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Analysis of corpus callosum size depending on age and sex

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Abstract

Background: The aim of the study was to analyse changes in the size of the corpus callosum (CC) depending on age and sex and to establish the reference values of the morphometric indices of the CC in the Polish population.

Material and Methods: The results of MR studies of 1108 patients performed in the years 2010-2014 were analysed. Two independent radiologists evaluated cerebral images to exclude deviations from normal state. In patients divided according to sex and to 10 age groups, measurements of CC and brain dimensions were made and morphometric indices were calculated.

Results: The results of measurements related to the following parameters: lengths of longitudinal cross-section of CC (CD), CC thickness in the narrowest place - isthmus (EF), the largest linear dimension of the brain from the frontal pole to the occipital pole (AB), the longitudinal cross-section area of the CC (A1) and cerebral cross-section area (A2) as well as CD/AB and A1/A2 ratios are summarized in 7 figures and 3 tables.
Conclusions: It was demonstrated, that in all age groups there are statistically significant differences in the values of the analysed parameters and ratios of CC size. It was indicated, that there are no statistically significant differences between men and women in the CD, EF, and A1 parameters related to CC size, and the profiles of variations of these parameters are very similar. It was proved that there are statistical differences between women and men in parameters/indicators concerning of the brain size.

Key words: corpus callosum, MR, morphometry, age groups, sex

Introduction
The corpus callosum (CC) i.e. commissura magna is a white matter band located at the bottom of the longitudinal fissure of the brain that connects the two hemispheres of the brain. It plays a very important role, allowing information to be transmitted between the right and left hemisphere of the brain, thus integrating their activities and providing the ability to perform complex functions [9]. For this reason, this structure has been frequently and continues to be screened for morphological and morphometric evaluation [10, 19] and to determine the correlation of its developmental disorders and pathological states with the occurrence of specific clinical symptoms [2, 17, 26]. The numerous reports link the presence of morphological abnormalities of the corpus callosum with mental disorders, speech dysfunction and dyslexia, seizures [7], autism [12], Alzheimer's disease [15], cognitive processes [22] and other pathologies [26, 27]. There are also reports linking variants of the shape and size of the corpus callosum to gender and age and also to the size of the brain [1,4-6, 8, 10, 13, 14, 18, 19, 28, 30, 32,33]. The importance of researches on morphology and the function of corpus callosum underline the fact that in 2012 a separate organization dedicated to the development of researches to understand the role of this structure and to help people with developmental disorders of the corpus callosum was invoked - National Organization for Disorders of the Corpus Callosum (NODCC) [24].

The aim of the study was to analyse the changes of corpus callosum size depending on age and sex and to establish the reference values of morphometric indicators concerning corpus callosum in the Polish population.

Material and methods
The analysis was performed on 1108 patients, including 529 women and 579 men MR studies results, performed in the Magnetic Resonance Unit in the years 2010-2014, diagnosed with scanner Philips Achieva 1.5T. All of these individuals, on the basis of the information contained in the referral, had no CNS injury or CNS diseases or pathology. In each patient also performed a morphological evaluation of the brain image with particular emphasis on the corpus callosum; the evaluation was performed by two radiologists independently evaluated without finding any deviation from the normal state. Patients were divided into 10 age groups (0-5 / 6-10 / 11-15 / 16-20 / 21-30 / 31-40 / 41-50 / 51-60 / 61-70 /> 70), in each group. The M : W ratios were close to 1: 1, with the exception of 0-5 / 6-10 and 11-15, where men predominated (95:57 / 71:53 / 65:59 / 50:57 / 51:51 / 50:50 / 50:50 / 52:50 / 50:50).

Corpus callosum measurements were obtained based on MR studies performed in the frFSE sequences in T2-dependent images in sagittal plane, along the midline of the head (midsagittal).

