hypothalamus for treatment of chronic intractable cluster headaches: first reported series. Neurosurgery. 52(5): 1095–1099. PMID: 12699552.

[33] Király A, Szabó N, Párdutz Á, Tóth E, Tajti J, Csete G, Faragó P, Bodnár P, Szok D, Tuka B, Pálinkás É, Ertsey C, Vécsei L, Kincses ZT (2018) Macro- and microstructural alterations of the subcortical structures in episodic cluster headache. Cephalalgia. 38(4):662-673. https://doi.org/10.1177/0333102417703762

[34] May A, Ashburner J, Büchel C, McGonigle DJ, Friston KJ, Frackowiak RS, Goadsby PJ (1999) Correlation between structural and functional changes in brain in an idiopathic headache syndrome. Nat Med. 5(7):836–838. https://doi.org/10.1038/10561

[35] May A, Kaube H, Büchel C, Eichten C, Rijntjes M, Jüptner M, Weiller C, Diener CH (1998) Experimental cranial pain elicited by capsaicin: a PET study. Pain. 74:61–66. https://doi.org/10.1016/S0304-3959(97)00144-9

[36] Haane DY, de Ceuster LM, Geerlings RP, Dirkx TH, Koehler PJ (2013) Cluster headache and oxygen: is it possible to predict which patients will be relieved? A prospective cross-sectional correlation study. J Neurol. 260(10):2596-2605. https://doi.org/10.1007/s00415-013-7024-x.

[37] Leone M, Bussone G (2009) Pathophysiology of trigeminal autonomic cephalalgias. Lancet Neurol. 8(8):755–764. https://doi.org/10.1016/S1474-4422(09)70133-4

How to Cite;

Sahan MH, Bayar Muluk N, Kocturk F (2024) Evaluation of the Pons, Midbrain, Thalamus, Hippocampus, and Trigeminal Nerve with MRI in Patients with Cluster Headache. Eur J Ther. 30(6):797-807. https://doi.org/10.58600/eurjther2363