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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