Research Paper:
Morphometrical Evaluation of Corpus Callosum Using Mid-sagittal Brain MRI Images in Patients With Relapsing-Remitting Multiple Sclerosis

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ABSTRACT

Introduction: Corpus callosum (CC), an intracranial organ, is located in the midline of the cerebrum, communicating both the right and left hemispheres. CC undergoes morphological changes in Multiple Sclerosis (MS). The morphometrical changes of organs are directly associated with geographical regions; thus, this study aimed to investigate the morphological alteration of CC in patients with relapsing-remitting MS in Hamadan (Iran) in a retrospective study from April 2011 to April 2021.

Methods: Following inclusion and exclusion criteria, 54 and 128 Brain MRI images of RRMS patients and healthy individuals were examined morphologically using PmsDICOMViewer software. Two main morphological indices of area (mm^2) and longitudinal (mm) parameters were examined in midsagittal sections of Brain MRI images, including the area of CC (ACC) and associated segments, length of CC (LCC), and height of CC (HCC). Finally, the data were analyzed by SPSS software, version 19. $P<0.05$ was considered significant, and data were presented as Mean±SEM.

Results: Following MS onset, total ACC was decreased significantly ($P<0.05$) in MS patients than in control. Also, the area of rosterum/genu (ARG) and area of anterior half midbody of CC (AAMB) showed significant ($P<0.05$) incremental and decremental trends, respectively. In other indices, no significant differences were detected ($P>0.05$).

Conclusion: Morphometrical measurements of CC are associated with MS. By assessing the anterior half of CC in brain MRI images (ARG and AAMB), the diagnosis of MS can occur. Thus, the investigation results can be proposed as criteria for radiological confirmation of MS disease.

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1. Introduction

Multiple Sclerosis (MS), the most common disorder of the Central Nervous System (CNS), is a neuroinflammatory condition which first described by Jean-Martin Charcot in 1868 [1]. Following autoimmunity, demyelination occurs in which the myelin sheaths in the brainstem, optic nerves, and spine, as well as white matter adjacent to the lateral ventricles of the brain, are attacked and damaged by hyperactivity of white blood cells [2]. These inflammatory lesions disrupt the communication among various parts of the CNS. Consequently, some pathologic symptoms appeared, such as physical, mental, and psychological disorders.

By 1977, Just 26 patients with MS were identified in Iran, but 60,000 patients have been diagnosed with MS. The prevalence of MS in Iran is estimated at 45 per 100,000 [3]. In the early stages of MS, the myelin repair process occurs, but oligodendrocytes cannot completely regenerate the myelin sheath of axons. Repeated attacks can reduce the effect of successive myelin regeneration, and this process continues to form inflammatory plaques around the damaged axons. These plaques are the source of symptoms and are considered criteria for radiological diagnosis of MS in brain MRI images [4].

There are four clinical subtypes for MS: relapsing-remitting MS (RRMS), secondary progressive MS, primary progressive MS, and progressive relapsing MS [5]. MS begins approximately in 65%-80% of people in the form of RRMS. Since RRMS is the most common type of MS, this type of disease was selected for investigation in the current study.

CC is the main communication bundle of white matter consisting of many axons connecting two brain hemispheres. This organ acts as the most extensive communication neural pathway in primates and consists of $200\text{-}350\times10^6$ nervous fibers in humans [6]. The CC is the most common brain element involved in MS, which the multiple inflammatory plaques can diagnose.

Studies have shown that Brain MRI is the best imaging technique for people with MS symptoms. The diagnostic power of MRI is extremely high, and the imaging method is sensitive and convenient. MRI can show more brain and spinal cord lesions than CT scans, which can detect MS plaques in more detail. Thus, brain MRI images were used in this study to examine CC morphologically [7].

There are various reports of morphological changes of CC in MS disease [8]. Since the morphological dimensions of the human body, such as brain organs, are influenced by age, sex, and geography, we aimed to investigate the morphometrical changes of CC more accurately in RRMS patients referred to the Besat hospital (Hamadan, Iran) using mid-sagittal sections of brain MRI images in 10 years from April 2011 to April 2021.

