Cumhuriyet Sci. J., 43(4) (2022) 569-576
DOI: https://doi.org/10.17776/csj.1144272

Cumhuriyet Science Journal

| csj.cumhuriyet.edu.tr | Founded: 2002 ISSN: 2587-2680 e-ISSN: 2587-246X Publisher: Sivas Cumhuriyet University

Evaluation of Thalamus Volumes in Patients with Diabetic Polyneuropathy Using Magnetic Resonance Imaging Method

Aysegul Ozturk[1,a,*], Vedat Sabancioglullari[2,b], Yasar Tastemur[2,c], Ibrahim Oztoprak[3,d]

[1]*Departments of Medical Services and Techniques, Sivas Cumhuriyet University, Vocational School of Health Services, Sivas, Türkiye*
[2]*Departments of Anatomy, Sivas Cumhuriyet University, School of Medicine, Sivas, Türkiye*
[3]*Departments of Radiology, Canakkale On Sekiz Mart University, School of Medicine, Canakkale, Türkiye*
**Corresponding author*

Research Article

History
Received: 15/07/2022
Accepted: 09/12/2022

ABSTRACT

The neurological process in diabetes is not limited to peripheral nerves but also affects the central nervous system (CNS). In addition, magnetic resonance images (MRI) showing that this condition can occur early in the neuropathic process are also available. This study was conducted to investigate whether peripheral sensory nerve dysfunction causes changes in thalamus volume in patients with diabetic polyneuropathy (DPNP) who experience sensory loss. Our study is a retrospective study consisting of diabetes mellitus (DM), DPNP and a healthy control group, where brain MRI of 204 individuals aged between 20-90 with no neurological disorder that might affect thalamus. Morphometric measurements for thalamus and cerebrum volumetry were performed in conventional MRI. In order to measure the microstructural changes of thalamus, the apparent diffusion coefficient (ADC) was calculated by the diffusion-weighted imaging method. In conclusion of our measurements, it was found that individuals with DM and DPNP had a decrease in volume of both thalami($p<0.05$) and cerebrum($p<0.05$). However, no significant difference was found in ADC values($p>0.05$). According to the results of research, DM and DPNP affect not only the peripheral nervous system but also the CNS. This effect caused atrophy of thalamus and cerebrum in patients of all age groups.

Keywords: Diabetes mellitus, Diabetic polyneuropathy, Thalamus, Magnetic resonance imaging.

[a] *fztaysegul@yahoo.com* *https://orcid.org/0000-0001-8130-7968*
[b] *vsabanci@yahoo.com.tr* *https://orcid.org/0000-0001-9059-6554*
[c] *dryasar58@hotmail.com* *https://orcid.org/0000-0002-2016-0592*
[d] *ibrahimoztoprak@comu.edu.tr* *https://orcid.org/0000-0002-4334-0350*

Introduction

Diabetes Mellitus (DM) is a very common disease in the world and it is estimated that 629 million people will be affected by this disease by 2045 [1]. DM prevalence is constantly increasing with factors such as a rapidly rising population, aging, urbanization, increasing obesity, and sedentary life. One of the most important complications in patients with diabetes is diabetic neuropathy. 50% of patients with diabetic neuropathy have diabetic polyneuropathy [2-4].

Diabetic polyneuropathy is caused by an imbalance between destruction and repair of nerve fibers. Damage to the nerves affects autonomic and distal sensory fibers more. After the disease affects the nerve endings, symptoms first begin in the distal of the lower extremities, and then progress to the proximal. After exceeding knee level, it first affects the distal of the upper extremities, then the proximal and the distal sensory nerve fibers of the intercostal nerves. In rare cases, with the influence of the trigeminal nerve, there are complaints with regard to head region as well. Almost all sensory messages, such as heat and pain, are lost if the progression of the disease is not prevented [5-7].

The afferents of all these sensory messages end up in nuc. ventralis posterolateralis (VPL) core of thalamus before being transmitted to the cortex. Thalamus organizes the information to be transmitted and sends it to the relevant parts of the cortex [8].

Scientific studies in the literature on the effects of sensory nerve dysfunction on thalamus volume in adult diabetes and diabetic polyneuropathy population are quite limited. In this regard, our purpose is mainly to detect thalamus volumes belonging to diabetes, diabetic polyneuropathy and healthy adult population and to investigate whether sensory nerve dysfunction causes changes in thalamus volume, especially in patients with diabetic polyneuropathy who experience sensory loss.

Material and Method

Ethics Committee Approval

Prior to starting the study, permission was obtained from Sivas Cumhuriyet University Non-invasive Clinical Research Ethics Committee with decision No. 02/30 dated 20th February 2019.

Study Group

The patient group in the study is composed of 74 (45 females, 29 males) adult individuals with diabetes and 57 (29 females, 28 males) adult individuals with diabetic polyneuropathy, aged between 20 and 90, diagnosed with diabetes mellitus and diabetic polyneuropathy at Sivas Cumhuriyet University Faculty of Medicine between January 2013 and April 2019, who applied to Radiology Department of our hospital to have brain MRI.

The control group in the study is composed of 73 (44 females. 29 males) adult individuals aged between 20 and 90, not diagnosed with diabetes mellitus and diabetic polyneuropathy, whose MRI images are archived in the hospital and who do not have any psychological or neurological disorders.

Four hundred patient files were screened in order to form groups of the study we conducted retrospectively.

Patients with a diagnosis of infarction, lesions that occupy space in the brain, bleeding, etc. other than microinfarcts contained in MRI reports in screened files, were excluded from the study. Images of patients who did not have any pathology other than microinfarts in MRI reports or were considered normal were included in the study. Similarly, patients with psychological disorders, neurological deficits, or neurological examination positives were not included in the study.

