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Volumetric Analysis of Brain Structures and Evaluation of Neurological Symptoms in Patients With Sjögren's Syndrome: Anatomical, Radiological, and Neurological Study

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ABSTRACT

Sjögren's disease is an autoimmune disease that affects the body's glands. In this study, the volumes of many anatomical structures in the brains of female patients diagnosed with Sjögren's Syndrome (SS) were measured, and their neurological symptoms were evaluated. In our study, brain Magnetic Resonance Imaging (MRI) of 21 female patients with SS and 34 healthy women were evaluated, and the volumes of some anatomical structures were measured. After calculating the volumes, it was determined that the total temporal lobe volumes, right temporal lobe volumes, and 4th ventricle volumes of patients with SS were significantly smaller compared to the control group. In SS patients, the volume of the right corpus amygdaloideum was found to be significantly smaller than the left side. Volume measurements of other anatomical structures, except vermis volume, were smaller than those in the control group but statistically insignificant. When patients with primary and secondary SS were compared: left corpus amygdaloideum volume, left insular cortex volume, total corpus amygdaloideum volume, and total insular cortex volume were found to be significantly smaller in secondary SS patients. Our study shows that structures related to the limbic lobe are more affected in patients with secondary SS. The most common neurological symptoms in patients are vertigo, headaches, and forgetfulness. Headache symptoms correlate with nucleus accumbens and third ventricle volume. SS can cause neurological symptoms in patients and affect the anatomical structures of the brain, even if their neurological examinations are normal. We recommend early diagnosis and treatment of the disease and regular neurological check-ups.

Keywords: Sjögren's Syndrome (SS), Brain, Anatomy, Volume

INTRODUCTION

Sjögren's Syndrome (SS) is a systemic chronic autoimmune disease of unknown etiology, characterized by immune damage to the salivary and lacrimal glands, leading to dry mouth (xerostomia) and dry eyes (xerophthalmia). Dryness can also cause a clinical picture that affects other mucosal surfaces, such as the respiratory tract, digestive system, and vagina [1].

Sjögren's syndrome is divided into two types: Primary Sjögren's Syndrome (pSS) and secondary Sjögren's Syndrome (sSS). Other autoimmune diseases are not observed in pSS and are characterized by keratoconjunctiva sicca (dry eyes) and xerostomia (dry mouth), collectively referred to as sicca syndrome (Latin word sicca, meaning “dry”). Vaginal, dermal, and nasal dryness may be added to these findings. pSS is a chronic, complex systemic autoimmune disease that mostly affects adult women and still has no specific treatment. Although the involvement of the salivary and lacrimal glands is the hallmark of the disease, during the progression of pSS, various organs and systems, including the nervous and musculoskeletal systems, such as the lungs, kidneys, and liver, may be involved in the disease [2].

SS can also occur in association with another autoimmune disease (i.e., polyautoimmunity), the most frequent being autoimmune thyroid disease, rheumatoid arthritis, and systemic lupus erythematosus. When this occurs, the disease is designated Sss [3].

Although the etiopathogenesis of the disease is unknown, studies show that it is caused by genetic, hormonal (estrogen) factors, and viruses such as Epstein-Barr Virus **(**EBV), Hepatitis C Virus **(**HCV), Human T-lymphotropic virus **(**HTLV), and Human Immunodeficiency Virus **(**HIV) [4]. There is an immune regulation disorder due to a significant increase in B cell activity. Accordingly, in approximately 2/3 of patients with pSS, ANA (55%-97%) and RF (32%-90%), anti-Ro/SS-A (40%-60%) and anti-La/SS-B (50%) antibodies are positive [5]. The prevalence of SS is estimated to be approximately 3% in individuals aged 50 and over, with a female-to-male ratio of 9:1. Clinical findings are often vague and misinterpreted. Therefore, misdiagnosis of SS is common, and approximately half of all patients are thought to be undiagnosed [6]. Birlik et al. found the prevalence of pSS in our country to be 0.35% [7].

The aim of this study is to investigate and reveal the changes that occur in some anatomical regions of the brain in diagnosed Sjögren's patients, about which less research has been done, and the diversity of neurological symptoms in the patients.

