

## Age-related changes in the cerebral hemispheres of male and female brains: A morphometric study using magnetic resonance imaging scans

**Nataliia Maryenko\***

PhD in Medical Sciences, Doctoral Student  
Kharkiv National Medical University  
61022, 4 Nauky Ave., Kharkiv, Ukraine  
<https://orcid.org/0000-0002-7980-7039>

**Abstract.** Understanding the differences in brain ageing between males and females and the varying sensitivity of morphometric parameters to ageing are crucial for developing algorithms and protocols for objective and quantitative brain morphology evaluation in clinical practice. This study aimed to determine simple and applicable morphometric parameters for quantifying cerebral atrophic changes associated with ageing and to identify specific characteristics of these changes in ageing male and female brains. Two-dimensional magnetic resonance brain images from 100 participants without confirmed pathology of the nervous system, aged 18 to 86 years, were examined. The sample comprised 44 males and 56 females. Each participant underwent an assessment of five sections: four in the frontal plane (coronal sections) and one in the horizontal plane (axial section). The assessment involved the determination of perimeter and area values. Two measurement approaches were employed: one focusing solely on the visible surface of the cerebral hemispheres, and the other tracing the pial surface within the sulci. Derived indices, including perimeter-to-area ratios, shape factors, and ratios of perimeters and areas, were computed based on the acquired data. The study revealed more pronounced changes in absolute cross-sectional area values corresponding to overall brain tissue with ageing in males. However, no significant sex difference was observed in the age dynamics of relative values. The ratio of two cross-sectional brain areas, considering sulcal content and excluding it, has been identified as the most sensitive parameter to age-related changes in both male and female brains. This ratio could serve as an additional morphometric parameter for diagnostic purposes in examining cerebral structure

**Keywords:** ageing; morphometry; sex differences; tomography

### ✦ INTRODUCTION

The human brain undergoes an intricate and dynamic ageing process, characterised by morphological changes in various brain structures that can influence diverse functions of the nervous system. Currently, morphological alterations in the ageing brain can be evaluated non-invasively using diagnostic neuroimaging techniques, with magnetic resonance imaging (MRI) usually being the method of choice [1]. As highlighted by M.E. MacDonald *et al.* [1], MRI findings during healthy brain ageing encompass a wide range of structural and quantitative changes, with the most common including loss of brain volume and cortical thickness, which can be discerned through morphometry. The significance of studying age-related

changes is emphasised by the resemblance of normal ageing changes to those observed in pathological brain ageing, as evident in neurodegenerative diseases like Alzheimer's. The study by A. Chandra *et al.* [2] concludes that brain MRI serves as an informative biomarker for diagnosing Alzheimer's disease and mild cognitive impairment. However, the development of diagnostic criteria is still pending. The comprehensive review by D.B. Dubal [3] underscores the differing vulnerability of male and female brains to neurodegenerative changes. This is further supported by the conclusions drawn by T. Zalewska *et al.* [4], suggesting notable distinctions between male and female brains concerning neurodegenerative diseases and brain

### Suggested Citation:

Maryenko N. Age-related changes in the cerebral hemispheres of male and female brains: A morphometric study using magnetic resonance imaging scans. *Bull Med Biol Res.* 2024;6(1):34–42 . DOI: 10.61751/bmbr/1.2024.34

\*Corresponding author



ischaemia. Therefore, a crucial aspect of studying brain ageing, including Alzheimer's disease, is to ascertain the sex-specific characteristics of brain ageing in males and females, along with discerning changes in healthy ageing from those indicative of neurodegeneration.

Sexual dimorphism has been observed in various brain structures, as evidenced by morphometric studies utilizing diverse methodologies. For instance, a study by O. Boiagina & O. Vovk [5] utilizing MRI reported larger dimensions (circular area) of the corpus callosum in males compared to females. Similarly, research conducted by O. Slobodian *et al.* [6] on MRI brain scans revealed significant differences in the brain ventricular system between aged males and females with reported interhemispheric asymmetry in males.

Studies focusing on MRI-based morphometry of the overall cerebral hemispheres often employ either surface-based or volumetric morphometric approaches. For instance, D. Brennan *et al.* [7] utilised surface-based measurements of the cerebral cortex, including cortical thickness, cortical surface area, cortical volume, and sulcal depth, and developed a brain sex-predicting classifier based on these measurements.

P. Podgórski *et al.* [8] employed both volumetric and surface-based cortical measurements in their comprehensive morphometric investigation targeting brain ageing in males and females. Their study encompassed volumetric measurements of white matter, grey matter, and cerebrospinal fluid, along with the identification of surface-based parameters such as cortical thickness, sulcal depth, gyrification index, and fractal dimension.

Several studies have prioritised the volumetric approach when comparing age-related atrophic changes in male and female brains. For instance, in the study conducted by F. Sang *et al.* [9], a volumetric approach was chosen to measure total grey and white matter volumes in males and females. Similarly, A.M. Stickel *et al.* [10] utilised

volumetric measurements to assess global brain volume and grey matter volumes in specific brain regions such as the hippocampus, temporal, and occipital lobes. The study by Y. Wang *et al.* [11] employed volumetry to investigate subcortical volumes and their asymmetry in males and females during ageing. Additionally, N. Sambuco [12] applied a volumetric approach to assess the hippocampus and the amygdala in ageing male and female brains.

However, most of the surface-based and volumetric measurements require three-dimensional modelling, complicating the implementation of these metrics into clinical practice. Therefore, the simple morphometric approaches and algorithms adopted for two-dimensional MRI images commonly used in clinical practice deserve further exploration. This study aimed to identify straightforward and practical morphometric measures for assessing age-related cerebral atrophy and to delineate distinctive features of these alterations in the ageing brains of both men and women.