MRI Protocol

The same imaging protocol was applied to all individuals included in the study. Morphometric MRI analysis; Routine brain MRI analysis was performed using 20 channel coils in 1.5 Tesla MRI devices

(Magnetom Aera, Siemens, Germany). Parameters in MRI images; T1 SE axial images; Slice thickness: 5 mm, TE: 5.6, TR: 402, FOV: 220, FA: 150, Matrix: 300x512, NSA: 3 T2 SE axial images; Slice thickness: 5 mm, TE: 102, TR: 4350, FOV:220, FA: 150, Matrix: 320x1024, NSA: 2 FLAIR axial images; Slice thickness: 5 mm, TE: 92, TR: 9000, FOV: 230, FA: 150, Matrix: 320x1024, NSA: 1

DAG was performed using an echo-planar (EP) imaging sequence (TR: 5000ms; TE: 130 ms; FA: 90/180; NEX: 1; FOV: 270 x 320 mm; matrix: 128 x 128; slice thickness: 5 mm; slice spacing: 2 mm; b value: 0 and 1000 s/mm2) To measure diffusion on three axes (x, y and z), diffusion gradients were applied in three orthogonal plans.

Image Analysis

T2-weighted MRI sequences were used for morphometric measurements of thalamus. In Coronal sections, measurements were performed on T2-weighted images passing through ventriculus lateralis and tertius. The vertical length of the thalamus was measured in Coronal sections, while the transverse length was obtained from sections in the axial plane [9]. The upper limit of thalamus in the coronal section was determined as the lateral ventricle and the lower limit was determined as the substantia nigra (Figure 1) [10]. For measurements in the axial section, the largest diameter image of the cranium containing the cornu anterior and cornu posterior of the ventriculus lateralis was used. The anterior border of the thalamus in the axial section was determined as the posterior of the foramen interventricularen, the posterior border was determined as the pulvinar thalami, the medial border was determined as the 3rd ventricle, the lateral border was determined as the crus posterior of the capsula interna [11]. Thalamus volume was obtained by multiplying the anteroposterior diameter, transverse diameter, vertical diameter of the thalamus, and the number π/6 (T1×T3×T5×π/6).

As for thalamus morphometry, the following measurements were made on T2-weighted axial and coronal MRI images (Figure 1).

T1: anteroposterior length of the left thalamus
T2: anteroposterior length of the right thalamus
T3: transverse length of the left thalamus
T4: transverse length of the right thalamus
T5: vertical length of the left thalamus
T6: vertical length of the right thalamus
Tl: volume of the left thalamus
Tr: volume of the right thalamus
Tt: total volume of the thalamus

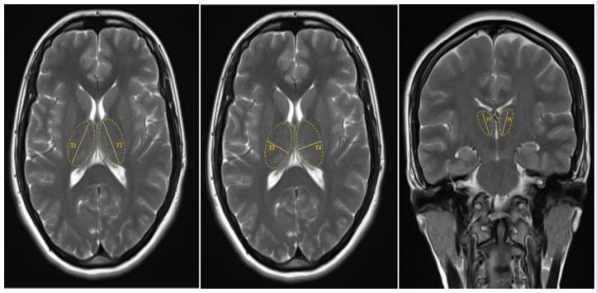

Figure 1. Measurement reference points for thalamus diameters in axial and coronal section

In T1 midsagittal sections, anteroposterior diameter of cerebrum (C1) was found by measuring the distance between polus frontalis and polus occipitalis, cerebrum height (C3) was found by measuring the distance between corpus mamillare and the peak point of cerebrum for cerebrum morphometry. In T2 axial sections, cerebrum transverse diameter (C2) was determined by measuring the distance between the two furthest points of the cerebral hemispheres [12]. Cerebrum volume was calculated by multiplying anteroposterior diameter, transverse diameter, height of cerebrum and the number π/6 (C1×C2×C3×π/6).

As for cerebrum morphometry, the following measurements were made on T2 axial and T1 sagittal MRI images (Figure 2).

C1: anteroposterior diameter of cerebrum
C2: transverse diameter of cerebrum
C3: cerebrum height
Ct: volume of cerebrum

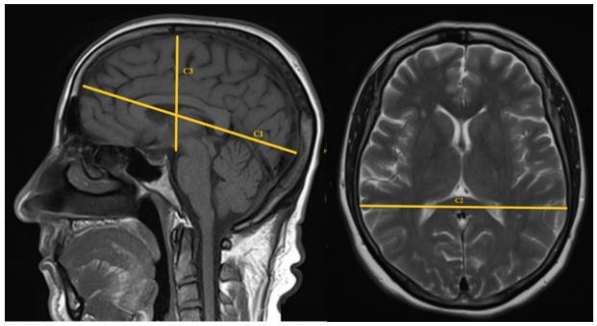

Figure 2. Measurement reference points for cerebrum in axial and coronal section

ADC maps were used to measure mean ADC value of thalamus quantitatively. In order to prevent contamination of other tissues with ADC value of thalamus, the capsula located in the lateral of both thalami were taken far enough from the interna and from the ventriculus tertius in medial, and in the central part, as wide a size as possible of the thalamus was selected. Stardardized ROIs (ROI: region of interest) were placed in thalami by considering circular area of analysis 0.5 cm^2 in order to determine mean ADC values of thalamus (Figure 3).