MATERIALS AND METHODS

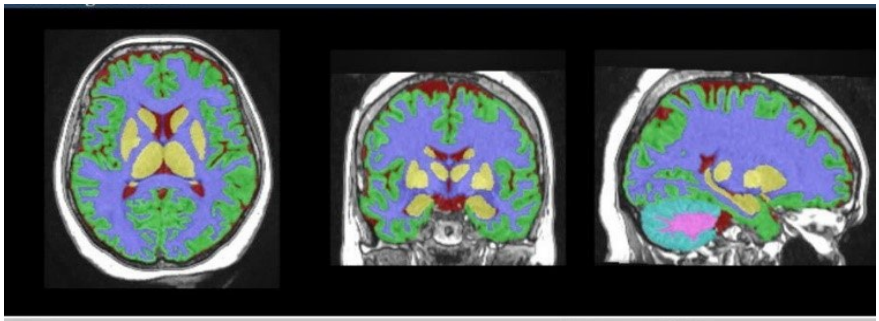
Ethics Committee permission for our study was received from the Kırıkkale University Non-invasive Research Ethics Committee with meeting number 2021/10 and protocol number 2021.05.07. Our study group consists of 21 female patients diagnosed with Sjögren's disease in the rheumatology outpatient clinic of our hospital. Of these patients, 71.4% (15 people) have pSS disease, and 28.6% (6 people) have sSS disease. The number of control groups is 34. Sjögren's syndrome patients were evaluated as Group 1, and the control group was evaluated as Group 2. Patients diagnosed with Sjögren's who had one or more neurological symptoms had a neurological evaluation, and had a non-contrast cranial Magnetic Resonance Imaging (MRI) were included in the study (Group 1).

People with known or previous neurological diseases (such as cerebrovascular disease, multiple sclerosis, dementia, Parkinson's, myasthenia gravis, and Alzheimer's), people diagnosed with psychiatric diseases (such as depression, schizophrenia, and psychotic disorder), people with a history of cranial surgery, people with major metabolic disorders, and those with major risk cardiovascular disease were not included in the study group (Group 2).

Volume calculation from MRI images: Brain MRIs were imaged with a 1.5T MRI scanner with the cranial coil (1.5T GE SIGNA EXPLORER 2022, USA). The axial T1-weighted MP-RAGE series was evaluated (TR: 1500 ms, TE: 2.8 ms, field of view: 240 mm × 240 mm, slice thickness: 1.0 mm, flip angle: 12). The volBrain system was used for volume evaluation of the anatomical structures to be measured in the study. MRI images were taken from the PACS system, and the images in DICOM format (.dcm) were converted to NIFTI format (.nii). dcm2niix software was used for this. Images in NIFTI format were then uploaded to the volBrain system. Automatic quantitative analysis of MRI images was performed through the software within the system. With quantitative analysis in the volBrain system, data reports were obtained in PDF format. In the reports, the volumes of the objective structures we wish to measure include absolute values measured in cm^3.

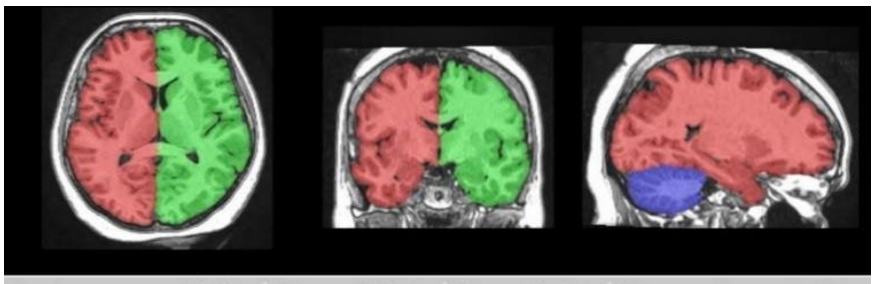
The study of Wozniak was used as a volume measurement method [8]. Volume measurements of the following anatomical structures were made:

