DOI: https://doi.org/10.17816/rmmar660874 EDN: WVSWMQ

Magnetic Resonance Imaging-Based Frontal Lobe Morphometry in Pediatric Patients

Nikolay N. Semibratov[1], Vladimir A. Fokin[2], Gennadiy E. Trufanov[2], Aleksandr Yu. Efimtsev[2], Konstantin B. Abramov[2], Gleb V. Kondratiev[3], Anatoly G. Levchuk[2]

[1] Saint Petersburg Clinical Scientific and Practical Center for Specialised Types of Medical Care (Oncological), Saint Petersburg, Russia;
[2] Almazov National Medical Research Centre, Saint Petersburg, Russia;
[3] Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia

ABSTRACT

BACKGROUND: Magnetic resonance imaging-based morphometry is a highly informative, noninvasive method for early diagnosis of structural brain changes, which facilitates their quantitative and qualitative evaluation. The frontal lobes increase significantly in size during brain development, which is associated with their important role in cognitive functions and environmental adaptations. Frontal lobe morphometry in pediatric patients can be used to identify abnormalities and understand normal developmental processes in early childhood.

AIM: To identify any changes in the morphometry of the frontal lobes in neurologically healthy children and to analyze how these changes may vary across sex and age groups.

METHODS: The study included 49 children aged 6 months to 18 years. The observations were categorized into two age groups: from 0 to 7 years (17 children) and from 7 to 18 years (32 children). Automatic magnetic resonance imaging-based morphometry was performed with FreeSurfer software used to determine morphometric parameters, including frontal lobe volume, surface area, and cortical thickness.

RESULTS: The findings showed age-related variations in the frontal lobe volume, area, and thickness. There were no significant sex-specific differences in the morphometric parameters between the age groups. However, relative values of the morphometric parameters calculated as a percentage of intracranial volume were higher in boys than in girls. The obtained results demonstrate both symmetrical and asymmetrical changes, thereby underscoring the multidirectional nature of the frontal lobe development during human growth.

CONCLUSION: Magnetic resonance imaging-based morphometry is a highly effective method for identifying the developmental patterns of the frontal lobes in neurologically healthy children. The morphometric parameters outlined in this study may serve as reference values in the assessment of pediatric populations diagnosed with neurodegenerative diseases.

Keywords: brain; children; frontal lobe; magnetic resonance imaging-based morphometry; magnetic resonance imaging; growth and development; aging.

To cite this article
Semibratov NN, Fokin VA, Trufanov GE, Efimtsev AYu., Abramov KB, Kondratiev GV, Levchuk AG. Magnetic Resonance Imaging-Based Frontal Lobe Morphometry in Pediatric Patients. *Russian Military Medical Academy Reports*. 2025;44(2):141–150. DOI: 10.17816/rmmar660874 EDN: WVSWMQ

Submitted: 21.03.2025 **Accepted:** 10.04.2025 **Published**: 30.06.2025

DOI: https://doi.org/10.17816/rmmar660874 EDN: WVSWMQ

Особенности магнитно-резонансной морфометрии в исследовании структур лобных долей у детей

Н.Н. Семибратов[1], В.А. Фокин[2], Г.Е. Труфанов[2], А.Ю. Ефимцев[2], К.Б. Абрамов[2], Г.В. Кондратьев[3], А.Г. Левчук[2]

[1] Санкт-Петербургский клинический научно-практический центр специализированных видов медицинской помощи (онкологический) им. Н.П. Напалкова, Санкт-Петербург, Россия;
[2] Национальный медицинский исследовательский центр им. В.А. Алмазова, Санкт-Петербург, Россия;
[3] Санкт-Петербургский государственный педиатрический медицинский университет, Санкт-Петербург, Россия

АННОТАЦИЯ

Актуальность. Магнитно-резонансная морфометрия является высокоинформативным неинвазивным методом для ранней диагностики структурных изменений головного мозга, позволяющим оценивать их количественно и качественно. Лобные доли в процессе развития значительно увеличиваются в размерах, что связано с их важной ролью в когнитивных функциях и адаптации к окружающей среде. Исследование морфометрии лобных долей у детей может помочь в выявлении патологии и понимании нормальных процессов их развития в ранние годы жизни.

Цель — выявление особенностей изменения морфометрических характеристик структур лобных долей головного мозга у неврологически здоровых детей, а также анализ их зависимости от пола и возраста.