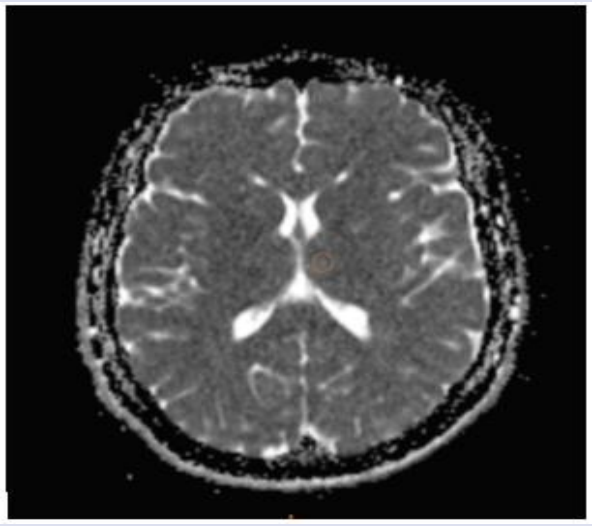

Figure 3. ADC map on thalamus in axial section

Statistical Analysis

The data obtained from our study were evaluated using SPSS 23.0 program. The normality of the data was evaluated using the Kolmogorov-Smirnov test. If the data met parametric conditions, it was analyzed using the independent sample t test for two independent groups and the F test (ANOVA) for more than two groups. Whereas ANOVA was used for comparison of more than two groups, Tukey test was used in those providing homogeneity hypothesis, and Tamhane's T2 tests were used in those, not providing homogeneity hypothesis, to determine which group was different from the others. Mann Whitney U test was used for two independent groups and Kruskal Wallis test was used for more than two independent groups, in groups not providing parametric test hypotheses. Level of significance was considered 0.05.

Results

A total of 204 individuals between the ages of 20 and 90 were included in the study, 118 (57.3%) of whom were female and 86 (42.3%) were male. Mean age of females was found to be 58.32±15.29; mean age of males was found to be 58.63±17.01; and total mean age was found to be 58.45±16.00.

Of the individuals included in the study, 73 were in healthy control group, 74 had DM, and 57 had diabetic polyneuropathy. The mean age was 60.89 in individuals with diabetic polyneuropathy, 59.00 in individuals with DM and 55.93 in healthy controls.

In our study, the size and volume of thalamus of DPNP, DM and healthy control group were divided into age groups and compared. According to the results obtained from the study, patients with DM and DPNP in all age groups had a decrease in left, right and total thalamus volume compared to healthy individuals ($p<0.05$) (Figure 4).

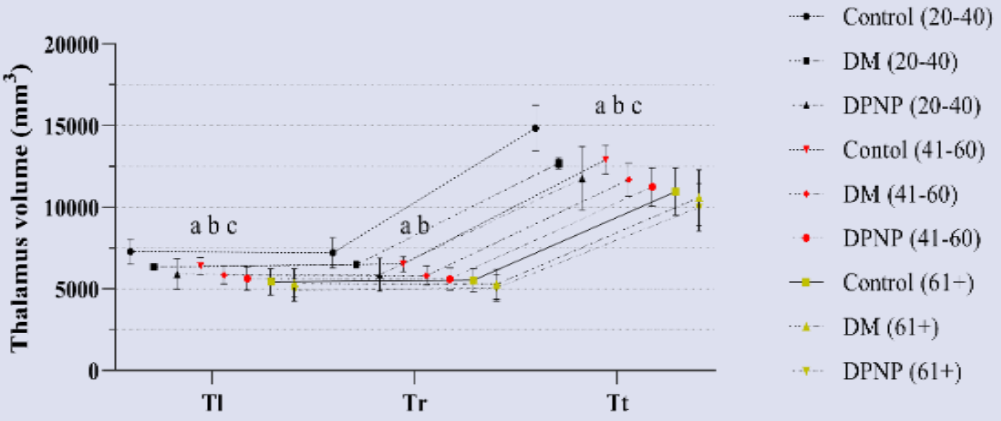

Figure 4. Thalamus volumes of all age groups in the Diabetic Polyneuropathy, Diabetes Mellitus and control; data were expressed as mean ±SD. In all groups; a comparison of thalamus volumes (mm^3) in individuals age 20-40, 41-60, 61 plus. a; $p < 0.05$ 20-40 age (DPNP, DM, Control), b; $p < 0.05$ 41-60 age (DPNP, DM, Control), c; $p < 0.05$ 61 plus (DPNP, DM, Control) (*Tl;volume of the left thalamus, Tr; volume of the right thalamus, Tt; total volume of the thalamus, DM; diabetes mellitus, DPNP; Diabetic polyneuropathy).*

In our study, it was found that thalamus anteroposterior and transverse lengths in all age groups were smaller in individuals with DM and DPNP ($p<0.05$) (Figure 5). The fact that diseases caused neuronal and axonal loss in thalamus resulted in atrophy in thalamus volume.

Size and volume of thalamus of DM, DPNP and healthy individuals were compared by gender. Left, right, and total thalamus volumes in males and females of all ages were negatively affected by DPNP and DM ($p<0.05$). DM and DPNP similarly affected both genders, causing a decrease in thalamus volume.

Morphometric measurements of thalamus of DPNP, DM and healthy individuals were compared by age groups. According to these results, the size and volume of thalamus of each patient and healthy person decreased with the effect of aging ($p<0.05$).