## ✦ MATERIALS AND METHODS

This work is a continuation of the previous study [13], where a comprehensive morphometric analysis was conducted using parameters derived from Euclidean ("classical") geometry. The current study expands on this by focusing on the sex differences in brain ageing. The morphometric analysis was carried out at the Histology, Cytology, and Embryology department of Kharkiv National Medical University (KNMU) during 2022 and 2023.

This research analysed MRI brain scans from a cohort comprising 100 individuals, consisting of 44 males and 56 females, aged between 18 and 86 years, with a mean age of  $41.72 \pm 1.58$  years. The mean age for males was  $41.43 \pm 1.68$  years, ranging from 18 to 86 years, and for females, it was  $41.95 \pm 1.51$  years, ranging from 18 to 72 years. Table 1 shows the distribution of the study participants according to age and sex.

**Table 1.** The distribution of study participants according to age and sex

Age range, years	Males, N	Females, N	Total, N
18-30	14	17	31
31-45	14	15	29
46-60	8	16	24
61-86	8	8	16
Total	44	56	100

**Source:** compiled by the author

A 1.5 Tesla Siemens Magnetom Symphony magnetic resonance scanner (Siemens, Germany) was utilised for brain imaging. Two sequences were chosen for the study: T2 and fluid-attenuated inversion recovery (FLAIR). The MRI brain scans had the following specifications: a resolution of 72 dpi, with the absolute scale configured at 3 pixels = 1 mm. The distance between sections (slice thickness) was set at 5 mm.

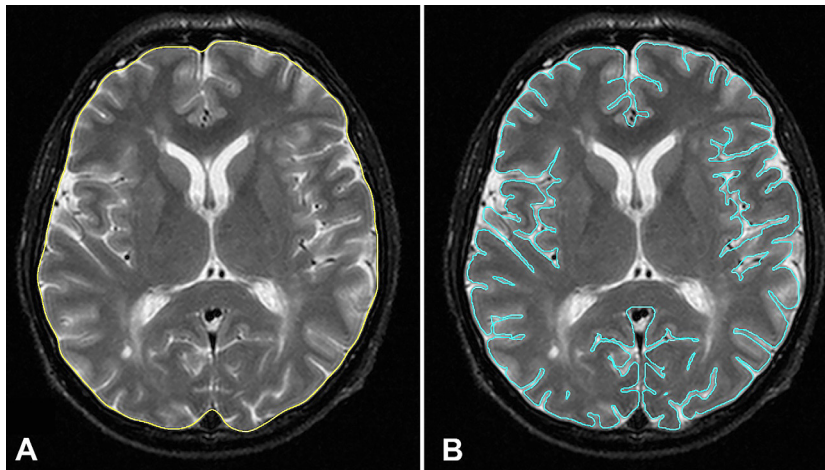
For each participant, a series of tomographic sections (slices) from five distinct brain locations was selected. The frontal plane was utilised to acquire four coronal sections, designated as coronal 1 to 4, while the horizontal plane was

used to obtain one axial section (consequently, designated as axial). These specific sections were identified using precise anatomical landmarks: the first coronal section (coronal 1) corresponded to the level of the anterior poles of the temporal lobes, the second (coronal 2) to the level of the mammillary bodies, the third (coronal 3) to the level of the quadrigeminal plate, and the fourth (coronal 4) to the level of the splenium of the corpus callosum. The fifth, axial, section, was positioned at the level of the upper-middle portion of the thalamus. The chosen sections were selected based on their alignment with anatomical landmarks,

facilitating their easy identification and ensuring the representation of diverse regions within the cerebral hemispheres. Moreover, these sections are recognised for their association with common sites of pathological changes observed in neurodegenerative diseases [14].

The morphometric analysis relied on two fundamental parameters derived from Euclidean geometry: perimeter ( $P$ ) and area ( $A$ ). Both the perimeter and area were determined twice, in two stages (Fig. 1). The first stage involved measuring the perimeter and area, considering solely the superficially visible cerebral surface (Fig. 1A). The second stage involved measuring the perimeter and area encompassing the entire pial surface, including the surface

hidden in the sulci (Fig. 1B). Consequently, four primary parameters were obtained: perimeter  $P_A$ , representing the length of the visible cerebral surface contour; perimeter  $P_B$ , representing the length of the overall pial surface contour, encompassing sulci; area  $A_A$ , representing the cross-sectional overall brain area, including regions enclosed inside the sulci; and area  $A_B$ , representing the cross-sectional area of the overall brain tissue, excluding regions enclosed inside the sulci. Perimeter and area measurements were conducted using Adobe Photoshop CS5 Graphics Editor. Following scale fitting, the respective regions were outlined using the “select” tool, followed by measurement using the “analysis” tool.



**Figure 1.** Two stages (A and B) for the morphometric analysis of MRI brain scans; axial section

**Notes:** A – measurement of perimeter  $P_A$  and area  $A_A$  along the superficially visible pial surface of the cerebral cortex; B – measurement of perimeter  $P_B$  and area  $A_B$  encompassing the entire pial surface of the cerebral cortex, with the pial surface hidden in the sulci

**Source:** the image is sourced from Kharkiv Radiologic Center; labelled by the author

Subsequently, several morphometric indices were computed from the acquired perimeter and area values. These included the following parameters: the perimeter-to-area ratios ( $P_A/A_A$  and  $P_B/A_B$ ), the shape factors (circularity) ( $SF_A$  and  $SF_B$ ), the ratio of two perimeters, or the gyrification index ( $P_B/P_A$ ), and the ratio of two areas ( $A_B/A_A$ ). The shape factors  $SF_A$  and  $SF_B$  (circularity) were calculated using the following formula:

$$SF = \frac{4\pi \times A}{P^2}, \quad (1)$$

where  $SF$  is the shape factor,  $A$  is the area, and  $P$  is the perimeter [15].