Материалы и методы. В исследование вошли 49 детей в возрасте от 6 месяцев до 18 лет. Все наблюдения были разделены на две возрастные группы: от 0 до 7 лет (17 человек), от 7 до 18 лет (32 человека). Была проведена автоматическая магнитно-резонансная морфометрия с помощью программного обеспечения FreeSurfer с определением морфометрических показателей: объема для каждой структуры лобной доли, площади поверхности и толщины коры.

Результаты. Полученные данные исследования продемонстрировали возрастные различия в объеме, площади и толщине различных структур лобных долей у детей. Статистически значимых половых различий в морфометрических показателях структур, представленных в данном исследовании возрастных групп, выявлено не было. Вместе с тем относительные размеры морфометрических показателей этих структур, рассчитанные относительно внутричерепного объема, были больше у мальчиков, чем у девочек. Полученные результаты показывают как симметричные, так и асимметричные изменения, что подчеркивает разнонаправленную динамику развития структур лобных долей по мере взросления человека.

Заключение. Магнитно-резонансная морфометрия — эффективный метод выявления особенностей развития структур лобных долей головного мозга у неврологически здоровых детей. Представленные в работе морфометрические показатели могут быть использованы в качестве ориентировочных значений при изучении групп детей с нейродегенеративными заболеваниями.

Ключевые слова: головной мозг; дети; лобная доля; магнитно-резонансная морфометрия; магнитно-резонансная томография; рост и развитие; старение.

Как цитировать

Семибратов Н.Н., Фокин В.А., Труфанов Г.Е., Ефимцев А.Ю., Абрамов К.Б., Кондратьев Г.В., Левчук А.Г. Особенности магнитно-резонансной морфометрии в исследовании структур лобных долей у детей // Известия Российской военно-медицинской академии. 2025. Т. 44, № 2. С. 141–150. DOI: 10.17816/rmmar660874 EDN: WVSWMQ

Рукопись получена: 21.03.2025 **Рукопись одобрена**: 10.04.2025 **Опубликована**: 30.06.2025

BACKGROUND

The brain undergoes substantial morphometric changes throughout ontogenesis, particularly during childhood. Such changes depend on the child's age and sex [1–3]. The most intensive development of the nervous system occurs during the first 3 months after birth. By 3 years of age, neuronal differentiation, characterized by axonal growth, myelination, and the growth and increased branching of dendrites, is largely completed. By 8 years of age, the cerebral cortex structurally resembles that of an adult [4]. The brain volume peaks at ~10.5 and 14.5 years in girls and boys, respectively [2]. The mean brain volume is 7%–10% greater in adult men than in women [1, 2, 5].

The frontal lobes are among the most highly developed regions, with significant increases in size during development. In adults, the prefrontal cortex constitutes nearly one-third of the total neocortical surface area. Its relatively late maturation is explained by the delayed myelination of axonal connections. This and other markers of morphological development in the prefrontal cortex are associated with its critical role in cognitive functions and environmental adaptation [6]. Magnetic resonance imaging (MRI) has shown that the gray matter volume in the frontal lobes reaches its maximum at ~11 and 12 years in girls and boys, respectively [7].

MRI-based morphometry is an automated, operator-independent neuroimage analysis method that provides quantitative data on the volumes of individual brain structures, cortical surface area, and cortical thickness [8]. The present study reports the results of morphometric analysis reflecting the effects of age and sex on frontal lobe development in children. Understanding the trajectory of these alterations in normal brain development is essential for interpreting neuroimaging data in clinical practice.

This work aimed to investigate normal frontal lobe development in children without neurologic pathology using MRI morphometry.

METHODS

This study was conducted at the V.A. Almazov National Medical Research Center, Ministry of Health of the Russian Federation, Saint Petersburg, Russia. It included the retrospective and prospective stages of data collection from September 2016 to May 2024. A total of 49 children (30 boys and 19 girls) aged 2 months to 18 years were enrolled. The mean age was 7.94 ± 5.08 years. None had any magnetic resonance imaging (MRI)–detectable structural abnormalities in the brain or clinical symptoms. Written informed consent was obtained from the patients' parents. Anesthesia was provided in cases where examination without it was not feasible.