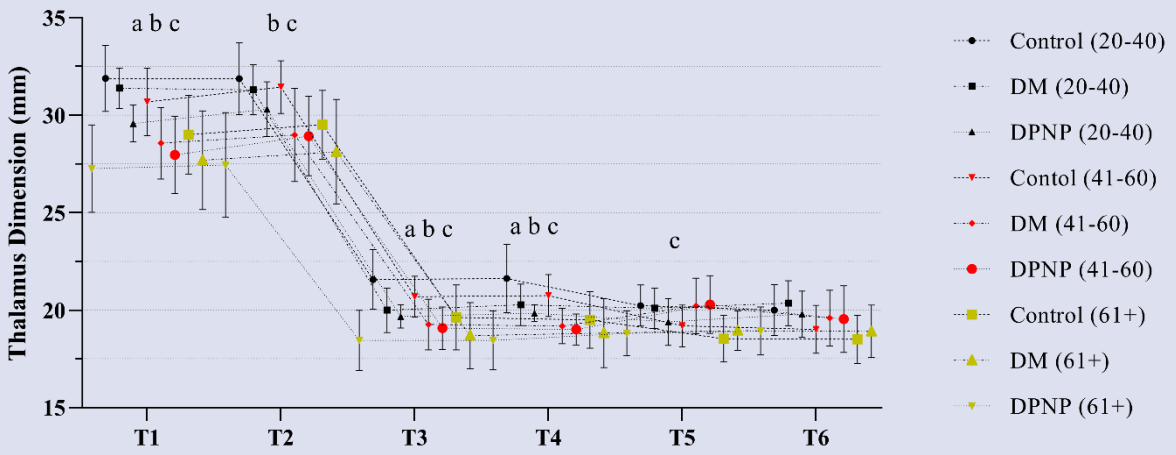

Figure 5. Thalamus dimensions of all age groups in the Diabetic Polyneuropathy, Diabetes Mellitus and control; data were expressed as mean±SD. In all groups; Comparison of thalamus dimensions (mm) in individuals age 20-40,41-60,61 plus. a; $p < 0.05$ 20-40 age (DPNP, DM, Control), b; $p < 0.05$ 41-60 age (DPNP, DM, Control), c; $p < 0.05$ 61 plus (DPNP, DM, Control)(T1; anteroposterior length of the left thalamus, T2; anteroposterior length of the right thalamus, T3; transverse length of the left thalamus, T4; transverse length of the right thalamus, T5; vertical length of the left thalamus, T6; vertical length of the right thalamus, DM; diabetes mellitus, DPNP; Diabetic polyneuropathy).

In our study, size and volume of cerebrum of DM, DPNP and healthy individuals were analyzed based on ages. In our results, volume, anteroposterior and transverse diameter ıf cerebrum of individuals aged 2 to 40 years are smaller in patients compared to the healthy individuals ($p<0.05$). There is a significant difference in C3 and Ct parameters in 41-60 age group and C2, C3 and Ct parameters in individuals 61 and above age group ($p<0.05$). According to these results, it was concluded that patients with DM and DPNP in the all age groups had a loss in cerebrum size and volume (Figure 6, Figure 7).

When we examined cerebrum sizes of individuals with DM and DPNP based on age groups, it was found that there was a decrease in C3 and Ct parameters of individuals with DPNP and all parameters of individuals with DM, as age increases ($p<0.05$). Similarly, a decrease in cerebrum volume was found in healthy individuals, as age increases ($p<0.05$).

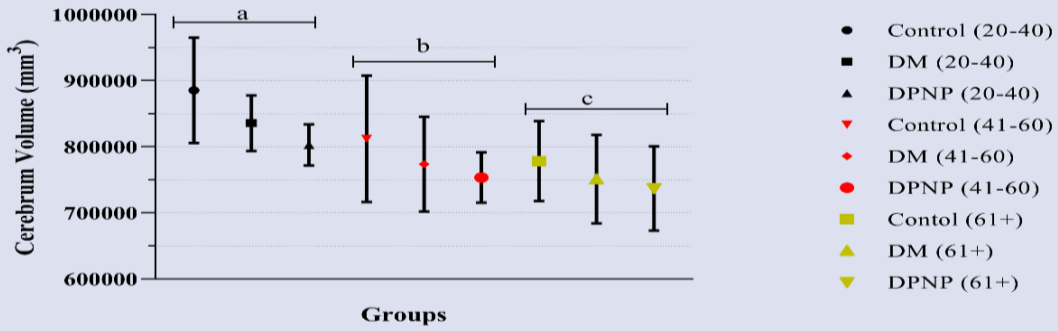

Figure 6. Cerebrum volumes of all age groups in the Diabetic Polyneuropathy, Diabetes Mellitus and control; data were expressed as mean±SD. In all groups; Comparison of cerebrum volumes (mm3) in individuals age 20-40,41-60,61 plus. a; $p < 0.05$ 20-40 age (DPNP, DM, Control), b; $p < 0.05$ 41-60 age (DPNP, DM, Control), c; $p < 0.05$ 61 plus (DPNP, DM, Control). *(DM; diabetes mellitus, DPNP; Diabetic polyneuropathy).*