2. Materials and Methods

Human samples collection

The total population of individuals was 54 RRMS and 128 healthy people as case and control groups, respectively. Inclusion criteria included the patients with definite RRMS, approved under the supervision of radiologists and neurologists. In this process, following neurological assessments, radiological examinations were applied to confirm the MS disease. Besides, all non-neurological patients or individuals with no apparent disease diagnosis and no definite pathologic conditions were considered a healthy control group. Exclusion criteria included individuals with previous neurological diseases or neurosurgeries excluded from the study [9].

Individuals categorization

Subjects were classified into two main groups healthy and RRMS. Also, the healthy group individuals were classified into genders (male and female) and age groups (20-30, 30-40, 40-50, 50-60, 60-70, and 70-80 years).

Data collection tools

T2-weighted brain MRI images with the intensity of 1.5 Tesla were selected for data extraction using Pms-DICOMviewer software (PHILIPS, R3.0-SP13, 2018, Philips Medical Systems Nederland, B.V., Vinpluis 4-6, 5684PC, Best, The Netherlands). All examinations were performed in the Midsagittal section using anatomical landmarks of the cerebral aqueduct and the great cerebral vein (Figure 1). The software accuracy was 0.01 mm or mm^2, and to reduce potential bias during measurements, whole parameters were measured twice, and the associated mean was used for data analysis. Longitudinal and area parameters were reported in mm and mm^2, respectively.

Morphometrical protocols of CC and associated segments

As depicted in Figure 2, for CC morphometry and to standardize the measurements, two primary subcallosal and TS-EOP baselines were used for whole images. Subcallosal baseline is an axis connecting the lowest points of the anterior and posterior CC. Also, the TS-EOP line passes through the tuberculum sella (TS) anteriorly and the External Occipital Protuberance (EOP) posteriorly. Above the baselines, a 90°-angle was used to accurately detect images' anterior or posterior points. Finally, area and longitudinal variables were measured for each image as follows:

1) Length of the cerebrum (LC): This variable is the direct distance between the anterior (in the frontal lobe) and posterior (in occipital lobe) poles of the brain in MRI images. Following TS-EOP line tracing, the 90°-angle was used to detect the anterior and posterior points of the brain.

2) Length of CC (LCC): This variable calculates the distance between anterior and posterior points of CC. In this method, after tracing the subcallosal baseline and using 90°-angle, these two points were marked, and the associated length was measured.

3) Height of CC (HCC): The subcallosal baseline was traced, and the 90°-angle was used. The distance between the subcallosal baseline and the highest point of CC was considered HCC.

4) Area of the cerebrum (AC): The Smoothed Polygon tool was hired in the midsagittal section of brain MRI images. The whole brain surface surrounded by meninges was marked as an area of cerebrum other than the surface of CC and cerebellum. This index was measured as an essential interfering factor affecting the size of ACC. This bias can be eliminated by forming the ACC/AC ratio.

5) Area of CC (ACC): Using the Polygon tool, the margin of CC was marked, and the surface was calculated.

6) CC segmentation and area calculation: First, the anterior-posterior length of the corpus callosum was calculated and divided into four different segments based on the Hofer & Frohm criteria for CC topography [10], including 1/6, 1/3, 1/6, 1/12, and 1/4, respectively from anterior to posterior direction. Whole five associated areas were marked and named as areas of rosterum/genu (ARG), anterior midbody (AAMB), posterior midbody (APMB), isthmus (AI), and splenium (AS). To inhibit the effect of interfering factors, the area of ACC was divided into the area of AC (ACC/AC ratio). The area of segmentation of CC was divided into the ACC (ARG/ACC, AAMB/ACC, APMB/ACC, AI/ACC, and AS/ACC ratios), and also the ratio of LCC/LC was defined.

Statistical analysis

After collecting numerical measurements, the data were statistically analyzed by SPSS software v. 19. The Kolmogorov-Smirnov test confirmed data distribution. The analysis was performed using a student's t-test and ANOVA. The Results were reported as Mean±SEM, and a significant level was considered $P<0.05$.

3. Results

According to Table 1, the total number of individuals studied in the current study was 182 (128 were healthy in the control group and 54 were RRMS patients). In control, 68 individuals were women, and 60 were men. Also, in the RRMS group, 31 females and 23 were males, respectively (Table 1).