White matter, gray matter, subcortical gray matter, cortical gray matter, total cerebrospinal fluid, total cerebrum, cerebellum, cerebrum/cerebellum ratio, cerebellum/vermis ratio, vermis, brainstem, total nucleus caudatus, right nucleus caudatus, left nucleus caudatus, total hippocampus, left hippocampus, right hippocampus, total globus pallidus, right globus pallidus, left globus pallidus, total thalamus, right thalamus, left thalamus, total frontal lobe, right frontal lobe, left frontal lobe, total temporal lobe, right temporal lobe, left temporal lobe, total parietal lobe, right parietal lobe, left parietal lobe, total occipital lobe, right occipital lobe, left occipital lobe, total limbic cortex, right limbic cortex, left limbic cortex, total insular cortex, right insular cortex, left insular cortex, total lateral ventricle, right lateral ventricle, left lateral ventricle, third ventricle, fourth ventricle, total nucleus accumbens, right nucleus accumbens, left nucleus accumbens, total corpus amygdaloideum, right corpus amygdaloideum, left corpus amygdaloideum, total putamen, right putamen, left putamen volumes (Figures 1-3).



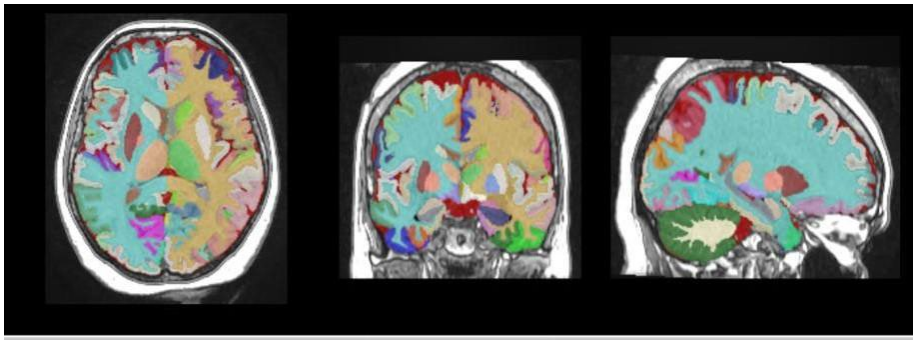
Tissue	Volume (cm^3/%)	
White Matter (WM)	538.55 (39.749)	[32.729, 42.594]
Normal Appearing White Matter	538.36 (39.735)	[32.668, 42.614]
Abnormal Appearing White Matter	0.19 (0.014)	[0.000, 0.248]
Grey Matter (GM)	683.99 (50.484)	[44.191, 51.769]
Subcortical Grey Matter	44.31 (3.270)	[2.644, 3.361]
Cortical Grey Matter	541.46 (39.964)	[34.096, 40.512]

Figure 1 White and gray matter volume measurements



Structure	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asymmetry (%)
Cerebrum	1096.53 (80.933)	548.71 (40.499)	547.82 (40.433)	0.1629
	[71.426, 79.680]	[35.746, 39.933]	[35.619, 39.808]	[-1.548, 2.217]
Cerebrum WM	510.76 (37.698)	254.72 (18.800)	256.04 (18.898)	-0.5160
	[30.650, 39.843]	[15.375, 19.984]	[15.259, 19.875]	[-1.614, 2.884]
Cerebrum GM	585.77 (43.235)	293.99 (21.699)	291.78 (21.536)	0.7549
	[36.940, 43.673]	[18.466, 21.854]	[18.451, 21.842]	[-1.869, 2.014]
Cerebellum *	118.08 (8.715)	59.17 (4.367)	58.91 (4.348)	0.4429
	[8.122, 10.747]	[4.078, 5.395]	[4.035, 5.361]	[-2.337, 4.018]
Cerebellum WM	27.79 (2.051)	14.06 (1.038)	13.73 (1.013)	2.4191
	[1.862, 2.968]	[0.939, 1.511]	[0.919, 1.461]	[-2.850, 8.595]
Cerebellum GM	98.22 (7.250)	45.11 (3.329)	45.18 (3.335)	-0.1653
	[6.457, 8.889]	[2.946, 4.077]	[2.941, 4.074]	[-3.777, 4.004]