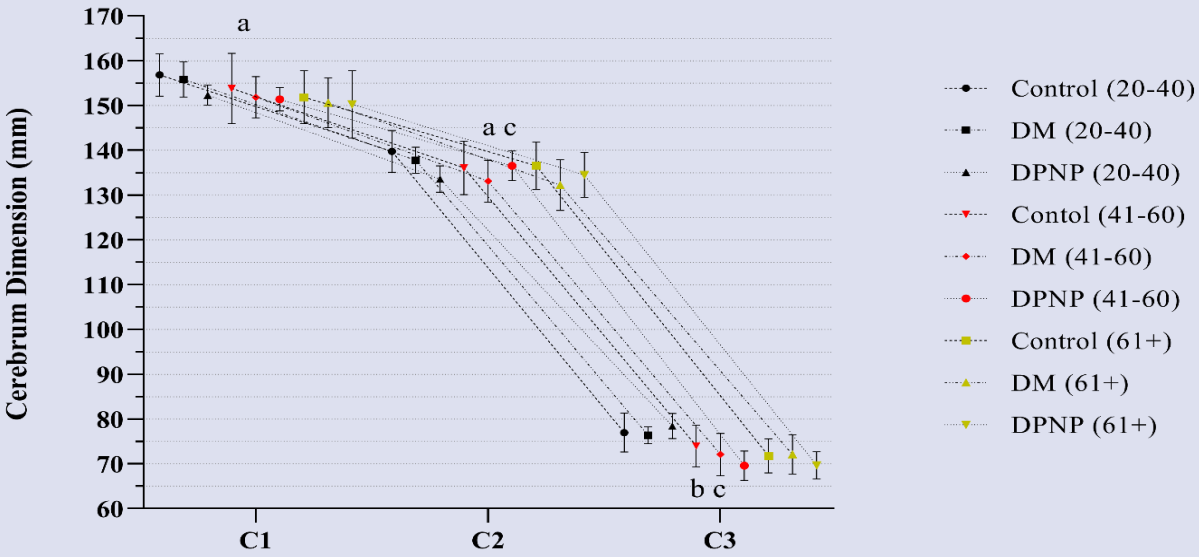

Figure 7. Cerebrum dimensions of all age groups in the Diabetic Polyneuropathy, Diabetes Mellitus and control; data were expressed as mean±SD. In all groups; Comparison of cerebrum dimensions (mm) in individuals age 20-40,41-60,61 plus. a; $p < 0.05$ 20-40 age (DPNP, DM, Control), b; $p < 0.05$ 41-60 age (DPNP, DM, Control), c; $p < 0.05$ 61 plus (DPNP, DM, Control).(C1; anteroposterior diameter of cerebrum, C2; transverse diameter of cerebrum, C3; cerebrum height, DM; diabetes mellitus, DPNP; Diabetic polyneuropathy).

In our study, mean ADC values of thalamus of DPNP, DM and healthy individuals were examined using the DAG method, which reflects the structural and dynamic properties of brain tissue. In conclusion of our results, it was found that the mean ADC value of thalamus in all age groups was higher in DPNP and DM compared to healthy ones, but was not statistically significant ($p>0.05$) (Figure 8).

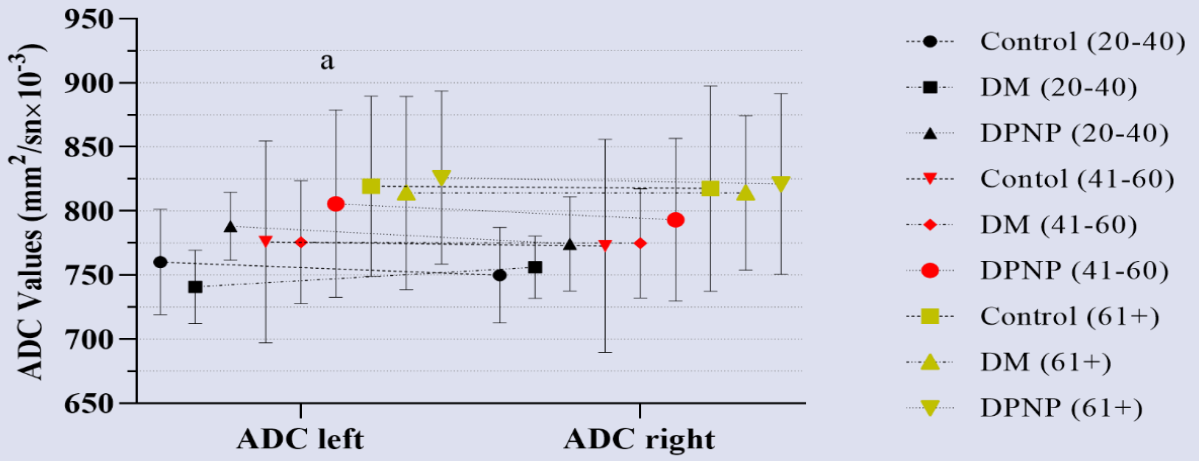

Figure 8. Thalamus ADC values of all age groups in the Diabetic Polyneuropathy, Diabetes Mellitus and control; data were expressed as mean±SD. In all groups; Comparison of thalamus ADC values (mm2/sn×10-3) cerebrum dimensions (mm) in individuals age 20-40,41-60,61 plus. a; $p < 0.05$ 20-40 age (DPNP, DM, Control), b; $p < 0.05$ 41-60 age (DPNP, DM, Control), c; $p < 0.05$ 61 plus (DPNP, DM, Control) *(DM; diabetes mellitus, DPNP; Diabetic polyneuropathy)*.

Discussion

Diabetic neuropathy, one of the most common complications in diabetes, is observed in almost half of diabetic patients [2, 13].

Recent studies have shown that the neurological process in diabetes is not limited to peripheral nerves but also affects the central nervous system. In addition, MRI images showing that this condition can occur early in the neuropathic process are also available [14]. Therefore, researching whether cerebral structures are affected by neuropathic process, assists to have more comprehensive information about the disease.

Selvereajah et al. found grey matter volume of patients with painful diabetic peripheral neuropathy (DPN) to be 585.4 cm^3 and grey matter volume pf patients with painless diabetic peripheral neuropathy (DPN) to be 599.6 cm^3 and peripheral grey matter volume of healthy

control individuals to be 626.5 cm^3 in the study that they examined cerebral volume. In this study, it was found that the gray matter volume of both the painful and painless DPN group decreased at similar rates compared to the healthy control individuals. [15].

As for thalamus, grey matter structure of cerebrum, they stated that volume of thalamus of individuals with painful and painless distal symmetric polyneuropathy (DSP) is less than that of healthy individuals [15].

In their study, Gustin et al. [16] stated that neuropathic pain leads to changes in brain structures. In this study, individuals with trigeminal neuropathic pain (TNP) were compared with individuals with temporomandibular pain (TMP) and healthy volunteers. In conclusion of the study, they found significant volume loss in the nucleus accumbens and thalamus of individuals with TNP, while they reported no volume loss in individuals with TMPD.

Our results are also similar to those in the literature. Accordingly, DM and DPNP lead to atrophy in volume of thalamus. Unlike other studies, these diseases were found to be effective in all age groups.

In their thalamic morphometric measurements, compared with regards to age factor of healthy individuals, Mohammadi et al. [9] stated that anteroposterior, transverse, and vertical length of thalamus of individuals aged 31 to 40 was the highest, while individuals aged 51 and above had the shortest thalamic length. In conclusion of their study, they showed that thalamic sizes slowly increase until the age of 31 to 40 and increasingly decrease after the age of 51.