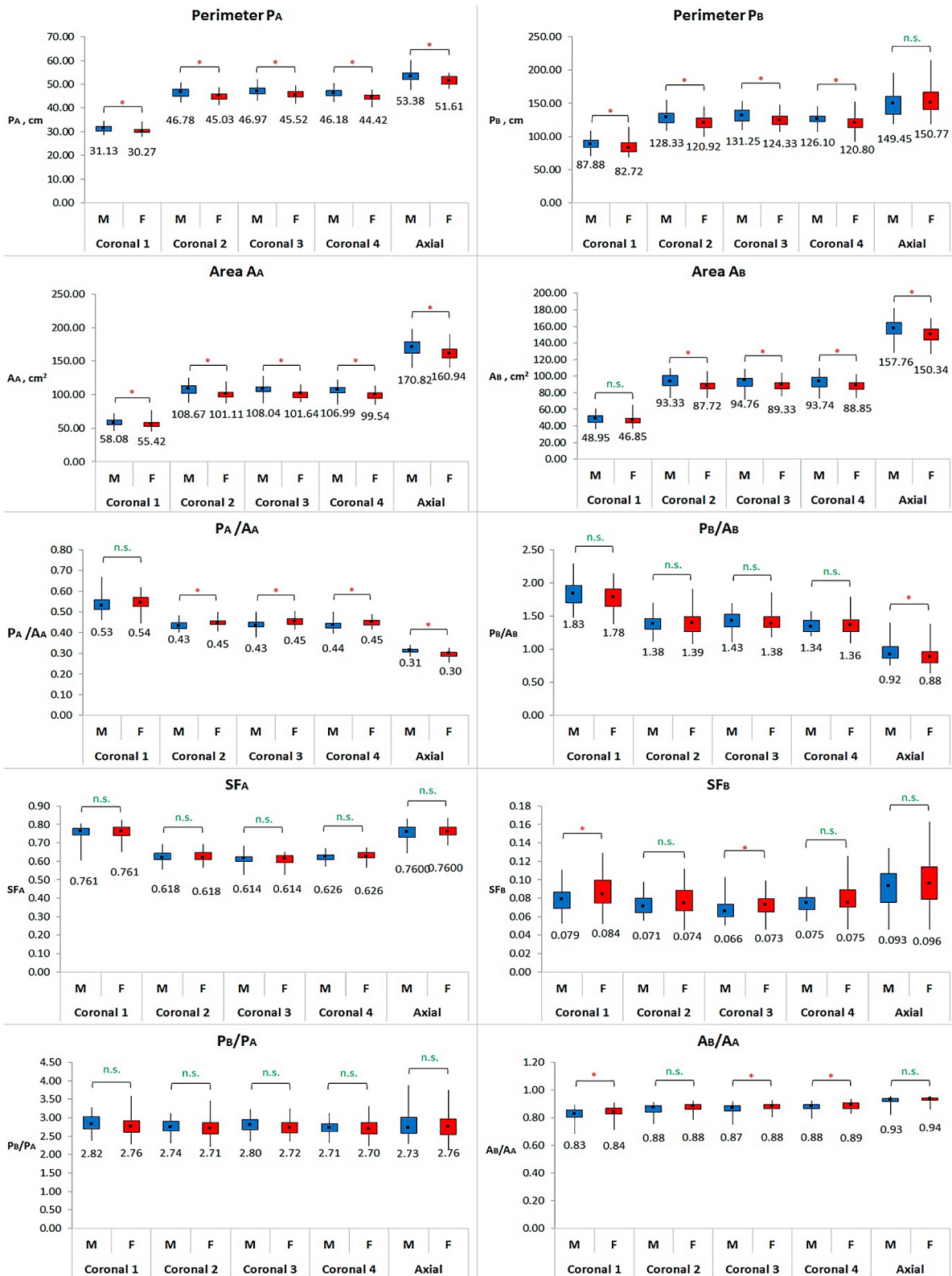
Statistical data processing involved Microsoft Excel 2016. The median values (percentile 50), interquartile ranges (Q1, or percentile 25, and Q3, or percentile 75), and minimum, and maximum values of the studied parameters were computed. The statistical significance of differences between morphometric parameters in males and females was evaluated using the Mann-Whitney U test. Spearman's rank correlation coefficient ( $r$ ) was calculated to evaluate relationships between the studied morphometric parameters and age, with significance determined by the Student  $t$ -test. The F test was applied to compare linear regression equations characterizing the age dynamics of the studied

parameters in males and females (where age is an independent variable, and studied parameters are dependent variables). The significance level for all results was established at  $\alpha=0.05$ .

Brain scanning was conducted at the Kharkiv Radiologic Center for diagnostic purposes. The MRI brain scans were evaluated by radiology experts, and data from individuals without confirmed brain pathology on MRI were included in the study. These individuals were considered to have relatively normal brain anatomy. The study participants provided written informed consent. Anonymised MRI data were obtained under the requirements of the Kharkiv Radiologic Center. The study received approval from the Commission on Ethics and Bioethics of KNMU (Minutes of the Commission Meetings No. 10 dated November 7, 2018, and No. 5 dated February 1, 2023) for research involving human subjects. The study was conducted in compliance with the fundamental bioethical principles outlined in the Declaration of Helsinki [16].