Alteration of longitudinal and area variables in RRMS and healthy individuals in both genders based on age groups

According to Table 2, ACC was significantly ($P<0.05$) lower in RRMSMS patients than in healthy individuals representing the effect of disease on decreasing the total surface of CC. Also, the ARG and AAMB indices were decreased and increased in RRMS patients than in control individuals (significant at $P<0.05$). Other area segments of CC (APMB, AI, and AS) showed non-significant changes in MS patients than healthy control ($P>0.05$). Also, the results approved non-significant ($P>0.05$) alteration in longitudinal variables (HCC and LCC) in MS patients than control individuals.

4. Discussion

The results of this study showed that following the incidence of MS, the area of corpus luteum (ACC) decreases (6.35±1.03 in healthy and 5.26±1.52 in MS patients). By examining the segments of CC in MS people, the ARG index was increased (25.85±3.16 and 27.50±4.47 in healthy and MS patients, respectively), and the AAMB was decreased (23.99±3.65 and 22.65±3.14 in healthy and MS patients, respectively). Also, no significant changes were found in other segments of CC.

Many environmental and genetic factors are involved in the development of MS. For example, according to several articles, migration can change the possibility of MS occurrence [11]. In several articles, some of these factors are achievable and controllable, and some are inaccessible and therefore uncontrollable. Researchers in designing the process of studying brain changes following MS induction can not inhibit such factors [12].

In the current project, there are various uncontrollablefactors which could affect the results including environment, living habits, genetic basis, brain inflammation, neural infection, and the prescribed drugs.". Also, since this investigation was applied to human samples, so the rate of drug use is out of control, and according to the research ethics, there is no permission to change the drug doses. On the other hand, although radiologists and neurologists were hired to achieve their goals, in order not to go beyond the regulations of our research, which was based on Gross Anatomy, we emphasized the same conditions of the subjects in terms of neurology and radiology since “definitive diagnosis of inflammation” is important.

It is not enough just to show the symptoms of the disease. Still, in the process of confirming the disease, it will be necessary to perform clinical and paraclinical tests by the relevant specialists. Therefore, two radiology and neurology specialists have been used in this research. These specialists perform clinical trials such as movement tests and clinical trials such as Cerebrospinal Fluid to analyze oligoclonal bands of immunoglobulin with lumbar puncture and then radiological examinations through brain MRI images and use of gadolinium as a contrast agent with an intravenous injection to display plaques.

The McDonald’s criterion, which emphasizes clinical, laboratory, and radiological evidence of lesions at different times and regions [13], reported the certainty of the disease to us. Thus, we may conclude that according to ethical standards, to carry out a research project, patient drugs should not be changed or reduced by accepting the interfering factors and considering that these factors affect the research result.

Experts worked to unify the options to make the data as uniform as possible. In diagnosing inflammatory bowel disease using MRI stereotypes, studying factors and variables related to corpus luteum, especially the ACC variable, is more important than other variables. Over time, inflammatory bowel disease is more affected than other variables. Due to the precision of digital tools and software related to measuring one-dimensional, two-dimensional, and even three-dimensional variables, measuring the cross-sectional dimensions of radiological stereotypes has become more accessible and more accurate [14].

Accordingly, in this study, in addition to the longitudinal variables related to the corpus callosum, by examining the two-dimensional variables, we have tried to increase the accuracy of the results and, finally, to pay more attention and examine the corpus callosum changes, correlation, and relationships between variables. These relationships are presented as regressions to determine the relationship between the studied factors.

Numerous articles have suggested that measuring the cross-sectional area of the corpus luteum can be an appropriate criterion for confirming inflammatory MS disease [15]. In different studies on the patients with inflammatory bowel disease, not only has its cross-section been considered, but also changes in the segments of this body in order to innovate in the method of analyzing the cross-section of this body by observing the changes more closely.

In most of the articles, although the number of infected people was less than fifty and the number of people in the control group was the same. Still, this study reduced the number of people with inflammation to 54 and healthy to 128. This number of samples will increase the validity of the research results. In this study, only one type of fixed-profile MRI was used to collect the stereotypes.

In several articles, using multiple devices has reduced the stereotype’s accuracy, obscuring the output results [14]. Paying attention to all the details, especially the variables measured with hand tools, the need for uniformity is undeniable. For example, after the stereotypes were prepared by one type of MRI machine, they were analyzed by one person with one kind of software, and the data were analyzed by one type of statistical software.