Figure 2 Cerebellar volume measurements



Subcortical	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asymmetry (%)
Accumbens	0.79 (0.059)	0.38 (0.028)	0.41 (0.030)	-7.2993
	[0.031, 0.060]	[0.013, 0.029]	[0.016, 0.032]	[-36.302, 11.350]
Amygdala	2.08 (0.154)	1.07 (0.079)	1.01 (0.074)	6.3348
	[0.118, 0.173]	[0.060, 0.086]	[0.057, 0.088]	[-12.167, 13.398]

Figure 3 Nucleus accumbens and corpus amygdaloideum volume measurements

The records of the patients in Group 1 in the hospital data system were examined. According to the anamnesis results, it was determined that the patients had symptoms of vertigo, headache, numbness in hands and feet, visual disturbances, and forgetfulness. In the neurological examination, diplopia and nystagmus findings were detected in three patients. Neurological examinations of the other patients in Group 1 are normal. The relationship between volume and neurological symptoms was evaluated statistically. It was recorded how many years they had been sick after the diagnosis. All patients are under treatment and taking medication. The relationship between disease duration and volume was evaluated statistically. In addition, blood biochemical were examined, and kidney function tests, liver function tests, B12 levels, and thyroid function tests were checked.

Statistical analysis: Compliance of measured volumes with normal distribution was analysed with the Shapiro-Wilk test. Descriptive statistics of measurements that comply with normal distribution are shown as Mean ± SD and, non-normal distribution are shown as Median and Interquartile Range. Independent-sample T and Mann-Whitney U tests were used to compare volumes by groups. The distribution of categorical variables according to groups was evaluated with the Chi-square test. Spearman correlation analysis was performed for the relationship of categorical variables with volumes. The statistical significance level was taken as $p \leq 0.05$ and SPSS (ver. 26) program was used in the calculations.

RESULTS

Our study group consists of female patients. The average age is 52 ± 14 for Group 1 Sjögren's syndrome patients and 51 ± 16 for the Group 2 control group 71.4% of the patients have pSS, and 28.6% have sSS (Tables 1 and 2).

Table 1 Distribution of demographic data

	Group 1				**Group 2**			
	Min	Max	Median	IQR	Min	Max	Median	IQR
Age	28	63	52,00	14	30	65	51,00	16

The average of the measured volumes and the p values obtained as a result of statistical analysis are shown in (Table 2).

Table 2 Volume averages and comparisons in cm^3 of Sjögren's patients (Group 1) and control (Group 2)

Volume	**Group 1**				**Group 2**				**t**	**p**
	Min	Max	Mean	SD	Min	Max	Mean	SD		
White matter	357,06	577,45	450,42	59,98	281,65	594,18	474,16	68,41	-1,309	0,196
Gray matter	534,69	732,58	639,91	57,08	486,07	817,51	662,99	71,12	-1,257	0,214
Subcortical gray matter	33,57	46,03	39,77	3,51	27,81	49,99	41,58	4,72	-1,512	0,136