## ★ RESULTS

Descriptive statistical data of morphometric parameter values are presented in Figure 2. This figure illustrates the comparison of median values for the studied parameters in males and females, along with the distribution of values.



**Figure 2.** Descriptive statistics for morphometric parameters of cerebral hemispheres in males and females

**Notes:** M – males; F – females;  $P_A$  – perimeter measured along the visible cerebral surface only;  $P_B$  – perimeter measured along the entire cerebral pial surface;  $A_A$  – area measured along the visible cerebral surface only;  $A_B$  – area measured along the entire cerebral pial surface;  $SFA_A$  – shape factor (circularity) calculated from  $P_A$  and  $A_A$  values;  $SFA_B$  – shape factor (circularity) calculated from  $P_B$  and  $A_B$  values; the box plots depict the distribution of values, with median values provided below each box plot; \* –  $p < 0.05$  (significant sex difference); n.s. –  $p > 0.05$  (non-significant sex difference)

**Source:** compiled by the author

As can be seen from Figure c2, the absolute values of both perimeter measures ( $P_A$  and  $P_B$ ) were significantly larger in males in all examined brain sections, except for perimeter  $P_B$  in the axial section. Similarly, both area values ( $A_A$  and  $A_B$ ) were significantly larger in males in all sections, except for area  $A_B$  in the first coronal section. This observation was expected and can be attributed to the sexual dimorphism in the absolute brain and head size between males and females.

When comparing derived indices in males and females, a diverse pattern was observed, depending on the section and parameter. The perimeter-to-area ratio  $P_A/A_A$  was statistically significantly different in all sections except the first coronal. However, the other perimeter-to-area ratio  $P_B/A_B$  did not statistically differ between males and females in all sections, except for the axial section.

Both shape factors did not differ between males and females in most sections (except for shape factor  $SF_B$  in

the first and third coronal sections). The gyrification index (the ratio of two perimeters,  $P_B/P_A$ ) did not statistically differ between males and females in all sections. These findings suggest that there are no significant differences in the overall brain shape and gyrification degree between males and females, as assessed on the two-dimensional cross-sectional tomographic images.

The area ratio  $A_B/A_A$  was slightly higher in females in all investigated locations; however, a statistically significant difference was noted in the first, third, and fourth coronal sections.

Despite the presence of sexual dimorphism in brain structure and dimensions, it's important to note that some differences may arise from distinct patterns of brain ageing. To assess age-related changes, correlation analysis was conducted, as outlined in Table 2. The examined parameters demonstrated varying strength and direction of correlation relationships with age (Table 2).

**Table 2.** Correlation relationships between morphometric parameters of cerebral hemispheres and age in male and female brains

Parameter	Sex group	Brain section					
		Coronal 1	Coronal 2	Coronal 3	Coronal 4	Axial	All sections (average value)
$P_A$	Males	-0.212	-0.153	0.063	0.025	0.105	-0.019
	Females	-0.182	0.077	0.269	0.221	0.032	0.128
$P_B$	Males	-0.285	-0.083	0.133	-0.186	-0.008	-0.090
	Females	-0.209	-0.198	-0.033	-0.046	0.223	-0.045
$A_A$	Males	-0.194	-0.228	-0.166	-0.062	-0.027	-0.152
	Females	-0.222	-0.017	0.121	0.201	-0.017	0.037
$A_B$	Males	-0.442*	-0.374*	-0.428*	-0.191	-0.177	-0.384*
	Females	-0.392*	-0.268	-0.085	-0.041	-0.139	-0.189
$P_A/A_A$	Males	0.169	0.229	0.332*	0.141	0.220	0.232
	Females	0.212	0.087	0.080	-0.080	0.159	0.124
$P_B/A_B$	Males	0.245	0.400*	0.492*	0.055	0.145	0.379*
	Females	0.181	0.058	0.106	0.081	0.239	0.140
$SF_A$	Males	0.000	-0.082	-0.292	-0.189	-0.192	-0.370*
	Females	-0.108	-0.213	-0.283*	-0.166	-0.132	-0.324*
$SF_B$	Males	0.001	-0.178	-0.362*	0.080	-0.080	-0.170
	Females	-0.023	0.025	-0.076	-0.013	-0.240	-0.129
$P_B/P_A$	Males	-0.211	-0.031	0.098	-0.236	-0.008	-0.087
	Females	-0.167	-0.161	-0.177	-0.113	0.200	-0.110
$A_B/A_A$	Males	-0.429*	-0.561*	-0.568*	-0.388*	-0.445*	-0.549*
	Females	-0.521*	-0.503*	-0.545*	-0.514*	-0.379*	-0.579*

**Notes:** independent variable – age;  $P_A$  – perimeter measured along the visible cerebral surface only;  $P_B$  – perimeter measured along the entire cerebral pial surface;  $A_A$  – area measured along the visible cerebral surface only;  $A_B$  – area measured along the entire cerebral pial surface;  $SF_A$  – shape factor (circularity) calculated from  $P_A$  and  $A_A$  values;  $SF_B$  – shape factor (circularity) calculated from  $P_B$  and  $A_B$  values; \* –  $p < 0.05$

**Source:** compiled by the author

The values of both perimeters ( $P_A$  and  $P_B$ ) did not show statistically significant correlations with age in both males and females. Similarly, statistically significant correlations between age and area  $A_A$  were not observed. However, area  $A_B$  showed a statistically significant decrease with age in males in the first, second, and third coronal sections, while

in females, a statistically significant decrease in this parameter was found only in the first coronal section. Therefore, this finding corresponds to a decrease in overall brain volume attributable to atrophic changes.