The dependence of the size of the corpuscle on the size of the brain makes it invalid just to examine the size of the corpus callosum in the form of the ACC variable. By defining the relative dependence of ACC on AC, we sought to neutralize the intervening variable. The same principle is defined relative to the significant variables. It has been mentioned in several articles that the total surface area of the corpus callosum decreases [16].

Based on published articles, Khader and his colleagues concluded that the study of a corpus luteum plays a key role in confirming inflammatory bowel disease, so they analyzed the body. They examined 26 people with inflammation and 32 healthy people as a control group. The point is that healthy people were the same age as those with inflammatory bowel disease. Their study showed that with anthrax in both the anterior and posterior parts of the trunk, there was a decrease in size. In other segments of the corpus callosum, there was no correlation with the duration of the disease.

The first and most important difference between this study with the current study is the use of the DTI method to examine the corpus callosum, while in this project, MRI has been used. The advanced DTI method is the MRI method. In our review, the final report fundamentally differs from the report from Khader's activity.

We reported a change in the ARG as an incremental change and in the AAMB as a decreasing change, but in this study, only a reduction in the trunk size of the corpus callosum was noted. The DD variable, considered in both studies, is that in our study, the ACC/AC and AAMB/ACC variables decrease over time (DD increase). Still, in Khader's study, there is no significant relationship between DD and corpus callosum segments. The disadvantage of Khader's study is the small number of samples, with 22 women and 4 men with ASD.

The next point is in the method of segmentation of the corpus callosum. They used the Witelson method, while current research emphasizes the Hofer & Frohm method. Because Whitlson based the concepts of Gross Anatomy on the corpus callosum, Hofer & Frohm segmented it based on Tractology methods.

The studies performed for the current study, if examined in terms of brain area, have different results than those analyzed brain area, too, so this point has not been taken into account in Khader's study [16].

Yulin et al. examined the callus in 15 patients with inflammatory bowel disease and 12 healthy individuals as a control group using the DTI method. An important factor they considered for their research was the concept of DD, which averaged 2.7 years. We also evaluated this factor in our study but divided it into 5-year groups. They did not classify the corpus callosum according to Witelson or Hofer & Frohm but divided it into three parts: anterior, trunk, and posterior. All three body parts significantly change with an increase in DD (within 2.7 years) and show a decrease in size [17]. An important point to be drawn from this study is the duration of the disease, known as the DD variable. Cercignani et al. selected 78 people with inflammatory bowel disease. They did not distinguish between different types of inflammation and chose people of each kind. In addition, 26 healthy individuals were used as a control group but did not mention that the control group was age- and sex-matched to people with inflammatory bowel disease. The results of their work also indicate a decrease in the level of the corpus callosum [18].

Sullivan et al. investigated the relationship between corpus callosum and age and gender [19]. The stereotypes examined were all in the mid-sagittal period. The age of the study was in the range of 21-71 years. The final report was published so that the corpus callosum's size and the brain's dimensions are more extensive in men than in women, so there is a gender difference between these two variables. On the other hand, it was stated that the size of the corpus callosum was not related to age and did not change significantly with age. The important thing they noticed was that they measured the size of the brain surface as the size of the corpus callosum, which is why they reported gender differences but rejected age-related changes.

In the current study, the existence of a relationship between the cross-sectional area of the corpus luteum and the cross-sectional area of the brain was proved. On the other hand, the relationship was expressed in regression in tables. According to this principle, we used the concept of "ratio" in our information [19]. Studies by Gupta et al. examined the corpus callosum in two ways: in the first stage, the corpses were morphologically examined after fixation with formalin, and in the second stage, another group of people was analyzed by brain MRI.

The results showed that the LCC values for men and women were 7.62±0.62 and 7.10±0.041, respectively. With P-value values of 0.03, it was concluded that LC is more extensive in men than women. So there is a gender difference for LC. HCC is also a variable that changes significantly with age. In this study, what should not be overlooked is that LCC is essentially a dependent factorassociated with LC. The larger the length of the brain, the larger the longitudinal size of the corpus callosum. "Gupta and colleagues reported a different findings due to the not considering the LC factor." On the other hand, the non-uniformity of variables and methods of examining them can harm the results. The results of our study are based on the fact that

Table 1. Total number of individuals in both groups of healthy and multiple sclerosis

Gender	Healthy status	
	Healthy (n)	RRMS (N)
Male	60	23
Female	68	31
Total number of individuals	128	54

All data were presented as many individuals. RRMS: relapsing-remitting multiple sclerosis.
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neither LCC is sex-dependent nor HCC is significantly different over time [20].