Cortical gray matter	404,25	579,86	498,98	47,77	363,92	656,14	519,18	61,03	-1,291	0,202
Cerebrospinal fluid	65,12	244,73	143,22	44,64	78,61	236,11	165,33	44,54	-1,787	0,080
Total cerebrum	799,33	1152,71	961,83	100,26	688,90	1260,68	1006,39	126,24	-1,371	0,176
Total cerebellum	95,21	146,87	119,85	12,90	95,26	150,87	122,28	12,43	-0,693	0,491
Vermis	7,42	10,45	8,65	0,90	6,97	9,99	8,50	0,88	0,610	0,544
Cerebrum/cerebellum ratio	6	9	7	1	6	9	8	1	394,50	0,481
Cerebellum/vermis ratio	10	15	13	1	11	16	14	2	453,00	0,084
Brainstem	16,25	24,84	19,02	2,15	14,73	23,37	19,14	2,11	-0,209	0,836
Total nucleus caudatus	5,49	8,76	6,90	0,87	4,92	9,18	7,44	1,16	-1,837	0,072
Right nucleus caudatus	2,73	4,35	3,48	0,45	2,37	4,61	3,73	0,58	-1,704	0,094
Left nucleus caudatus	2,70	4,40	3,42	0,43	2,54	4,78	3,70	0,59	-1,943	0,057
Total hippocampus	6,86	9,19	7,95	0,64	5,05	9,94	8,04	0,94	-0,419	0,677
Left Hippocampus	3,45	4,75	3,95	0,32	2,62	4,96	4,00	0,45	-0,422	0,675
Right hippocampus	3,27	4,54	4,08	0,49	2,43	4,98	4,1	0,49	392,50	0,538
Total globus pallidus	2,11	3,45	2,68	0,32	1,96	3,43	2,75	0,33	-0,815	0,418
Right globus pallidus	1,04	1,74	1,36	0,16	0,93	1,75	1,40	0,18	-0,886	0,380
Left globus pallidus	1,07	1,71	1,33	0,17	0,96	1,67	1,35	0,17	-0,575	0,567
Total thalamus	9,13	13,88	11,29	1,33	8,45	14,32	11,55	1,40	-0,695	0,490
Right thalamus	4,67	6,84	5,64	0,61	4,11	7,18	5,76	0,72	-0,645	0,522
Left tthalamus	4,46	7,04	5,65	0,73	4,34	7,14	5,79	0,70	-0,729	0,469
Total frontal lobe	127,64	194,28	163,60	17,23	115,64	237,86	172,24	22,46	-1,507	0,138
Right frontal lobe	64,91	97,66	82,33	8,59	56,80	118,04	86,57	11,15	-1,489	0,142
Left frontal lobe	62,73	96,62	81,27	8,70	58,85	119,81	85,67	11,41	-1,513	0,136
Total temporal lobe	90,85	117,15	102,56	19,04	65,47	129,76	1,11,855	14,86	483,00	0,029*
Right temporal lobe	46,09	59,27	50,62	8,13	29,32	64,23	55,76	6,83	484,50	0,027*
Left temporal lobe	44,76	59,02	52,52	4,61	36,15	65,80	55,18	6,17	-1,701	0,095
Total parietal lobe	75,28	115,76	96,25	10,86	65,45	118,43	97,82	12,70	-0,469	0,641
Right parietal lobe	39,93	56,83	48,50	4,97	31,75	60,09	48,88	6,23	-0,239	0,812
Left parietal lobe	35,35	59,00	47,75	6,08	33,69	60,31	48,94	6,67	0,661	0,512
Total occipital lobe	58,72	82,50	69,75	6,85	54,28	87,77	71,71	8,45	-0,895	0,375
Right occipital lobe	30,50	41,43	35,65	3,62	26,63	44,39	36,47	4,37	-0,715	0,478
Left occipital lobe	28,21	41,07	34,10	3,44	27,61	43,38	35,24	4,27	-1,037	0,304
Total limbic cortex	29,75	47,12	38,02	4,02	29,23	53,01	40,31	5,00	-1,771	0,082
Right limbic cortex	15,19	23,02	18,59	1,93	14,07	26,82	19,87	2,76	-1,863	0,068
Left limbic cortex	14,56	24,10	19,43	2,25	15,15	26,75	20,44	2,43	-1,532	0,132
Total insular cortex	21,52	31,61	27,22	4,22	19,32	57,69	27,695	5,41	405,00	0,406
Right insular cortex	10,56	16,17	13,26	1,41	8,97	17,47	13,69	1,90	-0,892	0,376
Left insular cortex	10,93	15,91	13,64	1,49	9,77	17,12	13,77	1,74	-0,284	0,778
Total nucleus accumbens	0,41	0,79	0,62	0,16	0,29	1,01	0,66	0,10	428,00	0,218

