Examination of Age Related Volume Changes in Brain by Magnetic Resonance Imaging Method

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Abstract

Aim: Normal brain aging is accompanied by cognitive decline. Determination of age-related changes in the brain helps in understanding the healthy aging process. Our aim was to examine the volume changes occurring due to advanced age by investigating the age-related changes in brain during normal aging process.

Method: This study was carried out on the magnetic resonance (MR) images of 29 healthy subjects consisting of 13 males and 16 females between the ages of 20 to 80. Volumes of right and left cerebral hemispheres, right and left frontal lobes, and right and left temporal lobes were measured by Cavalieri sections method on MR images.

Findings: A significant age-related decline in the volumes of all investigated regions ($p<0.05$) was observed. The decline in volume is higher in males in comparison to females. Additionally, it has been observed that in male subjects, the volume of right hemisphere, right frontal lobe and right temporal lobe showed more signs of atrophy than left side; whereas in females, the volume of right frontal lobe showed a more prominent decline than its left frontal lobe.

Conclusion: An age-related decline in brain volume has been detected for both sexes; however male subjects suffered a more prominent decline than females. We believe that the reason behind this more significant decline might be the effect of gonodal hormones.

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Keywords: Aging, brain, MRI.

Manyetik Rezonans Görüntüleme Yöntemi ile Beyinde Yaşa Bağlı Hacim Değişikliklerinin İncelenmesi

Öz

Amaç: Normal beyin yaşlanmasına yaşa bağlı bilişsel kayıp eşlik eder. Beyinde yaşlanmaya bağlı değişimlerin tespiti sağlıklı yaşlanma sürecini anlamakta yardımcı olacaktır. Amacımız beyinde yaşa bağlı hacim değişikliklerinin incelenmesiyle yaşlılıkta beyinde görülen patolojik değişimleri tespit ederek bu hacim değişikliklerinin cinsiyet ile ilişkili olarak farklılık gösterip göstermediğini tespit etmektir.

Yöntem: Çalışma, yaşları 20-80 arasında değişen, 13 erkek ve 16 kadın bireyden oluşan toplam 29 kişilik bir grubun manyetik rezonans (MR) görüntüleri ile gerçekleştirilmiştir. MR görüntülerinde sağ ve sol serebral yarıkürelerin, sağ ve sol frontal ve temporal lobların hacimleri Cavlieri yöntemi ile ölçülmüştür.

Bulgular: Volümlerdeki bu azalma oranının erkeklerde kadınlardan daha fazla olduğu saptandı. Erkeklerde sağ serebral yarıkürelerin volümü, sağ ve sol frontal ve temporal lobların hacimlerinde sol tarafta göre daha çok atrofi olduğu, kadınlarda ise sağ frontal lob hacminin, sol frontal lob hacminden daha çok azaldığı görüldü.

Sonuç: Sonuç olarak yaşlanma ile beyin volümünde her iki cinsde erkeklerde daha fazla olmak üzere azalma saptandı. Erkeklerde volüm kaybının daha fazla olmasında gonodal hormonların etkisi olabileceği düşünüldü.

Anahtar Sözcükler: Yaşlanma, beyin, MRG.

Introduction

Aging might be defined as gradual changes in body structure and functions that are not resulted from any illness or trauma[1,2,3]. The aging process develops is effected by the genetic material and metabolism of an individual[4,5] and is also sensitive to environmental factors[6,7].

The significant changes in the elder people's brain were first explained in literature about hemispheres 160 years ago. In 1838, Esguirol stated that with increasing age there would be atrophy in cerebral gyri and expansion in cerebral sulci[8]. The studies on human brain have revealed that with the increasing age, the gross weight[9,10] and volume of brain decrease[11,12], cerebral ventricles expand[13,14], overall cerebral sulci expand[15,16], and the selective loss in brain tissue is observed. In one of the first quantitative studies regarding the age-related changes in brain, Brody asserted that “In every single day of our adult life, we lose more than 100.000 neurons[14]”. Later Brody and Vljayashankar claimed that the ratio of cell loss differed from one section to other and it might not be appropriate to make a daily estimation[15]. Haug et al. have shown that some parts of the brain such as cortex striatum and parietal lobe were not losing significant amount of neurons, but between the ages 18 and 84, 15-20% of the neurons in neostriatum and prefrontal area were losing[16]. Additionally, Haug et al. stated that besides the quantitative decrease, the diameter of cell bodies were also decreasing. By using stereological methods, Pakkenberg et al. have calculated that we lose about 10% of our neurons between the ages 20 and 90[17]. We aimed to enlighten the pathological changes occurring in advanced age by detecting the age-related changes in brain during normal aging process. Based on this of brain, we have aimed to collect data regarding the age-related changes in tissue integrity and morphology by scanning healthy volunteers between the age of 20-30 and 70-80, to detect whether the effects of aging change according to gender in different brain regions.