In another article, Gupta et al. examined gender differences in the thickness of the splenic segment of the corpus callosum. The people they used for their examination include those referred to a hospital for screening. After neurological examination, MRI images of the brain were obtained. The result was that no gender differences were reported for the splenic part of the corpus luteum. He and his colleagues attributed the difference between different studies centered on the corpus callosum to several factors: measuring the corpus callosum with other methods and the small number of samples studied [21].

In 2000, Evangelou et al. found that only the size of the corpus callosum was reduced. We agree with this to some extent, but with the point that it is true that the size of the trunk of the corpus callosum decreases, but only in the anterior part, not the posterior. AAMB decreases in level, and APMB does not change significantly. Second, not all variables decrease, but ARG/ACC increases and other segments remain unchanged [22]. The action plan of Evangelou et al. differs significantly from our project in several fundamental respects. First, he divided the cross-sectional area of the corpus callosum into three parts: anterior, middle, and posterior, but we increased this division to five. Second, our studies of living humans were performed with the help of Brain MRI stereotypes while he and his colleagues worked on the corpse with manual measurements.

The fact that the corpse was examined a few hours after death and how changes in the brain were controlled after death are questions that may have led to differences in the results of our research. Ciccarelli et al. Found that with MS, only two parts of the nose and spleen decreased in size [23]. We confirm the changes of the rostrum section and the knee in the form of the ARG variable; however, regarding the evolution of the splenic section, it is necessary to pay attention to two points. First, in our study, the splenic section was unchanged; second, in several articles, the strong evidence of this section in various diseases has been emphasized.

Griffin et al. presented a variety of observations of the corpus callosum with DTI studies [24]. The critical point in these studies is the use of the new DTI method, which is a more advanced form of MRI. The following vital point is the small number of people studied, which was 28 for the inflammatory group and 27 for healthy people. Their study did not report a significant difference in the corpus callosum in a person with MS [24]. It should be noted that the thinner the nerve fibers, the more likely they are to be damaged during inflammation [17].

On the other hand, pathological studies have shown that in the process of inflammation, the number of fibers passing through the corpus callosum is significantly reduced [24]. According to Arboitz et al., in the splenic region, thin fibers are denser, and on the other hand, the densest part of the corpus callosum is the posterior part. According to our research, the two parts with dense fibers, namely the splenic part and the posterior part of the trunk (APMB), do not significantly change the MS process, and perhaps the cause can be related to the same density of corpus callosum segments. The pattern by which several factors influence the corpus callosum changes in the course of inflammation. One of these factors depends on the thickness and density of nerve fibers [17].

Another factor is Wallerian scars, which affect the corresponding part of the corpus callosum wherever it occurs in the brain [23]. Rueda et al. examined the corpus luteum by dividing it the same way we used it. Still, with the help of DTI imaging, all cohorts of the corpus callosum were significantly different in the person with OMI [25]. In articles, one of the weaknesses in the studies of people with MS is that they use immunomodulatory drugs in their treatment routine, which will inevitably be effective due to work. Since

Table 2. Findings of areas and longitudinal variables in healthy and RRMS based on the age groups in both genders