Right nucleus accumbens	0,17	0,38	0,30	0,08	0,11	0,48	0,31	0,04	415,00	0,313
Left nucleus accumbens	0,22	0,41	0,34	0,08	0,19	0,53	0,35	0,07	421,00	0,266
Total corpus amygdaloideum	1,51	2,22	1,82	0,31	0,78	2,47	1,915	0,25	455,50	0,088
Right corpus amygdaloideum	0,75	1,14	0,92	0,14	0,34	1,25	0,97	0,13	466,00	0,059
Left corpus amygdaloideum	0,75	1,07	0,91	0,18	0,45	1,23	0,94	0,14	438,00	0,160
Total putamen	5,67	9,64	7,94	1,63	5,64	13,23	8,205	1,56	407,00	0,386
Right putamen	2,84	4,77	3,92	0,67	2,67	6,62	4,07	0,90	420,50	0,271
Left putamen	2,83	4,92	3,95	0,90	2,98	6,61	4,06	0,74	421,50	0,264
Total lateral ventricle	3,82	34,32	9,88	10,61	4,20	28,71	11,27	12,04	396,00	0,499
Right lateral ventricle	1,89	15,94	4,99	4,82	1,74	15,02	5,39	6,09	377,50	0,722
Left lateral ventricle	1,70	20,59	5,13	5,62	2,46	17,36	6,54	6,65	403,00	0,425
Third ventricle	0,30	2,73	0,88	0,81	0,55	3,17	1,015	0,77	405,50	0,401
Fourth ventricle	0,69	1,97	1,27	0,36	0,82	2,50	1,53	0,40	-2,417	0,019*
*: $p < 0.05$										

The significant results are shown in table 3 when the volumes of primary and secondary Sjogren's patients are compared (Table 3).

Table 3 Volume comparisons in cm^3 of primary and secondary Sjögren's patients

Volume	Primary				Secondary				t	p
	Min	Max	Mean	SD	Min	Max	Mean	SD		
Total corpus amygdaloideum	1,56	2,22	1,94	0,21	1,51	1,92	1,66	0,29	15,50	0,018*
Left corpus amygdaloideum	0,78	1,07	0,94	0,12	0,75	0,97	0,79	0,13	12,00	0,008*
Left insular cortex	10,96	15,91	14,17	1,30	10,93	13,60	12,32	1,09	3,069	0,006*
Total insular cortex	21,52	31,61	27,65	2,60	22	27,22	24,565	3,01	14,00	0,014*
*: $p < 0.05$										

The significant results between Sjögren's syndrome patients and the control group are as follows:

Right temporal lobe volume was found to be significantly smaller than the control group (p=0.027), total temporal lobe volume was significantly smaller than the control group (p=0.029), and 4^{th} ventricle volume was significantly smaller than the control group (p=0.019).

Except for vermis volume, all other volume measurements were found to be smaller in Sjögren's syndrome patients, although they were not statistically significant.

Significant results between patients with primary and secondary Sjögren's syndrome are as follows:

Left corpus amygdaloideum volume (p=0.008), left insular cortex volume (p=0.006), total corpus amygdaloideum volume (p= 0.018), and total insular cortex volume (p=0.014) were found to be significantly smaller in sSS patients. In addition, although not statistically significant, gray matter, cerebrum, nucleus caudatus, thalamus, frontal lobe, temporal lobe, parietal lobe, occipital lobe, limbic cortex, insular cortex, corpus amygdaloideum, and putamen volumes were found to be smaller in sSS patients. Structures connected to the limbic lobe are more affected. In pSS, the volumes of white matter, hippocampus, pallidum, 4^{th} ventricle, and cerebellum are smaller than in sSS patients but are not significant.

Right and left volume differences in Sjögren's syndrome patients: In Sjögren's syndrome patients, the right side nucleus

accumbens volume was found to be significantly smaller than the left side (p=0.033).

Vertigo symptoms were detected in 66.7%, headache in 61.9%, forgetfulness in 52.4%, numbness in hands and feet in 28.6%, and visual impairment in 14.3% of patients with Sjögren's syndrome.

When the relationship between neurological symptoms and volume was investigated, it was determined that there was a positive correlation between headache and left nucleus accumbens volume (r0.447, p=0.042) and a negative correlation with third ventricle volume (r=-0.462, p=0.035).