The following linear measurements and surface areas were performed in sagittal plane of the brain (Figure 1, 2):

Fig. 1,2
CD – length of longitudinal section of corpus callosum
EF - thickness of corpus callosum in the narrowest place - isthmus
AB - largest linear dimension of the brain on the level CD

Measurements of the cross-sectional areas:
A1 - cross-sectional area of corpus callosum in midline plane (midsagittal)
A2 - cross-sectional area of the brain in midline plane (midsagittal)

In addition, the parameters expressing relative ratios of measured structures were added. The introduction of these parameters was aimed obtaining indicators independent from the dimensions of the head / brain.

The following relative ratios were calculated:
A1 / A2 – i.e. the ratio of the area of the cross-sectional area of corpus callosum to the area of the cerebral cross-sectional area in the midline
CD / AB – i.e. the ratio of the length of the corpus callosum to the length of the brain in the sagittal section of the midline

The collected material was subjected to statistical analysis. The analysis was based on a two-
way analysis of variance, Tukey's HSD test, and a non-parametric analysis at the final stage using the Kruskal-Wallis ANOVA test.

**Results**

Figures 3-9 and tables I-III show selected, important parameters of this analysis. The CD parameter (length of the longitudinal section of corpus callosum) was analysed by sex and subsequent age groups. Results are shown in Figure 3.

Fig.3

The analysis of the CD parameter shows that this value varies with age, wherein for the size of corpus callosum rapid increase in the age of 0-10 is characteristic, followed by a short plateau phase over a period of 11-15 years, then the parameter values gradually increase to achieve the peak in a period of 41-50 years of age. After 50 years of age, this parameter gradually decreases in order to note the growth in patients over 70 years of age. There are also differences in CD parameter values depending on sex. There is no difference in CD values in the ages of 0-10 whereas between 11 and 70 years of age the value of this parameter is slightly higher for men than for women, but these differences are not statistically significant.

The AB parameter (the largest linear dimension of the brain from frontal to occipital) was analysed by sex and subsequent age groups. The results are summarized in Figure 4.

Fig.4

The value of AB parameters rapidly increases in the period of 0-10 years of age in both men and women. Then we observe a quiet growth phase up to 15 years of age in women and up to 30 years of age in men followed by a decrease in the value of AB parameter in both sexes of similar severity during the 50s. It is worth noting that the value of the AB parameter for 41-50 years of age in both sexes is half the value of this parameter from 0-10 years of age. In the period of 51-70 years of age AB parameter values in both sexes remain stable. Over the lifetime, the values of AB parameter are higher for men than for women, which is statistically significant.

The analysis of the EF parameter (thickness of corpus callosum in the narrowest place - isthmus) was performed on the basis of sex and age groups. The results are summarized in Figure 5.

Fig.5

For the EF parameter, there is a gradual increase in its value in both sexes up to 40 years of age, followed by a gradual decline in its value over the age of 70, while the EF value for both
sexes in the age group above 70 years of age corresponds to its value in the age of 10-15 years. It is worth adding that in the period 15-20 years the absolute value of the EF parameter is higher in men, while in the period 21-30 years and 51-70 years it is higher in women, what is not statistically significant. Between 0-15 years of age and 31-40 years of age the values of this parameter in both sexes are very similar.

A CD / AB index corresponding to the ratio of the corpus callosum length to the length of the brain in cross-sectional area in the midline was generated and analysed according to sex and age groups. The results are summarized in Figure 6

Fig.6
The CD / AB indicator shows gradual linear growth in subsequent age groups in both sexes. Only in the period of 11-15 years of age and 41-60 years of age in women and 41-70 years of age in men its value stabilizes. In all age groups except 11-15 years, the value of this parameter in women is higher than in men, what is statistically significant.

The A1 parameter (cross sectional area of corpus callosum in cross sectional area in the plane passing through the midline) was analysed by sex and subsequent age groups. The results are summarized in Figure 7.