Age Group	Healthy Status	Gender	Mean±SEM							
			ACC	ARG	AAMB	APMB	AI	AS	HCC	LCC
20-30	Healthy	Male	6.42±1.13	25.42±3.48	26.23±3.71	10.47±1.11	5.32±0.87	33.16±2.83	24.68±3.45	42.60±2.38
		Female	6.10±0.82	26.52±3.82	25.34±4.31	10.54±1.01	4.9±0.85	33.28±3.65	24.60±1.11	42.93±2.43
	RRMS	Male	6.03±1.37	26.48±5.33	23.64±2.78	11.57±1.84	4.89±0.30	34.51±3.72	27.58±1.37	44.11±2.15
		Female	6.10±0.97	27.2±2.72	24.68±3.36	10.78±1.54	5.53±1.28	33.61±3.91	24.76±2.40	43.05±1.75
30-40	Healthy	Male	6.52±1.08	25.54±3.09	25.37±5.23	11.05±1.16	5.37±1.07	33.62±3.55	25.89±3.25	42.98±1.67
		Female	6.72±1.23	25.23±3.14	23.18±3.80	10.70±1.91	4.84±0.99	34.17±4.70	23.70±2.27	43.66±1.97
	RRMS	Male	7.11±1.76	24.93±4.80	25.12±6.34	11.14±0.27	4.96±0.20	34.21±2.68	26.33±0.94	43.0l±1.51
		Female	4.89±1.54	28.37±5.59	22.52±2.71	10.94±1.60	4.71±126	33.81±5.31	25.02±3.38	43.18±1.72
40-50	Healthy	M	5.8±0.72	27.89±2.71	23.32±1.30	10.46±1.04	5.15±0.54	33.86±1.24	24.14±2.00	43.06±2.73
		F	6.61±1.00	25.65±1.72	23.15±2.17	10.64±0.78	5.46±0.99	35.64±2.52	25.97±3.26	45.00±2.15
	RRMS	M	3.91±1.44	29.09±3.68	21.76±3.11	10.39±2.27	4.35±1.20	35.21±4.04	22.85±2.27	42.34±2.42
		F	4.04±1.95	25.92±3.51	21.17±2.81	10.81±2.00	5.41±1.27	36.95±5.33	24.24±4.53	44.78±4.36
50-60	Healthy	Male	6.77±0.93	26.90±3.12	27.71±1.24	10.77±1.04	4.78±0.80	35.60±4.l8	28.10±2.36	45.49±2.1 7
		Female	6.14±0.83	26.08±2.85	22.50±1.69	10.69±0.89	5.12±0.93	36.35±4.02	24.23±2.56	44.15±2.07
	RRMS	Male	7.45	27.00	21.86	12.17	6.60	32.59	26.20	47.32
		Female	6.30±1.27	27.18±1.20	23.07±1.12	11.14±1.96	5.13±0.65	34.34±3.05	26.23±3.79	44.02 3.23
60-70	Healthy	M	5.89±1.38	23.28±3.52	22.87±3.27	l1.28±1.17	5.78±1.02	37.42±2.35	24.84±3.23	44.17±2.07
		F	5.89±0.82	27.00±0.41	21.86±2.26	11.02±1.21	4.97±0.68	35.45±1.23	25.65±3.81	44.26±1.72
	RRMS	M	4.59	24.04	18.76	12.45	3.88	40.70	-	45.47
		F	-	-	-	-	-	-	-	-
70-80	Healthy	Male	6.18±1.39	25.4±4.61	22.05±3.83	10.36±1.04	5.55±1.01	37.19±2.78	28.48±2.72	44.03±2.34
		Female	6.24	28.13	22.49	8.99	4.16	37.12	26.44	41.86
	RRMS	Male	4.64±0.36	27.66±7.91	19.12±1.10	10.66±2.00	4.42±1.66	38.79±4.03	-	45.24±2.38
		Female	-	-	-	-	-	-	-	-
	P		0.000	0.01	0.02	0.25	0.14	0.87	0.81	0.65

RRMS: relapsing-remitting multiple sclerosis, F: female, and M: male.

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our society is made up of humans, this variable cannot be removed, and its effect must be accepted [25].

5. Conclusion

Examining the results of this study, it can be stated that with MS, the corpus callosum area changes significantly. This change is directed to the anterior half of this organ so that the Rostrum and Genu sections increase the cross-section, and the anterior section midbody will reduce the cross-section. Therefore, this finding can be considered valuable data and other findings as a non-invasive protocol for assessing the presence or absence of MS using Brain MRI stereotypes.