The patient's kidney function tests, liver function tests, B12 levels, and thyroid function tests were within normal limits.

There was no statistically significant relationship between disease durations and volumes.

Additional findings detected in the general MRI images of the patients were a few millimetric nonspecific hyperintense appearances in both cerebral hemispheres; atrophic appearances in both cerebral hemispheres were also detected. Focal/punctual increased FLAIR/T2 signal intensities in both periventricular white matter and centrum semiovale, thin band-like intensity on the lateral ventricle wall and frontal hat appearance, periventricular thick halo with bifrontoparietal centrum semiovale, corona radiata, bilateral periventricular deep white matter and subcortical hyperintense appearances that merged in spots were observed in the white matter, and in one patient, an encephalomalasic area was observed in the left parietal hemisphere.

DISCUSSION

Neurological involvement in Sjögren's syndrome is seen in approximately 20%-25% of patients. Central nervous system findings are observed in 13%, and peripheral nervous system findings are observed in 87% [9]. Sjögren's syndrome, the first symptom of which is an epileptic seizure, has been reported [10].

Previous studies have described cerebral cortical atrophy, a decrease in cortex and deep gray matter, ventricular dilatation and volume increase, decreased cerebral blood flow, and hypersensitivity in white matter in Sjögren's syndrome. Cerebellar degeneration, atrophy, and gray matter reduction may be observed. Vasculitis, vagal stimulation, trigeminal neuropathy, autonomic and sensory neuropathy, T cell invasion in the spinal dorsal root, and sympathetic ganglion are other reported findings. Depending on nervous system involvement, symptoms of fatigue, polyneuritis, mononeuritis, encephalopathy, cerebellar syndrome, brainstem syndrome, and cranial nerve disorders may occur [11]. Delalende et al. reported that in chronic myelopathy, motor neuron disease, optic neuropathy, peripheral nervous system involvement, and polyneuropathy, 75% had T2-weighted hyperintensities [12]. Small vessel vasculitis in the central nervous system, diffuse white matter abnormalities on MRI, and peripheral neuropathy were observed in 35% of pSS patients [13]. Soliotis et al. reported that there is a wider range of neurological findings, such as migraine, optic neuritis, hemiparesis, aseptic meningitis, and hyperreflexia [14].

The volume of both gray and white matter is reduced in pSS patients. In the gray matter, the cortical regions were bilaterally affected, mainly in the occipital, parietal, and frontal lobes; furthermore, the thalamus, caudate nucleus, and cerebellar hemispheres were diminished. As for the white matter, small areas with decreased volume could be observed throughout the brain, especially in the frontal and occipital lobes, cerebellum, and corpus callosum. In comparison with the controls, patients with pSS had decreased gray matter volume in the cortex, deep gray matter, and cerebellum. The associated loss of white matter volume was observed in areas corresponding to gray matter atrophy and in the corpus callosum [15]. In our study, the volumes of the cerebral cortex, subcortical gray matter, white matter, cerebellum, thalamus, nucleus caudatus, and limbic cortex were smaller than the control group but statistically insignificant.

It has been reported that in pSS patients, decreased structural connectivity is detected in the frontal and parietal lobes and some parts of the temporal and occipital lobes, and the most characteristic MRI finding is significantly increased white matter hyperintensities. Ventricular volume was found to be significantly increased in the same study [15]. Reduced gray matter volume was observed in patients with pSS bilaterally in the cortical regions, mainly in the occipital, parietal, and frontal lobes, and in the thalamus, caudate nucleus, and cerebellar hemispheres. Cortical atrophy and ventricular dilatation can also occur in pSS [16].

In our study, total cerebellum volume was found to be smaller in Sjögren's patients. The vermis volume was found to be larger. In Sjögren's patients, the cerebrum/cerebellum volume ratio, and cerebellum/vermis ratio are smaller than the control group. The cerebellar hemisphere volume has decreased, but the vermis volume has not. However, these findings are not statistically significant. Total cerebellar volume, vermis volume, cerebrum/cerebellum volume ratio and cerebellum/vermis volume ratio were examined for the first time in our study in Sjögren's patients.