In their study with regard to age groups in healthy individuals, Sen et al. found no difference in terms of thalamic size and volume [11].

According to the conclusion of our study, thalamic morphometric measurements of DPNP, DM, and healthy individuals were found to decrease as age increases .

In their study with regards to gender, Mohammadi et al. found anteroposterior, transverse, and vertical lengths of thalamus of males to be longer than those of females [9].

In their study that they compared thalamic sizes by gender, Sen et al. [11], reported that transverse diameter of thalamus was longer in males, however vertical and anterposterior diameters were similar in both genders.

In our study, anteroposterior and vertical diameters of thalamus in individuals with DM aged 20-40 years, transverse and vertical diameter sizes of thalamus in individuals with DPNP were longer in males compared to females, while in individuals aged 41-60 and 61 years and older, there were no significant differences between the genders. In healthy individuals in all age groups, the thalamus transverse diameter and volume were statistically greater in males than females.

Cerebral volumetric measurements cannot identify tissue properties, i.e. cellular components, but help to measure the extent and magnitude of disease effects. Volumetric measurements of cerebral structures provide valuable information about the pathological mechanisms of diseases. In this context, MRI measurements of volume of cerebrum provide reliable and strong inferences about the disease, providing information about clinical status and progress [17].

In their study, Musen et al. [18] stated that grey matter volume in the cerebellar region and occipital and temporal lobe of patients with Type 1 diabetes was reduced by 4.5%.

In their study, Selverajah et al. [15] found brain volume in painful DPN to be 1470 cm^3, in painless DPN to be 1470 cm^3 and in healthy individuals to be 1510 cm^3. In general, cerebral grey matter volume of patients with DPN decreased by 5.4% compared to healthy controls. This study also showed that the regions first affected by the neuropathic process were the primary somatosensory cortex, supramarginal gyrus, and cingulate cortex.

Ge et al. [19] examined the effects of aging on cerebral grey matter, white matter, and total volume in healthy individuals. In their results, it was stated that the loss of grey matter volume began at the age of 20 and decreased at a constant rate, while the volume of white matter increased until the age of 40, and then decreased rapidly. As a result of changes in the volume of white and grey matter, they reported that the total cerebral volume did not change until the age of 40-50, and the loss of volume began after this age.

In their study, in which they compared the cerebral volume of females and males associated with aging, Gut et al. [20], compared the age group below and above the age of 55. According to these results, they stated that there was a negative correlation between aging and cerebral volume (r= -0.2) and cerebral volume loss occurs as a result of neuronal atrophy.

In their study, in which they examined the white matter volume of healthy individuals, Liu et al. [21] found that there was a significant difference ($p<0.05$) between young (20-40 ages), middle-aged (41-59), and old individuals (60-78). In conclusion of the study, they reported that the volume of white matter gradually increased until the age of 40, was at its highest level around the age of 50, and decreased rapidly after the age of 60.

In our results, it was concluded that size and volume of cerebrum of healthy individuals aged 20-40, 41-60, 61 years and older decreased depending on age. A decrease in cerebral volume can be caused by structural changes such as myelin loss and axonal destruction [22, 23, 24], increased perivascular spaces [25, 26], and dilatation of gliosis [27,28].

Conventional MRI cannot provide sufficient information about local perfusion changes in structures, and biochemical and microstructural differences. Therefore, various MRI methods (Diffusion Weighted Imaging (DWI), perfusion MRI, magnetization transfer imaging, and MRI spectroscopy) are used to obtain quantitative information about the data.

In their study, in which they used MRI spectroscopy to measure the change of cerebrum metabolites in diabetic neuropathic pain, Sorensen et al., found the amount of thalamic NAA (N-Acetylaspartate) in healthy individuals to

be higher than that of patients with diabetic neuropathy [29]. The decrease in NAA resonance is thought to be associated with neuronal/axonal loss, neuron viability, and dysfunction [30].

In their study they conducted with MRI spectroscopy in individuals with type 1 diabetes, diabetic neuropathy, and healthy individuals, Selvarajah et al. found the same voxel in two different TE (echo time) (short TE, long TE). Decreased NAA signal obtained in short TE indicates irreversible neuronal loss/contraction, and a decrease in the NAA/creatine ratio in long TE indicates a state of reversible neuronal damage/dysfunction. According to the study's conclusion, the NAA/creatine ratio in long TE decreased in Type 1 diabetes and diabetic neuropathy compared to healthy individuals however, there was no significant difference in NAA resonance in short TE. They reported that this condition reflected thalamic neuronal dysfunction in patients with DPN rather than neuron death [31].

In their MRI perfusion study, Selvarajah et al. [32], measured cerebral blood volume (rCBV), one of the markers of cerebral microvascular perfusion, in individuals with painful and painless diabetic peripheral neuropathy (DPN) and healthy individuals. According to the conclusion of the study, amount of rCBV of individuals with painful and painless DPN is higher compared to the healthy individuals. They stated that this situation might be caused by high thalamic neuronal activity. In another study conducted on experimental diabetes, it was similarly reported that increased neuronal activity caused neuropathic pain [33]. Studies conducted have shown that thalamic neurons can act as central generators or amplifiers of pain in diabetes.

Detection and evaluation of differentiation in brain tissue that occurs in the aging process is possible by the DAG method [34].

Karasu et al. [35] reported that the mean ADC values of corpus callosum, a white matter mass in the brain, increased significantly with the effect of aging. Mean ADC value of individuals aged 60 and below was found to be 730±44 $mm^2/sn \times 10^{-3}$, and that of individuals aged 60 and above was found to be 758±26 $mm^2/sn \times 10^{-3}$.