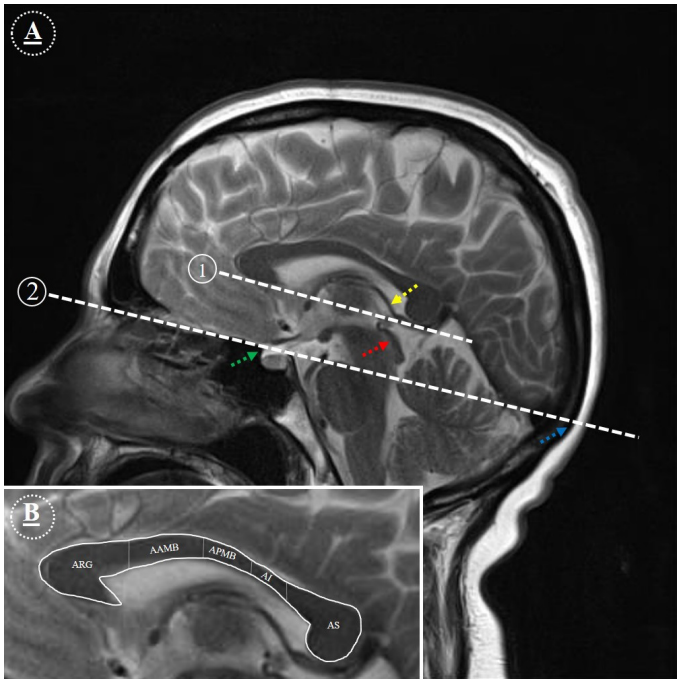

Figure 1. A: Brain MRI image in midsagittal section in a healthy individual

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Dashed-line 1 and 2 represented Subcallosal and TS-EOP baselines, respectively. Yellow arrow: Great cerebral vein, red arrow: cerebral aqueduct, green arrow: sella turcica, and blue arrow: external occipital protuberance. B: Corpus callosum margin with various segments including; ARG: area of rosterum and genu, AAMB: anterior midbody, APMB: area of posterior midbody, AI: area of the isthmus, and AS: area of the splenium.

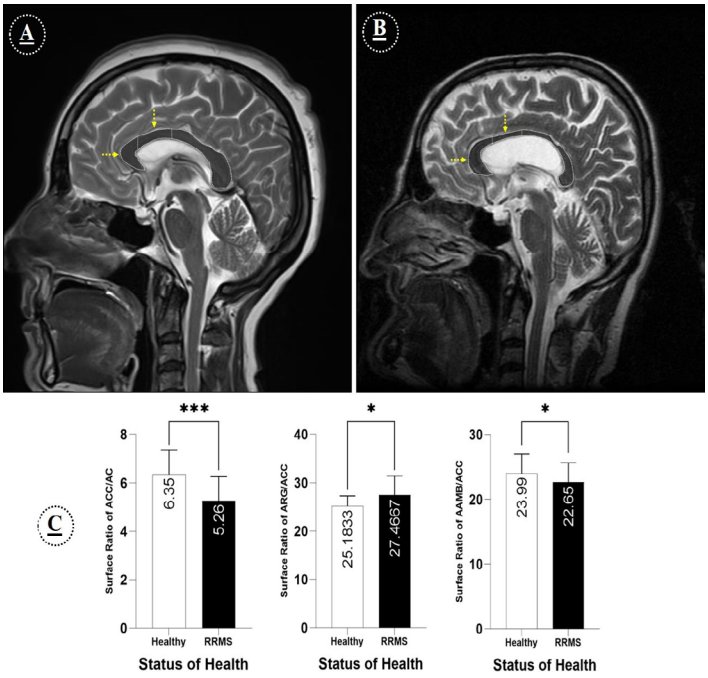

Figure 2. A: Brain MRI image in midsagittal section in a healthy individual

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The dashed line represented the total area of CC in healthy status. Yellow arrows indicated ARG (left arrow) and AAMB (right arrow) indices. B: Dashed line represented the total area of CC in RRMS patients. Yellow arrows indicated ARG (left arrow) and AAMB (right arrow) indices. C: Graphs of morphological CC alterations in healthy individuals compared to RRMS patients. All graphs were designed in ratios than AC and ACC. AC: area of cerebrum, ACC: area of corpus callosum, ARG: area of rosterum and genu, AAMB: area of anterior midbody, APMB: area of posterior midbody, AI: area of the isthmus, and AS: area of the splenium. * indicated significantly ($P<0.05$) levels.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were observed, and the patient information (such as first and last names, age, sex, period of the disease, place of living, and contact number) were preserved entirely. All research protocols have been supervised by the Ethics Committee of Hamadan University of Medical Sciences (Ethics Code: IR.UMSHA.REC.1399.892).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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