Material and Method

MR-images of 13 males and 16 females who were selected from a group of volunteers in the age range of 20 to 80; these volunteers answered a notice that was put up around the campuses of Liverpool University and Sheffield University. Among the volunteers who accepted to attend the study the ones who had no complains about cardiovascular, endocrine and neurological systems, and the ones whose background anamnesis was taken and found healthy were included the study. Additionally, right-left handedness scores were calculated and Intelligence Questions (IQ) tests were performed. Mental state scoring was also performed. Only right-handed individuals were included in the study. According to Edinburgh Handedness Scoring, (-) 100 is accepted as pure left-handed and (+) is accepted as pure right-handed. The individuals with zero or higher handedness scores were included the study. The educational background of the volunteers was not taken as reference. The education background varied between 9-1 years of education for men and 8-18 years of education for women.

The following volunteers who can be categorised into one of the following criteria were excluded from the study:

- Subjects with dementia,
- Subjects who had brain infection history,
- Subjects who experienced loss of consciousness as a result of head trauma,
- Subjects who have a psychiatric, neurological or cardiovascular system disorder and endocrine system-related illness,
- Subjects who use psychotropic medications,
- Subjects whose MR-images revealed any pathological alterations,
- Subjects who consume more than 54 grams of ethanol daily,
- Subjects whose systolic and diastolic blood pressure is above 150/100 mmHg in any measurement.

Imaging

MR-imaging was performed in University of Liverpool Magnetic Resonance and Image Analysis Research Centre (MARIARC) by using SIGNA 1.5 Tesla (GE Systems, Milwaukee, USA) whole body imaging system. The imaging protocol consisted of the following elements: Both sagittal and axial localizers were used. Participants, as receiver and donor, were scanned in supine position by using quartet-head coil that was provided by the manufacturing firm of the device. For each participant, in order to align the head in the nasion position, it was aligned with head coil by using laser aligning light. By using the foam head supports, the position of the head was fixed during the scanning. In order to minimize the acoustic noise-related disturbance earplugs were given to the participants. The participants' heart beats and capillary oxygenation was followed during the scan. A warning bell was given to the participants in case of claustrophobic feelings or for the cases that they asked to stop the study. Images obtained after scanning were transferred to ANALYZE image analysis program that operates in SPARC working station (SUN Microsystems, California, USA). ANALYZE was used for volume calculations.

1. Conversion: All raw images were converted to ANALYZE format.

2. Global Histogram: Based on the equipment-related factors, signal levels and brightness of the images differs from one subject to other one. It became possible to make the brightest point 240 by standardizing images of subjects with global histogram.

3. Re-Abstraction: 124 volumetric images were converted to 254 images by linear interpolation.

4. Three-Dimensional Levelling: The brain images of all subjects were set to a standard position by leveling a transverse plane that orthogonally passing through upper corner of the anterior and bottom corner of the posterior commissures and by leveling mid-sagittal plane.

5. Volumetric Analysis: The volumes of temporal lobe, cerebral hemisphere, and frontal lobe were calculated separately on coronal images as left and right hemisphere via point counting menu in ANALYZE by using Cavalieri method.

Limit Definitions Used for Volume Calculations

In order to define the limits of intracranial volume, cranial cavity was divided in two regions as supratentorial and infratentorial. For this study, the area that we called intracranial volume consists of all supratentorial area. This area involves cerebral matter (grey and white matters) and ventricular cavities that conveys cerebrospinal fluid. While measuring intracranial volume (ICV), the line above the sulcus pontocrualis level is taken into account and if sulcus pontocrualis cannot be seen, the line above the narrowest bottom part of the brain is counted.