Chun et al. [36] stated that the increase in diffusion with aging may be caused by the decrease in myelin fibrils in white matter. Therefore, the decrease in the myelin layer facilitates the diffusion ability of water [37].

Engelter et al. [37], in their study in which they examined the ADC values of the thalamus, found that the mean ADC value of the thalamus of individuals aged 60 and above increased significantly compared to the mean value of the thalamus of individuals aged 60 and below. According to this result, mean ADC values of thalamus increase as age increases.

In our study, the mean ADC values of thalamus of individuals were compared based on the age variable. While the mean ADC value of thalamus increased due to aging in individuals with DM and healthy individuals, no difference was found in individuals with DPNP. Differences in the structural properties of tissues are suggestive that they might also cause diffusibility of water.

Conclusion

In conclusion the results obtained from our study, it was shown that diabetes mellitus and diabetic polyneuropathy are not limited to peripheral nervous system involvement, but also affect the central nervous system. Besides, DM and DPNP can negatively affect volume of thalamus and cerebrum in individuals of all age groups, leading to atrophy. In this direction, we believe that clinical and laboratory results as well as MRI results can be useful in determining DM and DPNP diseases.

Besides thalamic nuclei are associated with motor activity, limbic system, pain, and visceral activity. A decrease in size volume of the thalamus in diabetes mellitus and diabetic polyneuropathy might cause dysfunctions in these activities. Therefore, we believe that regular patient follow-up is necessary to prevent complications that will negatively affect the lives of individuals with these diseases.

Acknowledgments

The authors would like to thank the Sivas Cumhuriyet University, Sivas, Turkey, for providing the necessary facilities to conduct this study. We would like to thank Research Assistant Handan Gunes for helpful critique and Assistant Professor Ahmet Sevki Taskiran for his critical suggestion and article editing.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] International Diabetes Federation. International diabetes federation: IDF Atlas. Brussels: Belgium (2017).

[2] Dyck P. J., Kratz K. M., Karnes J. L., Litchy W. J., Klein R., Pach J. M., Wilson D. M., O'Brien P. C., Melton L. J., 3rd & Service F. J. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study, *Neurology*, 43 (1993) 817–24.

[3] Pop-Busui, R., Boulton, A. J., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., Sosenko, J. M., & Ziegler, D. (2017). Diabetic Neuropathy: A Position Statement by the American Diabetes Association, *Diabetes Care*, 40(1) (2017) 136–154.

[4] Tesfaye, S., Chaturvedi, N., Eaton, S. E., Ward, J. D., Manes, C., Ionescu-Tirgoviste, C., Witte, D. R., Fuller, J. H. Vascular risk factors and diabetic neuropathy. Prospective epidemiological study showing that, apart from glycemic control, incident neuropathy is associated with modifiable cardiovascular risk factors, *N. Engl. J. Med.,* 352 (2005) 341–50.

[5] Said G., Diabetic neuropathy-A Review, *Nat. Clin. Prac. Neurol*., 3 (2007) 331-340.

[6] Albers JW., Diabetic Neuropathy: Mechanisms, Emerging Treatments and Subtypes, *Curr. Neurol. Neurosci. Rep*., 14 (2014) 473.

[7] Charnogursky G., Emanuele N.V., Emanuele M.A., Neurological Complications of diabetes, *Curr. Neuro.l Neurosci. Rep.,* 14 (2014) 457.

[8] McCormick D.A., Bal T., Sensory gating mechanisms of the thalamus, *Curr. Opin. Neurobiol.,* 4 (1994) 550–556.

[9] Mohammadi M.R., Hosseini S.H., Golalipour M.J., Morphometric measurements of the thalamus and interthalamic adhesion by MRI in the South-East of the Caspian Sea border, *Neurosciences*, 13(3) (2008) 272-275.

[10] Caetano S.C., Sassi R., Brambilla P., Harenski K., Nicoletti M., Mallinger A.G., Frank E., Kupfer D.J., Keshavan M.S., Soares J.C., MRI study of thalamic volumes in bipolar and unipolar patients and healthy individuals, *Psychiatry Res*., 108 (2001) 161–168.

[11] Sen F., Ulubay H., Ozeksi P., Sargon M.F., Tascioglu A.B. Morphometric measurements of the thalamus and interthalamic adhesion by MR imaging, *Neuroanatomy*., 4 (2005) 10-12.

[12] Tastemur Y., Sabancioguları V., Salk I., Cimen M. The Relationship of the Posterior Cranial Fossa, the Cerebrum, and Cerebellum Morphometry with Tonsiller Herniation, *Iran J. Radiol.*, 14(1) (2017) e24436.

[13] Yasuda S., Miyazaki S., Kanda M., Goto Y., Suzuki M., Harano Y., Nonogi H., Intensive treatment of risk factors in patients with type-2 diabetes mellitus is associated with improvement of endothelial function coupled with a reduction in the levels of plasma asymmetric dimethylarginine and endogenous inhibitor of nitric oxide synthase, *Eur. Heart J.,* 27(10) (2006) 1159-65.

[14] Selvarajah, D., Wilkinson, I. D., Emery, C. J., Harris, N. D., Shaw, P. J., Witte, D. R., Griffiths, P. D., & Tesfaye, S. Early involvement of the spinal cord in diabetic peripheral neuropathy, Diabetes Care., 29 (2006) 2664–2669.

[15] Selvarajah D., Wilkinson I. D., Maxwell M., Davies J., Sankar A., Boland E., Gandhi R., Tracey I., Tesfaye S., Magnetic resonance neuroimaging study of brain structural differences in diabetic peripheral neuropathy, *Diabetes Care*, 37 (2014) 1681–8.

[16] Gustin S.M., Peck C.C., Wilcox S.L., Nash P.G., Murray G.M., Henderson L.A., Differentpain, different brain: thalamic anatomy in neuropathicandnon-neuropathic chronic pain syndromes, *J. Neurosci.,* 31 (2011) 5956–5964.