Fig.7
Similarly to the parameter EF, the A1 parameter behaves, which reaches its peak in both sexes in the 31-40 years of age group and the final value in the >70 year of age group in both sexes corresponds to that of the 11-15 years of age period. The value of this parameter is higher in men in age groups up to 5 years and 21-50 years whereas for women aged 11-15 and 60-70 years, what is not statistically significant.

The analysis of the A2 parameter (area of the cerebral cross sectional area in the plane passing through the midline) was performed, depending on sex and in subsequent age groups. The results are summarized in Figure 8.

Fig.8
The values of A2 parameter in the following age groups behave, similarly to the parameter AB. The phase of rapid growth in the period of 0-10 years of age can be distinguished, followed by the quiet growth phase, which reaches peak in 11-15 years of age in women whereas in 21-30 years of age in men. In subsequent age groups, the A2 value gradually decreases, with men experiencing a rapid decline in the 51-60 years of age group and a slightly lower decrease in the 41-50 years of age group. After a short stabilization of A2
parameter in women within the age of 41-50 years, its value gradually decreases until the age over 70 years of age. Whereas in men, between 51 and 70 years of age, the value of this parameter gradually slightly increases. Over the lifetime, the absolute value of A2 parameter is higher in men than in women, what is statistically significant, and the differences are the highest in the age range of 16-50 years. In the age range of 51-60 years AB parameter values approach to each other in both sexes, and in the subsequent age groups the AB parameter value in men gradually increases.

The A1 / A2 index (the ratio of cross-sectional area of corpus callosum to cross-sectional area of the brain in the midline) was calculated and analysed depending on sex and subsequent age groups. The results are summarized in Figure 9.

The A1 / A2 index values show a gradual increase in the age group of 0-40 years, with linear growth in women and with temporary stabilization in men over 11-20 years of age. In both sexes, the stabilization of the value of this parameter is visible in the period of 41-60 years of age, whereas in the subsequent age groups a slight decrease occurs. The absolute value of the A1 / A2 index is higher in all age groups (except 0-5) higher in women than in men, what is statistically significant.

In all age groups, there are statistically significant differences in all analysed measurements in the parametric and nonparametric approach. On the other hand, within the analysed differences concerning sex insignificant differences for sex in CD, EF and A1 measurements were demonstrated in the nonparametric approach. For all other parameters (AB, A2, A1 / A2, CD / AB) the sex differences in the nonparametric approach were statistically significant, as illustrated in the Table I.

The range of the reference values (mean values and standard deviation) for the performed measurements and calculated indexes in the age groups and for women and men are presented in the Tables II and III.