Both perimeter-to-area ratios did not show statistically significant correlations with age in most brain sections

in both males and females, except for  $P_A/A_A$  in the third coronal section and  $P_B/A_B$  in the second and third coronal sections in males. A similar pattern was found for both shape factor values: no significant changes in this parameter were observed with age in both males and females, except for shape factor  $SF_A$  in the third coronal section in females and shape factor  $SF_B$  in the third coronal section in males. Therefore, these findings suggest that there are no significant age-associated changes in the overall brain shape in both males and females.

The two-dimensional gyrification index  $P_B/P_A$  was not statistically significantly changed with age in both sex groups. The gyrification index allows for characterizing the convolutedness degree of the cerebral cortex surface – the more gyri the brain has on a particular tomographic section, the larger the area of the cortex surface hidden within the sulci, and the higher the ratio of perimeter  $P_B$  to perimeter  $P_A$ . It could be assumed that the gyrification index decreases with age, which may result from the smoothing of the surface of the cerebral cortex. However, concurrently with this, there is a deepening and widening of the sulci. Therefore, the relative portion of the perimeter corresponding to the cortical pial surface hidden within the sulci remains unchanged.

The area ratio  $A_B/A_A$  showed statistically significant negative correlations with age in both males and females in all examined brain sections. Compared to the related parameter, absolute area  $A_B$ , the ratio of the two areas showed higher correlations with age. The ratio of two areas can be considered a relative area value. The absolute area value can be influenced by variations in head and brain size, but the relative area offers advantages as it reduces the impact of absolute sizes and individual variability.

When comparing linear regression equations characterizing the age dynamics of the investigated parameters in two sex groups, most parameters were not significantly different in most sections. However, a statistically significant difference was observed between males and females in the linear regression equations characterizing the age dynamics of area  $A_B$  in the second and third coronal sections and the average area across all five sections ( $p < 0.05$ ).

To summarise the findings, the investigated morphometric parameters can be classified into three distinct groups. The first group comprises primary perimeter and area values ( $P_A, P_B, A_A, A_B$ ) that characterise the absolute dimensions of the brain. It is noteworthy that these parameters exhibited higher values in males, and more pronounced age-related changes in absolute area  $A_B$  were observed in males.

The second group of parameters consisted of calculated relative indices (perimeter-to-area ratios  $P_A/A_A$  and  $P_B/A_B$ , shape factors  $SF_A$  and  $SF_B$ , and gyrification index  $P_B/P_A$ ) characterizing the features of brain shape. These parameters showed nearly identical or closely matched values in both males and females across most tomographic sections. Additionally, this group of parameters did not demonstrate age-related changes in either sex group.

The third group comprises only one parameter – the ratio of areas  $A_B/A_A$ . This parameter exhibited significant correlation relationships with age, which were the strongest among all studied parameters. This parameter exhibited a similar association with age in both males and females, making it the most sensitive and informative measure when characterizing age-related changes in the brains of both sex groups.

## DISCUSSION

This study focused on determining simple and applicable morphometric parameters for cerebral hemispheres, easily measurable through conventional two-dimensional MRI brain scans. Specifically, parameters such as perimeter and area, derived from Euclidean geometry, were determined. Additionally, the study calculated additional morphometric indices and assessed their changes in age.

When comparing the age-related dynamics of various parameters, the calculated index  $A_B/A_A$  emerged as the most responsive to age-related changes. This index signifies the ratio of area  $A_B$ , corresponding to brain tissue excluding sulci, to area  $A_A$ , encompassing sulcal content. In contrast to absolute morphometric parameter values, this index demonstrated similar sensitivity to age-associated changes in both genders. The widening of sulci with age, attributed to brain tissue atrophy, leads to an increase in the volume corresponding to sulcal content, resulting in a reduction in the ratio  $A_B/A_A$ . The widening of sulci has been linked to the documented increase in cerebrospinal fluid volume as described by P. Podgórski *et al.* [8]. This finding further aligns with the MRI findings reported by O. Slobodian *et al.* [6] regarding age-related changes in the brain's ventricular system. Although those authors reported sex differences in brain ventricles in aged persons, the present study did not find sex differences in the age-associated increase of cerebrospinal fluid occupying the cerebral sulci.

The parameter most closely resembling the areas' ratio  $A_B/A_A$ , or relative brain area, is intracranial volume [17, 18], which serves as a three-dimensional counterpart to the studied parameter and intracranial area. The study by S. Yamada *et al.* [17] affirmed the reliability of estimating cerebrospinal fluid volume alongside intracranial volume measurement for characterizing ageing changes. However, S. Nerland *et al.* [18] reported that the methods for intracranial volume estimation significantly influence the reliability and informativeness of the obtained data. The main difference between approaches used in the present and previous studies, aside from dimensionality, lies in the method of measurement. The current approach involves measuring area  $A_A$  along the external visible surface of the hemispheres, whereas intracranial volume is defined by the inner surface of the skull bones. The current approach offers advantages by specifically characterizing sulcal widening without considering the influence of the space between the skull and brain, including the subarachnoid space, the volume of which can vary and impact the accuracy of age-related change determinations.

The observed differences in brain ageing between males and females can be elucidated by several factors. A notable finding is the more pronounced age-related decline in the absolute cross-sectional area  $A_B$  in males. This discrepancy suggests a greater volume loss in the male brain over time. Given that males typically possess larger absolute brain dimensions, they may exhibit a more substantial reduction in absolute size with ageing. However, it is noteworthy that the age dynamics of the relative area, indicated by the ratio of the two areas, did not exhibit significant differences between males and females. This implies that, when considering relative area values, which account for variations in head and brain size, the age-related changes are comparable between the sexes. Furthermore, other derived

parameters characterizing brain shape, including shape factor, perimeter-to-area ratio, and gyrification index, did not demonstrate significant age-related changes and did not show significant differences in terms of sex. These findings suggest that while there may be differences in absolute brain volume changes with age between males and females, overall brain shape and structural complexity remain relatively stable across genders throughout the ageing process.