Limit definitions of cerebral hemisphere: The region called as cerebral hemisphere is a whole part of cerebral matter and is above the tentorium cerebelli and pontocrural groove. However the volume of ventricles is not included this volume. In serial MR sections, the lower limit after the cerebellum is accepted as a line passing through the lowest point of third ventricle to the most lateral point of crus cerebri. If the third ventricle cannot be seen a line passing through the lowest point of interpeduncular fossa to the most lateral point of crus cerebri is used.

Limit definitions of temporal lobe: The temporal lobe is separated from the brain with a line passing through the lowest point of sulcus cinguli to ambient cistern. The line where the walls of lateral ventricles are joined is considered as the limit.

Limit definitions of frontal lobe: The beginning limit of frontal lobe is accepted as the first frontal section where corpus callosum is not seen**.**

Calculation of Volumes

First of all, the front and end borders were determined for the areas that the volume would be calculated. The first measured section was chosen randomly in compliance with stereological principles. The points that were within the limits of examined structure were counted and recorded separately for left and right hemispheres. By using the counted points, volume and standard deviation was estimated. To calculate the intracranial volume, a T2 oriented sequence was used. 40 sections that were perpendicular to Anterior Commissure – Posterior Commissure (AC-PC) line were used to calculate ICV; the thickness of the sections was 3 mm and the distance between the sections was 10 mm. The intracranial volume was used to determine the amount of cerebral atrophy. All volumes were considered as a ratio of supratentorial intracranial volume. In order to calculate the cerebral hemisphere, temporal lobe, frontal lobe and intracranial volume, the Cavalieri sections method and point counting technique were used. In order to ensure the stability of each structure, all measurements were repeated three times every 15^{th} day. The stability was determined with intra-class correlation.

Statistical Analysis

SPSS 10.0 software was used to analyze the data by Mann-Whitney U test and Wilcoxon tests.

Findings

When all subjects were grouped only according to their age as old and young, all region volumes were observed to be significantly greater in young subjects (Table 1).

Table 1: Comparison of brain regions between younger and older adults

	Age Group	**N**	**Mean (cm^3)**	**SD**	**P**
Right hemispherium cerebri volume	Young	15	718.23	67.65	0.000
	Old	14	622.39	50.30	
Left hemispherium cerebri volume	Young	15	722.49	58.48	0.001
	Old	14	647.26	55.87	
Right lobus frontalis volume	Young	15	91.36	17.32	0.000
	Old	14	66.29	10.98	

	Age Group	N	Mean (cm^3)	SD	p
Left lobus frontalis volume	Young	15	98.90	18.82	0.000
	Old	14	71.83	11.93	
Right lobus temporalis volume	Young	15	89.23	13.10	0.019
	Old	14	79.47	11.15	
Left lobus temporalis volume	Young	15	95.61	13.70	0.007
	Old	14	83.35	9.97	

When we calculated the proportion of these volumes to ICV, it was observed that for the subjects in the age range of 20 to 30, the ratio of the volume of cerebral hemisphere to ICV was 84%, and the ratio was declining to 78% for the subjects in the age range of 70 to 80 (Table 2).

Table 2: Comparison of brain region to ICV ratio between younger and older adults

	Age Group	N	Mean (cm^3)	SD	p
Right hemispherium cerebri / ICV	Young	15	41.96	2.33	0.001
	Old	14	38.68	3.12	
Left hemispherium cerebri / ICV	Young	15	42.23	1.92	0.004
	Old	14	40.12	1.68	
Right lobus frontalis / ICV	Young	15	5.315	0.80	0.000
	Old	14	4.12	0.70	
Left lobus frontalis / ICV	Young	15	5.75	0.86	0.000
	Old	14	4.46	0.73	
Right lobus temporalis / ICV	Young	15	5.20	0.52	0.01
	Old	14	4.91	0.32	
Left lobus temporalis / ICV	Young	15	5.59	0.67	0.004
	Old	14	5.15	0.27	

Approximately 6% decline was detected in the volume of cerebral hemisphere for both sex-groups ($p< 0.05$). When we examine the ratio of volumes of cerebral hemisphere, frontal lobe and temporal lobe to intracranial volume for men and women in all age groups, it has been detected that the left temporal lobe/ICV ratio is significantly higher at men ($p< 0.05$) (Table 3).