[17] Giorgio A., De Stefano N. Clinical use of brain volumetry*, J. Magn. Reson Imaging*, 37 (2013) 1–14

[18] Musen G., Lyoo I. K., Sparks C. R., Weinger K., Hwang J., Ryan C. M., Jimerson D. C., Hennen J., Renshaw P. F., Jacobson, A. M., Effects of type 1 diabetes on gray matter density as measured by voxel-based morphometry, *Diabetes*, 55 (2006) 326–333.

[19] Ge Y., Grossman R.I., Babb J.S., Rabin M.L., Mannon L.J., Kolson D.L., Age-related total gray matter and white matter changes in normal adult brain. Part I: Volumetric MR imaging analysis, *Am. J. Neuroradiol.,* 23 (2002) 1327-1333.

[20] Gur R. C., Mozley P. D., Resnick S. M., Gottlieb G. L., Kohn M., Zimmerman R., Herman G., Atlas S., Grossman R., Berretta, D., Gender differences in age effect on brain atrophy measured by magnetic resonance imaging, *Proc. Natl. Acad. Sci. USA*., 88 (1991) 2845–2849.

[21] Liu H., Wang L., Geng Z., Zhu Q., Song Z., Chang R,. Lv H., A voxel-based morphometric study of age- and sex-related changes in white matter volume in the normal aging brain, *Neuropsychiatric Disease and Treatment,* 12 (2016) 453–465

[22] Salat D.H., Kaye J.A., Janowsky J.S., Prefrontal gray and white matter volumes in healthy aging and Alzheimer disease, *Arch Neurol.,* 56 (1999) 338–344.

[23] Swieten J.C., Den Hout J.H.W., Ketel B.A., Hydra A., Wokke J.H.J., van Gijn J., Periventricular lesions in the white matter on magnetic resonance imaing in the elderly, *Brain*, 114 (1991) 761–774.

[24] Sze G., DeArmond S., Brant-Zawadski M., Davis R.L., Norman D., Newton T.H., Foci of MRI signal (pseudo lesions) anterior to the frontal horns: histologic correlations of a normal finding, *Am. J. Neuroradiol.,* 7 (1986) 381–387.

[25] Fazekas F., Kleinert R., Offenbacher H., Schmidt R., Kleinert G., Payer F., Radner H., Lechner H. Pathologic correlates of incidental MRI white matter signal hyperintensities*, Neurology*, 43 (1993) 1683–1689.

[26] Awad I.A., Johnson P.C., Spetzler R.F., Hodak J.A., Incidental subcortical lesions identified on magnetic resonance imaging in the elderly, II: postmortem pathological correlations, *Stroke*, 17 (1986) 1090–1097.

[27] Fazekas F., Kleinert R., Offenbacher H., Payer F., Schmidt R., Kleinert G., Radner H., Lechner H., The morphologic correlate of incidental white matter hyperintensities on MR images, *Am. J. Neuroradiol.,* 12 (1991) 915–921.

[28] Grafton S.T., Sumi S.M., Stimac G.K., Alvord E.C Jr., Shaw C.M., Nochilin D., Comparison of postmortem magnetic resonance imaging and neuropathologic findings in the cerebral white matter, *Arch Neurol*., 48 (1991) 293–298.

[29] Sorensen L., Siddall P.J., Trenell M.I., Yue D.K., Differences in metabolites in pain-processing brain regions in patients with diabetes and painful neuropathy, *Diabetes Care*, 31 (2008) 980–981.

[30] Nakano M., Ueda H., Li J.Y., Matsumoto M., Yanagihara T., Measurement of regional N-acetylaspartate after transient global ischemia in gerbils with and without ischemic tolerance: an index of neuronal survival, *Ann Neurol.,* 44 (1998) 334–340.

[31] Selvarajah D., Wilkinson I. D., Emery C. J., Shaw P. J., Griffiths P. D., Gandhi R., Tesfaye S., Thalamic neuronal dysfunction and chronic sensorimotor distal symmetrical polyneuropathy in patients with type 1 diabetes mellitus, *Diabetologia*, 51 (2008) 2088-2092.

[32] Selvarajah D., Wilkinson I.D., Gandhi R., Griffiths P.D., Tesfaye S., Microvascular perfusion abnormalities of the thalamus in painful but not painless diabetic polyneuropathy: a clue to the pathogenesis of pain in type 1 diabetes, *Diabetes Care.,* 34(3) (2011) 718–720.

[33] Fischer T.Z., Waxman S.G., Neuropathic pain in diabetes evidence for a central mechanism, *Nat. Rev. Neurol.,* 6(8) (2010) 462–466.

[34] Bilgili Y., Ünal B., Kendi T., Simsir İ., Erdal H., Huvaj S., Simay K., Bademci G., MRG ile normal görünümlü beyaz ve gri cevherde yaşlanmanın etkilerinin ADC değerleri ile saptanabilirliği, *Tanısal ve Girişimsel Radyoloji*, 10(1) (2004) 4-7.

[35] Karasu R., Bilgili Y., Korpus kallosumun difüzyon ağırlıklı ve konvansiyonel manyetik rezonans görüntüleme ile yaşa göre değerlendirilmesi, *Kırıkkale Üniversitesi Tıp Fakültesi Dergisi*, 20(1) (2018) 51-61.

[36] Chun T., Filippi C.G., Zimmerman R.D., Ulug A.M., Diffusion changes in the aging human brain, *AJNR*, 21 (2000) 1078-83.

[37] Engelter S.T., Provenzale J.M., Petrella J.R., DeLong D.M., MacFall JR., The effect of aging on the apparent diffusion coefficient of normal-appearing white matter, *AJR*, 175 (2000) 425-30.