A prior investigation, conducted on the identical sample as the current study, employed fractal analysis to assess cerebral atrophy in terms of ageing [19]. The fractal dimension of the cerebral hemispheres' pial surface was identified as a sensitive indicator of age-related changes. However, this parameter did not show differences in cerebral hemispheres' complexity and ageing dynamics between males and females. Several prior studies have reported more noticeable age-associated alterations in males compared to females, while others demonstrated no age-gender interactions, or earlier and stronger declines in cortical parameters in females. Thus, the study by O. Podgórski *et al.* [8] reported that while both male and female brains exhibited signs of ageing starting at approximately 45 years old, females exhibited more pronounced age-related changes in morphometric parameters of the cerebral cortex: the thickness of the cerebral cortex, depth of sulci, gyrification index, and fractal dimension). This conclusion is bolstered by the findings of the study conducted by F. Sang *et al.* [9], which described the more pronounced age-associated decline in brain grey matter volumes in females. Simultaneously, the authors have reported no sex-related differences in white matter ageing.

Conversely, A.M. Stickel *et al.* [10] reported contrasting results, concluding that global brain volumes, as well as the volume of grey matter in several brain regions, exhibited less decline with age in males compared to females. Additionally, the study by Y. Wang *et al.* [11] corroborates these findings, reporting a faster decline in the volumes of subcortical structures in males. The volumetric study by N. Sambuco [12] reported a larger amygdala in males, but after the volume normalization, no sex differences were evident in the ageing patterns of the hippocampus and the amygdala.

The diverse array of results in this study and previous research by other authors may be linked to the specific morphometric parameters chosen, with varying sensitivity to age-related changes and heterogeneity in the samples. The studies of L.M. Wierenga *et al.* [20] and N.J. Forde *et al.* [21] have described greater variability in morphometric parameters in males, consistent with the somewhat larger interquartile range of area  $A_b$  in males observed in the present study. The substantial variability of morphometric parameters in the male brain may influence results in sample formation and account for differing degrees of age-related changes. Given the variability in absolute values, using relative calculated indices, such as the  $A_b/A_A$  ratio or intracranial volume, is more appropriate and informative.

The gender and sex-related differences in morphological changes in the ageing brain, as assessed by morphometric studies, may influence the functional state of the brain. Thus, F. Cieri *et al.* [22] and Z. Yang *et al.* [23] in their studies have shown the impact of sex on brain functional topology and connectivity during normal ageing, mild cognitive impairment, and Alzheimer's disease.

Consequently, morphological and functional changes may contribute to sex differences in cognitive decline during ageing. It has been reported by B.H. Lee *et al.* [24] and K. Wolfova *et al.* [25] that behavioural symptoms may vary between males and females in normal ageing, as well as in cognitive and behavioural impairment. Among the potential factors influencing the diverse patterns of brain ageing in males and females are the effects of sex hormones, as reported by C. Gurvich *et al.* [26], variations in blood plasma lipid profiles, as concluded by Q. Tian *et al.* [27], and congenital features of brain microstructure, as considered by E.T. Reas *et al.* [28]. However, the exact nature of these sex differences is still under investigation. Understanding these differences is essential for developing diagnostic protocols and targeted interventions for age-related cognitive impairments.

## ✦ CONCLUSIONS

Firstly, this study sought to identify simple and applicable morphometric parameters to measure cerebral atrophy changes linked with ageing. Among the studied Euclidean geometry-derived parameters, the most sensitive parameter to age-related changes, identified across both genders, was the ratio of two cross-sectional brain areas, considering sulcal content and excluding it. It has shown significant negative correlation relationships with age:  $r = -0.549$  in males, and  $r = -0.579$  in females for the average value of all brain sections. This finding suggests its potential utility as an additional morphometric parameter for quantitatively assessing age-related atrophic brain changes within clinical practice. The morphometric approach used in the present study offers advantages such as simplicity, applicability, and compatibility with a wide range of software. This metric approach can serve as a standalone morphometric method as well as a supportive preliminary measurement to assess the necessity of more complicated morphometric studies.

Secondly, the study aimed to identify the specific characteristics of changes in the studied parameters in the ageing male and female brains. The present study revealed that as individuals age, males exhibit more pronounced alterations in the absolute size of the cross-sectional area corresponding to overall brain tissue compared to females. In contrast, the age-related trends of relative values showed no notable differences between male and female brains. The derivative indices characterizing brain shape did not show significant sex differences, nor did they show age-related changes. Since the values of several assessed parameters differed in males and females, it is highly advisable to take into account the values calculated for both genders. Further research in this area requires an assessment of the sensitivity and informativeness of morphometric parameters in diagnosing neurodegenerative diseases and distinguishing between normal brain ageing and neurodegenerative diseases.

## ✦ ACKNOWLEDGEMENTS

The author wishes to extend heartfelt thanks to the participants of this study, whose invaluable contribution made this research endeavour achievable.

## ✦ CONFLICT OF INTEREST

The author declares no conflict of interest.