Table 3: Comparison of brain region to ICV ratio between males and females

	Gender	N	Mean (cm3)	SD	p
Right hemispherium cerebri / ICV	Male	13	39.45	3.55	0.10
	Female	16	41.13	2.70	
Left hemispherium cerebri / ICV	Male	13	40.92	2.48	0.20
	Female	16	41.45	1.73	
Right lobus frontalis / ICV	Male	13	4.70	1.06	0.36
	Female	16	4.77	0.90	
Left lobus frontalis / ICV	Male	13	5.18	1.01	0.4
	Female	16	5.08	1.07	
Right lobus temporalis / ICV	Male	13	5.12	0.43	0.32
	Female	16	5.01	0.47	
Left lobus temporalis / ICV	Male	13	5.64	0.53	0.02
	Female	16	5.17	0.50	

It has been observed that the left temporal lobe/ICV volume ratio is higher than the right temporal lobe/ICV volume ratio and the volume of left cerebral hemisphere is higher than the volume of right cerebral hemisphere both in men and women (Figure 1 and 2).

Figure 1: Comparison of right and left hemispherium cerebri volume/ICV ratio in men and women

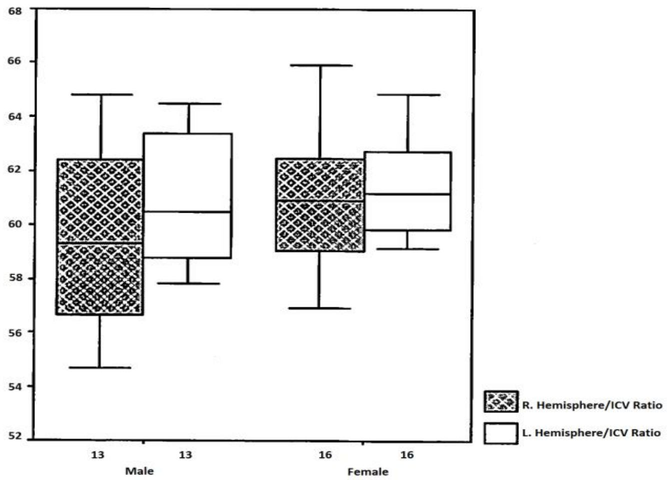
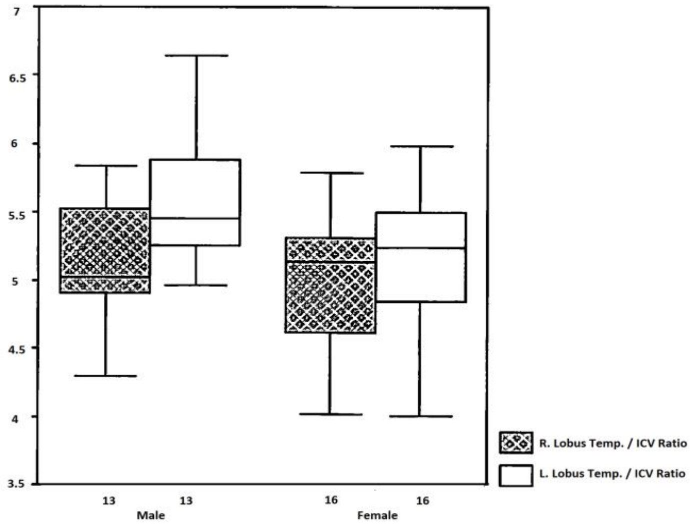


Figure 2: Comparison of right and left temporal lobe volume/ICV ratio in men and women



Discussion

This is a sectional study. The sectional studies enable us to reach data faster and relatively easier. The disadvantage of these studies is that they are being subjected to structural changes observed over generations. The researches like Goffey, Lucke et al. and Labouvie et al. have proved that it is possible to pinpoint systematic changes in consecutive generations among general population[18,19]. As a result of certain studies, it has been generally accepted that aging causes atrophy in gyrus and expansion in sulcus; however, which parts of human body shall be subjected to the first or the greatest effect of aging has been a controversial issue. Within the scope of this study, in order to detect the effects of aging on brain, we separately measured the right and left cerebral hemisphere volumes of young people and older people.