In our study, frontal, parietal, and occipital lobe volumes were measured smaller in Sjögren's patients, but this was not statistically significant. However, in our study, the right temporal lobe volume and total temporal lobe volume of Sjögren's patients were found to be significantly smaller than the control group. There has not been an article that has reached this conclusion before. The left corpus amygdaloideum volume, left insular cortex volume, total corpus amygdaloideum volume, and total insular cortex volume were found to be significantly smaller in sSS patients. Our findings show that the structures associated with the limbic lobe are more affected in sSS. A case of limbic encephalitis observed in a 42-year-old male pSS patient has been reported in the literature [17].

In our study, the 4th ventricle volume was found to be significantly smaller than the control group. Among the data on cerebrospinal fluid results in patients with Sjögren's syndrome, a single study reported a smaller volume [18].

Leuvsnes *et al*. found hippocampal volume in pSS to be smaller than in the control group [19]. In our study, hippocampus volume was small and not statistically significant.

There are no studies measuring the volume of the temporal lobe, nucleus accumbens, corpus amygdaloideum, insular cortex, nucleus caudatus, globus pallidus, and putamen in Sjögren's syndrome patients. Increased functional connections in the left hippocampus and left putamen have previously been detected in patients with pSS, but putamen volume has not been measured. Decreased low-frequency fluctuation amplitude was detected in the right Para hippocampal gyrus and right and left insula, but insular cortex volume was not examined [20]. A case of infarcts in the basal ganglia has been reported in Sjögren's syndrome, but volume measurement was not performed [21]. Studies reporting gray matter reduction in the nucleus caudatus have been reported, but volume was not measured [15].

In this study, the right nucleus accumbens volume was found to be significantly smaller than the left in Sjögren's patients. This shows that patients' motivation and vitality may change. There are no studies comparing right and left side volume in Sjögren's syndrome patients.

Modis et al., reported in their study that regional homogeneity was detected in the right cerebral hemisphere, left limbic lobe, right temporal gyrus, and parietal lobe, and decreased structural connectivity in the right occipital, temporal lobe, and right hippocampus in Sjögren's syndrome patients, but volume was not measured [15].

Tzarouchi et al., reported that a greater number of white matter hyperintensities smaller than 2 mm were found in pSS patients (median, 6; range, 0–24) than in controls (median, 0; range, 0–9) [16]. In our study, in 76% of the patients, a few millimetric nonspecific hyperintensities were detected in both cerebral hemispheres on T2-weighted MRI.

Urbanski et al., reported that vitamin B12 levels were low in patients with pSS [22]. In this study, the vitamin B12 levels of our patients were found to be within normal limits. Sjögren's patients are often associated with hypothyroidism [23]. In this study, the thyroid function tests of the patients were found to be at normal levels.

Impaired liver functions and cases of HCV infection, primary biliary cirrhosis, autoimmune hepatitis, and sclerosing cholangitis have been reported in pSS patients [24]. In this study, the liver function tests of the patients were found to be at normal levels. Renal dysfunction in pSS patients has been reported at a rate of 16.17% [25]. In this study, the kidney function tests of the patients were found to be at normal levels.

Our study also found that nucleus accumbens and third ventricle volume changes correlate with headache symptoms in Sjögren's syndrome patients.

CONCLUSIONS

Unlike our study, the temporal lobe, cerebellum, vermis, nucleus accumbens, corpus amygdaloideum, insular cortex, nucleus caudatus, globus pallidus, and putamen volume, cerebrum/cerebellum volume ratio, and cerebellum/vermis volume ratio in Sjögren's patients were measured for the first time.

In this study, neurological examinations of most Sjögren's syndrome patients were found to be normal, except for three patients (diplopia and nystagmus). However, patients have neurological symptoms, and the anatomical structures of the brain are affected. For this reason, we recommend that the disease be diagnosed early, patients receive treatment without delay, and neurological checks be performed regularly.

This study was presented as an e-poster at the 14th International Congress on Autoimmunity in Ljubljana, Slovenia on 17 – 20 May 2024.

Conflict of Interest

The authors declare no conflict of interest.

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