## ◆ REFERENCES

- [1] MacDonald ME, Pike GB. MRI of healthy brain ageing: A review. *NMR Biomed.* 2021;34(9):e4564. DOI: [10.1002/nbm.4564](https://doi.org/10.1002/nbm.4564)
- [2] Chandra A, Dervenoulas G, Politis M, Alzheimer's Disease Neuroimaging Initiative. Magnetic resonance imaging in Alzheimer's disease and mild cognitive impairment. *J Neurol.* 2019;266(6):1293–2. DOI: [10.1007/s00415-018-9016-3](https://doi.org/10.1007/s00415-018-9016-3)
- [3] Dubal DB. Sex difference in Alzheimer's disease: An updated, balanced and emerging perspective on differing vulnerabilities. *Handbook of Clin Neurol.* 2020;175:261–73. DOI: [10.1016/B978-0-444-64123-6.00018-7](https://doi.org/10.1016/B978-0-444-64123-6.00018-7)
- [4] Zalewska T, Pawelec P, Ziabska K, Ziemka-Nalecz M. Sexual dimorphism in neurodegenerative diseases and in brain ischemia. *Biomolecules.* 2023; 13(1):26. DOI: [10.3390/biom13010026](https://doi.org/10.3390/biom13010026)
- [5] Boiagina O, Vovk O. Method of the morphometric analysis of the corpus callosum form on the basis of MR-images and applicable to its natural preparations. *Inter Collegas.* 2019;6(3):150–54. DOI: [10.35339/ic.6.3.150-154](https://doi.org/10.35339/ic.6.3.150-154)
- [6] Slobodian O, Kryvetskiy V, Khmara T. Morphometric characteristics of the ventricular brain systems in the elderly age. *Clin Anat Oper Surg.* 2020;19(4):15–19. DOI: [10.24061/1727-0847.19.4.2020.45](https://doi.org/10.24061/1727-0847.19.4.2020.45)
- [7] Brennan D, Wu T, Fan J. Morphometrical brain markers of sex difference. *Cereb Cortex.* 2021;31(8):3641–49. DOI: [10.1093/cercor/bhab037](https://doi.org/10.1093/cercor/bhab037)
- [8] Podgórski P, Bładowska J, Sasiadek M, Zimny A. Novel volumetric and surface-based magnetic resonance indices of the aging brain – does male and female brain age in the same way? *Front Neurol.* 2021;12:645729. DOI: [10.3389/fneur.2021.645729](https://doi.org/10.3389/fneur.2021.645729)
- [9] Sang F, Chen Y, Chen K, Dang M, Gao S, Zhang Z. Sex differences in cortical morphometry and white matter microstructure during brain aging and their relationships to cognition. *Cereb Cortex.* 2021;31(11):5253–62. DOI: [10.1093/cercor/bhab155](https://doi.org/10.1093/cercor/bhab155)
- [10] Stickel AM, Tarraf W, González KA, Ivanovic V, Morlett Paredes A, Zeng D, et al. Characterizing age- and sex-related differences in brain structure among middle-aged and older Hispanic/Latino adults in the study of Latinos-investigation of neurocognitive aging magnetic resonance imaging (SOL-INCA MRI). *Neurobiol Aging.* 2023;126:58–66. DOI: [10.1016/j.neurobiolaging.2023.02.007](https://doi.org/10.1016/j.neurobiolaging.2023.02.007)
- [11] Wang Y, Xu Q, Luo J, Hu M, Zuo C. Effects of age and sex on subcortical volumes. *Front Aging Neurosci.* 2019;11:259. DOI: [10.3389/fnagi.2019.00259](https://doi.org/10.3389/fnagi.2019.00259)
- [12] Sambuco N. Sex differences in the aging brain? A voxel-based morphometry analysis of the hippocampus and the amygdala. *Neuroreport.* 2021;32(16):1320–24. DOI: [10.1097/WNR.0000000000001728](https://doi.org/10.1097/WNR.0000000000001728)
- [13] Maryenko N, Stepanenko O. Atrophic age-related changes in cerebral hemispheres: Euclidean geometry based morphometry of MRI brain scans. *Acta Morphol Anthropol.* 2023;30(3-4):40–52. DOI: [10.7546/AMA.30.3-4.2023.06](https://doi.org/10.7546/AMA.30.3-4.2023.06)
- [14] King RD, George AT, Jeon T, Hynan LS, Youn TS, Kennedy DN, et al. Characterization of atrophic changes in the cerebral cortex using fractal dimensional analysis. *Brain Imaging Behav.* 2009;3:154–66. DOI: [10.1007/s11682-008-9057-9](https://doi.org/10.1007/s11682-008-9057-9)
- [15] Underwood EE. *Quantitative stereology.* 2<sup>nd</sup> ed. Reading: Addison-Wesley Publishing Company; 1970. 274 p.
- [16] The World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects [Internet]. [cited 2023 Dec 21]. Available from: <https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/>
- [17] Yamada S, Otani T, Ii S, Kawano H, Nozaki K, Wada S, et al. Aging-related volume changes in the brain and cerebrospinal fluid using artificial intelligence-automated segmentation. *Eur Radiol.* 2023;33:7099–12. DOI: [10.1007/s00330-023-09632-x](https://doi.org/10.1007/s00330-023-09632-x)
- [18] Nerland S, Stokkan TS, Jørgensen KN, Wortinger LA, Richard G, Beck D, et al. A comparison of intracranial volume estimation methods and their cross-sectional and longitudinal associations with age. *Hum Brain Mapp.* 2022;43(15):4620–39. DOI: [10.1002/hbm.25978](https://doi.org/10.1002/hbm.25978)
- [19] Maryenko N, Stepanenko O. Quantitative characterization of age-related atrophic changes in cerebral hemispheres: A novel “contour smoothing” fractal analysis method. *Transl Res Anat.* 2023;33(8):100263. DOI: [10.1016/j.tria.2023.100263](https://doi.org/10.1016/j.tria.2023.100263)
- [20] Wierenga LM, Doucet GE, Dima D, Agartz I, Aghajani M, Akudjedu TN, et al. Greater male than female variability in regional brain structure across the lifespan. *Hum Brain Mapp.* 2022;43(1):470–99. DOI: [10.1002/hbm.25204](https://doi.org/10.1002/hbm.25204)
- [21] Forde NJ, Jeyachandra J, Joseph M, Jacobs GR, Dickie E, Satterthwaite TD, et al. Sex differences in variability of brain structure across the lifespan. *Cereb Cortex.* 2020;30(10):5420–30. DOI: [10.1093/cercor/bhaa123](https://doi.org/10.1093/cercor/bhaa123)
- [22] Cieri F, Yang Z, Cordes D, Caldwell JZK, Alzheimer's Disease Neuroimaging Initiative. Sex differences of brain functional topography revealed in normal aging and Alzheimer's disease cohort. *J Alzheimers Dis.* 2021;80(3):979–84. DOI: [10.3233/JAD-201596](https://doi.org/10.3233/JAD-201596)
- [23] Yang Z, Cieri F, Kinney JW, Cummings JL, Cordes D, Caldwell JZK, Alzheimer's Disease Neuroimaging Initiative. Brain functional topology differs by sex in cognitively normal older adults. *Cereb Cortex Commun.* 2022;3(3):tgac023. DOI: [10.1093/texcom/tgac023](https://doi.org/10.1093/texcom/tgac023)
- [24] Lee BH, Richard JE, de Leon RG, Yagi S, Galea LAM. Sex differences in cognition across aging. *Curr Top Behav Neurosci.* 2023;62:235–84. DOI: [10.1007/7854\\_2022\\_309](https://doi.org/10.1007/7854_2022_309)
- [25] Wolfova K, Creese B, Aarsland D, Ismail Z, Corbett A, Ballard C, et al. Gender/sex differences in the association of mild behavioral impairment with cognitive aging. *J Alzheimers Dis.* 2022;88(1):345–55. DOI: [10.3233/JAD-220040](https://doi.org/10.3233/JAD-220040)
- [26] Gurvich C, Thomas N, Kulkarni J. Sex differences in cognition and aging and the influence of sex hormones. *Handbook of Clin Neurol.* 2020;175:103–15. DOI: [10.1016/B978-0-444-64123-6.00008-4](https://doi.org/10.1016/B978-0-444-64123-6.00008-4)