Several researches like Gur et al., Coffey et al., Blatter et al. and Raz et al. have proved that there is an age-related global and selective decline in the cerebral hemisphere volume at the age range of 20 to 90 [18,20,21,22]. In a port-mortem study, Miller et al. have reported that mean volume of cerebral hemisphere stays roughly stable at the age range of 20 to 50; and then, for both sexes it starts to decline in the ratio of 2% decennially after the age of about 50 years[23]. According to the studies conducted so far, the decline in the ratio corresponds to 2% decline decennially. The ratio we have observed is lower which can be attributed to small sample size or differences in MR-imaging methods. In post-mortem studies, more atrophy in brain is expected as a result of fixation protocols for imaging and storage of brain tissues. Studies focusing on age-related volume changes in brain yielded conflicting results. In our study, mean volume of right frontal lobe was found 91.36±17.32 in young people and it declines to 66.29±10.98 in older adults; mean volume of left frontal lobe was found 98.90±18.82 in young adults and it declines to 71.83±11.93 in older adults. In this study we also observed a significant decline in the ratio of these volumes to ICV. Additionally, according to our results the frontal lobe volume declines 3% during aging process while the temporal lobe volume declines 0.7% which in accordance with the study conducted Coffey et al[24]. Cowell et al. conducted an MR-study on healthy adults where they observed an age-related decrease in brain volume for both lobes, but the decrease was higher in frontal lobe than temporal lobe[25]. On the other hand, De Carli, Murphy et al. conducted another MR-study on healthy males in the age range of 19 to 92 where they observed a meaningful age-related decline in posterior frontal lobe; however they did not find such decline in temporal lobe[26]. Along with these conclusions, when we examined if there would be any difference between men and women with regard to volume losses, we have observed that in young people left cerebral hemisphere volume/ICV, right and left frontal lobes/ICV, right and left temporal lobes/ICV ratios are higher in men than women while with increasing age right and left cerebral hemisphere volumes/ICV and right frontal lobe/ICV ratios are higher in women than men. Based on this, we conclude that the volume decline is higher in men than women. In accordance with our results Cowel et al. has indicated that the decline in frontal lobe and temporal lobe is higher in men than women[25]. Jiang Xu et al. has proved that atrophy evolves in brain with aging process and especially in men, right posterior frontal lobe volume shows more atrophy than women[27]. Besides, they have found that men develop age-related atrophy in medial temporal lobe, parietal lobe and cerebellum, but women do not. As a result, Jiang Xu et al. has observed that brain atrophy evolves at differentiating degrees with aging, but this changes are milder in women than men. Bhatia et al. have found a statistically meaningful difference between men and women in terms of whole brain and temporal lobe volume[28]. However, when the volumes are normalized by proportioning to ICV, they have observed that the gender difference disappears. In our study, the left frontal lobe volume in men/ICV ratio has found to be 0.5±0.5 higher than right frontal lobe volume/ICV ratio. Besides, left temporal lobe volume/ICV ratio has found to be 0.7±0.8 higher than right temporal lobe volume/ICV ratio, and left cerebral hemisphere volume has found 1.4±1.8 higher than right cerebral hemisphere volume. In case of women, however, only left frontal lobe volume/ICV ratio has meaningfully found 0.3±0.6 higher than right frontal lobe volume/ICV ratio ($p<0.05$). With regard to temporal lobe, De Carli and Murphy et al. have indicated that the right temporal lobe is bigger than the left temporal lobe, and this does not change with age[26]. Although age-related volume change has been detected by many researchers, the origin of the change has not been determined yet. Several studies have been conducted to determine the reasons behind this loss. Recent post-mortem studies of Double et al. have indicated that age-related white matter loss is more intense than grey matter loss[9]. Pfefferbaum et al. measured the amount of cortical grey matter and demonstrated a meaningful age-related decline, and 0.7 ml/year decrease in subjects in the age range of 21 to 70[29]. Even though the study of Pfefferbaum et al. has revealed that the white matter volume increases until the age of 20, Bartzokls et al. have indicated that the white matter volume in frontal lobe increases until the age of 44 and it increases until the age of 47 in temporal lobe[30].

Conclusion

We have observed that cerebral hemispheres, frontal lobe and temporal lobe volumes decline in relation to aging and this age-related decline in volumes is higher in men than in women. The right cerebral hemisphere, right frontal lobe and right temporal lobe were more atrophied than the left side in men and right frontal lobe was more atrophied than left frontal lobe in women. Considering the fact that the subjects were right-handed, higher atrophy in non-dominant hemisphere has been observed accordingly. The reason behind the more prominent atrophy in men might be a result of the effects of the gonodal hormones, which are still under investigation due to conflicting results of previous studies.

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