**Discussion**

The aim of the study was to analyse changes in the size of the corpus callosum, depending on age and sex. The point was to determine the morphometric parameters that are useful in the radiologist's day-to-day operation when assessing the corpus callosum. Many publications refer to the varied pathology of the corpus callosum and analyse the correlations of its
disorder with certain diseases, but the works on population norms related to the size of the corpus callosum is less common in the literature. Some previous works showed greater [6, 13, 14, 28] or similar [1, 4, 5, 16, 33] size of corpus callosum in women compared to men. In these works [5, 6, 14, 16, 28, 30, 33], the area of corpus callosum in the midline plane /midsagittal/, was measured what was a prerequisite for performing similar measurements in our work. Measurement of CC volume is much more difficult due to the difficulty of precisely defining the CC side limits and requires the use of dedicated software, which, although available, it is not widely used [18]. In own elaboration, the focus was on simple linear measurements and CC surface measurements, also demonstrating some correlations with the sex differentials of these parameters. It was demonstrated, that there are no statistically significant differences between women and men in terms of parameters related to the size of the corpus callosum, such as the length of its sagittal cross section (CD), the thickness in the isthmus (EF), or the area of the sagittal cross section (A1), what is consistent with previous work on CC morphometry [6, 11, 20, 21, 32]. Lee and et al. measured the volume of corpus callosum in the 20-year-olds and 40-year-olds groups of women and men in the Korean population, showing a significantly greater volume of the men corpus callosum than the women in the analysed age groups while there was no significant difference in corpus callosum volume between the 20-year-olds and 40-year-olds groups [16]. Takeda and Hirashima conclude that, like other authors, they did not show sex differences in measured CC size indexes in the Japanese population [32]. The meta-analysis by Dreisem and Raz, describing 43 works published in the twentieth century, has shown that the truth is the area of CC is higher in men than in women; however the area of CC cross-section in relation to cerebral size was higher in women than in men [6]. A similar conclusion can be drawn from Mitchell study and the results obtained in our study, where the ratio of the area of the CC cross-section to the area of the cerebral cross-section - $A1 / A2$ in midsagittal plane is higher in women, similarly as the length of CC cross-section in relation to the length of the brain cross-section - $CD / AB$ in this plane [20]. The interesting work by Tanaka-Arakawa indicates the dynamic and non-linear increase in dimensions of individual CC areas during the first two years, indicating the existing sex differences in the rate of development of individual CC parts during this period of life [31]. Our study also found that in both sexes dynamic development of CC over a period of 0-10 years of age, however, the analysed parameters of CC size did not show significant differences in sex, which is probably related to averaging measurements in
the 0-5 age group. Suganthi in 2003 studied the Indian population for differentiation of CC parameters [29]. One aspect of the study was the assessment of the CC (CD) cross sectional length in the age groups, which was found to be statistically significantly higher in men (tested group 18-40, 40-60 and > 60 years of age) than in women. In our work, this tendency was evident, however, in the statistical analysis it was not significant in particular age groups. Curious for unambiguous explanation was the fact that the CD parameter increases its value in the age group over 70 years of age. While initially fast (up to 10 years) and then mild increase in this parameter (up to 50 years of age) can be explained by the increasing amount of nerve fibres within CC and interhemispheric connections, which after 50 years of age begin to decline, it is the fact that in the age group over 70 years of age again gaining higher value, is probably due to the atrophic processes of the other brain structures, as a result of which the shape and morphology of the corpus callosum change. Similarly as in our study, gradual slight elongation in CC with age was observed and no significant sex differences in CC (A1) surface area. Also Mohammadi in the work on the Iranian population showed differences in the cross-sectional length of the CC (CD), but they were not statistically significant [21]. Due to the differences in the assessed age groups in individual studies [11, 18, 20, 21, 29, 31], the exact comparative assessment of the CD parameter in different populations is not reliable. In the work of 2015, Prendergast underwent a detailed analysis the changes in CC region size (described by Witelson) based on age and sex, finding differences between men and women only in the size of the genu of corpus callosum [25, 34]. Also in Mourgel work concerning the Greek population, although a small 41-member group, no statistically significant differences in CD dimension of corpus callosum between groups 45-65 and 66-80 years of age were found [23]. In this work, the dimensions of CC were compared to the brain sizes in midsagittal plane concluding, that these dimensions do not significantly change during life (age groups 24-80). Also the CD / AB ratio was analysed in our material, which value in patients group up to 50 years of age increased linearly and stabilized in the group of 51-70. The variability of the CD / AB indicator is most likely due to the rapid growth of corpus callosum size in comparison with the other structures of the brain in the period of 0-50 years of age, and subsequent stabilization of its value may be associated with cerebral atrophy. Arkedani in his work of 2013 proves that after a statistical correction of the size of the brain, the A1 (CCA) dimension in women is greater than in men [3]. This conclusion was not found statistically significant in our analysis. Analysis of parameters related to brain size (AB, A2,
CD / AB and A1 / A2) showed that there is statistically significant difference between women and men, where the absolute values of AB and A2 parameters are higher in men and CD / AB and A1 / A2 indexes are higher in women, so the sizes of the corpus callosum in women in relation to dimensions are relatively greater. Similar results, related to brain size can be found in the work of other authors [13, 20, 23]. Moreover our analysis found that the values of parameters related to brain size (AB, A2) rapidly increased in age groups of 0-10 years, what reflects a rapid increase in brain size in this life time. There are also interesting differences in the peak in both parameters (AB, A2) between men (21-30 years) and women (11-15 years), suggesting that the brain in women reach their target size earlier than in men.