- [27] Tian Q, Mitchell BA, Erus G, Davatzikos C, Moaddel R, Resnick SM, Ferrucci L. Sex differences in plasma lipid profiles of accelerated brain aging. *Neurobiol Aging*. 2023;129:178–84. DOI: [10.1016/j.neurobiolaging.2023.05.013](https://doi.org/10.1016/j.neurobiolaging.2023.05.013)
- [28] Reas ET, Hagler DJ, Zhong AJ, Lee RR, Dale AM, McEvoy LK. Brain microstructure mediates sex-specific patterns of cognitive aging. *Aging*. 2021;13(3):3218–38. DOI: [10.18632/aging.202561](https://doi.org/10.18632/aging.202561)

## **Вікові зміни великих півкуль головного мозку чоловіків та жінок: морфометричне дослідження магнітно-резонансних томограм**

**Наталія Мар'єнко**

Кандидат медичних наук, докторант  
Харківський національний медичний університет  
61022, просп. Науки 4, м. Харків, Україна  
<https://orcid.org/0000-0002-7980-7039>

**Анотація.** Розуміння відмінностей у старінні головного мозку чоловіків та жінок і різної чутливості морфометричних параметрів до вікових змін має важливе значення для розробки алгоритмів і протоколів для об'єктивної та кількісної оцінки будови головного мозку в клінічній практиці. Метою цього дослідження було визначити прості і застосовні морфометричні параметри для кількісної оцінки вікових змін у великих півкулях головного мозку та виявити специфічні особливості цих змін при старінні головного мозку у чоловіків і жінок. Були досліджені двовимірні магнітно-резонансні томограми головного мозку 100 осіб у віці від 18 до 86 років без підтвердженої патології нервової системи. До вибірки увійшли 44 чоловіка та 56 жінок. Дослідження головного мозку кожного учасника включало аналіз п'яти томографічних зрізів, у тому числі чотирьох у фронтальній площині (корональні зрізи) і одного у горизонтальній площині (аксіальний зріз). Морфометрія включала визначення значень периметра та площі. Було використано два підходи до вимірювання: один включав визначення периметра та площі відповідно до видимої поверхні півкуль головного мозку, а інший включав вимірювання цих показників відповідно до усієї поверхні півкуль, включно із поверхнею, прихованою в борознах. На основі отриманих значень периметра та площі були розраховані похідні індекси, у тому числі відношення периметра до площі, фактори форми та співвідношення периметрів і площ. Дослідження показало, що з віком у чоловіків спостерігаються більш виражені зміни абсолютних значень площі перерізу, що відповідає тканині мозку в цілому. Проте вікова динаміка відносних величин у чоловіків і жінок достовірно не відрізнялася. Виявлено, що співвідношення двох площ перерізу мозку, з урахуванням вмісту борозн та без нього, виявилось параметром, найчутливішим до вікових змін як у чоловіків, так і у жінок. Це співвідношення може слугувати додатковим морфометричним параметром для дослідження структури головного мозку з діагностичною метою

**Ключові слова:** старіння; морфометрія; статеві відмінності; томографія