**Conclusions**

1. In all age groups, there are statistically significant differences in the values of the analysed parameters and their ratios to the size of the corpus callosum and brain - what means, that the size of the corpus callosum varies considerably throughout human life.

2. There are statistically significant differences between women and men in terms of the following parameters and indicators AB, A2, A1 / A2, CD / AB.

3. There are no statistically significant differences between women and men in the measurements of corpus callosum: CD, EF and A1, and the variation profiles of these parameters depending on age in women and men are very similar.

4. The length of sagittal cross-section of corpus callosum (CD) in the period of 0-10 years of age increases rapidly and then grows slowly reaching a peak of 41-50 years of age and grows again slowly in the age group over 70 years.

5. The thickness of corpus callosum in the narrowest place (EF) reaches the peak within the period 30-40 years of age, and then gradually decreases, reaching in the age group over 70 years the size as within the period of 11-15 years of age.

6. The cross-section area of corpus callosum (A1) rapidly increases to 10 year of age, reaches the peak of its size within the period of 31-40 years of age and then gradually decreases, to finally reach in the age over 70 the size at the level of 11-15 years of age.

7. AB and A2 parameters related to brain size reach the peak of its size in different period in women (11-15 years of age) and in men (21-30 years of age).

**References**


LEGENDS OF FIGURES AND TABLES

Figure 1, 2. Scheme of linear measurements and areas of corpus callosum and brain.
Figure 3. CD value in age groups, depending on sex.
Figure 4. Values of AB parameter in age groups, depending on sex.
Figure 5. Values of EF parameter in age groups, depending on sex.
Figure 6. Value of CD/AB parameter in age groups, depending on sex.

Figure 7. Value of A1 parameter in age groups, depending on sex.

Figure 8. Value of A2 parameter in age groups, depending on sex.

Figure 9. Value of A1/A2 parameter in age groups, depending on sex.

Table I. Statistical differences of parameters values depending on sex – nonparametric approach.

Table II. Mean values (mv) and standard deviations (sd) of the analysed parameters and indexes divided for age groups in women. The values are presented in mm for CD, EF, AB measurements, in mm$^2$ for A1 and A2 measurements.

Table III. Mean values (mv) and standard deviations (sd) of the analysed parameters and indexes divided for age groups in men. The values are presented in mm for CD, EF, AB measurements, in mm$^2$ for A1 and A2 measurements.
Table I. Statistical differences of parameters values depending on sex – nonparametric approach.

U Mann-Whitney Test (with the correction to continuity) (Total base) in relation to variable: sex
Marked results are significant with p < 0.05
Disregard the incidents: 35;277;297;311;357;367;445;482;634;684;766;856;886;1031

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<td>144532.5</td>
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<td>0.364449</td>
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Table II. Mean values (mv) and standard deviations (sd) of the analysed parameters and indexes divided for age groups in women.

The values are presented in mm for CD, EF, AB measurements, in mm² for A1 and A2 measurements.

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Table III. Mean values (mv) and standard deviations (sd) of the analysed parameters and indexes divided for age groups in men.

The values are presented in mm for CD, EF, AB measurements, in mm$^2$ for A1 and A2 measurements.

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<td>540,89</td>
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<td>593,38</td>
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<td>572,06</td>
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<td>97,80</td>
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<td>130,80</td>
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<td>9048,00</td>
<td>9119,40</td>
<td>8863,30</td>
<td>8846,40</td>
<td>8804,50</td>
<td>8522,20</td>
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<td>910,2</td>
<td>1422,2</td>
<td>1464,6</td>
<td>763,8</td>
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<td>790,7</td>
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