Intervention

All participants underwent brain MRI on scanners with a magnetic field strength of 1.5 or 3.0 Tesla using a standardized brain imaging protocol with routine pulse sequences in three orthogonal planes (T1, T2, and TIRM), as well as magnetization-prepared rapid acquisition gradient echo (3DT1-MPRAGE), and a T1-weighted gradient-echo sequence with accelerated data acquisition. The parameters used were repetition time (TR): 2000 ms; echo time(TE): 4.38 ms; flip angle (FA): 10°; field of view (FOV): 250 mm; matrix: 256 × 256; slice thickness: 1 mm; number of slices: 160; and scan time: 11 min. Automated MRI morphometry was performed using the FreeSurfer 7.3.2 software to obtain parameters, including volume (mm^3), surface area (mm^2), and cortical thickness (mm) for each frontal lobe structure [9]. Post-processing consisted of sequential steps. The preparatory stages included Talairach linear transformation, intensity normalization, skull stripping, removal of the extracerebral tissues using surface deformation, separation of the cerebellum and brainstem from the cerebrum, and of the left and right hemispheres [9]. A deformable surface algorithm was employed to define the inner (gray–white) and outer (pial, gray–CSF) cortical surfaces [8]. Automated topological correction, surface inflation, and registration in a spherical atlas were also included in the processing pipeline [10]. Morphometric parameters of volume, surface area, and cortical thickness in the frontal lobe structures were compared and reported according to the built-in Desikan–Killiany atlas [11].

All observations were divided into two age groups: 0–7 years (17 participants) and 7–18 years (32 participants). These age ranges were selected to identify the key age-related changes in the morphometric parameters of the frontal lobe structures occurring during critical developmental periods.

Statistical analysis was performed using Jamovi version 2.3.28 and Microsoft Excel 2007 [12, 13]. Data were processed to determine the statistically significant differences between the groups. Quantitative variables were described as their means ± SD. For group comparisons, the non-parametric Mann–Whitney *U* test was applied to account for possible outliers and data asymmetry. A graphical representation of the segmented cerebral structures obtained with the FreeSurfer software package is shown in Fig. 1. Linear regression analysis was performed, and the percentage change in mean values was calculated to assess the trends in morphometric parameters (volume [mm^3], surface area [mm^2], and cortical thickness [mm]) of the frontal lobe structures. The formula used to calculate the percentage change of means was

$$\Delta P = ([M_{end} - M_{start}] / M_{start}) \times 100\%$$

where ΔP indicates the percentage change; M_{end}, the final mean value; and M_{start}, the initial mean value.

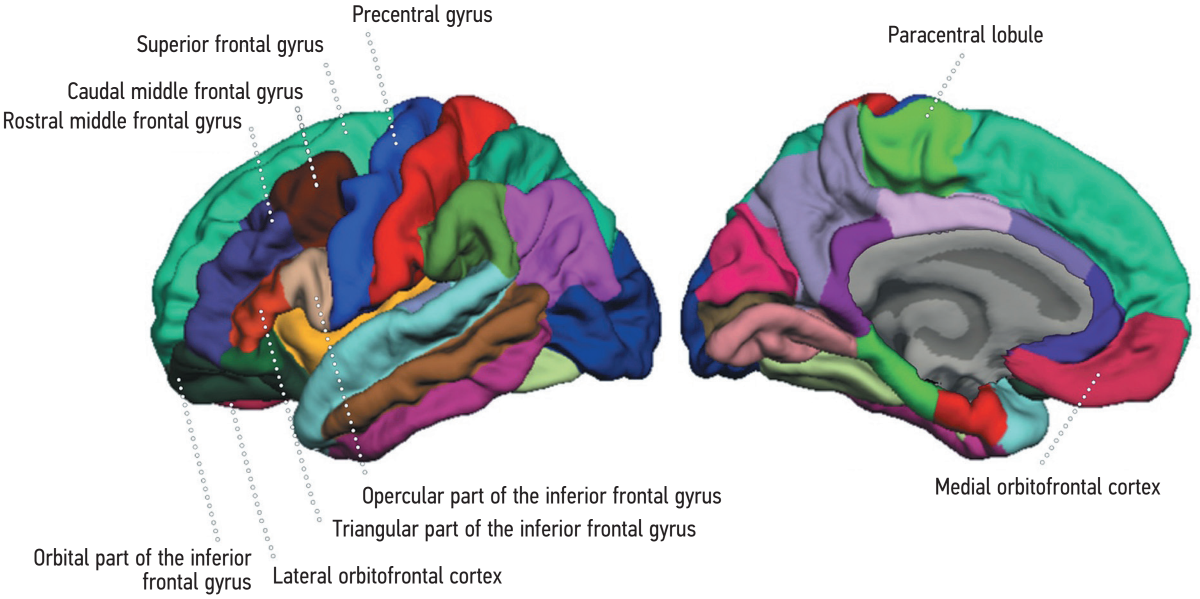

Fig. 1. Frontal lobe structures accessed from the Desikan–Killiany atlas: superolateral (left) and inferomedial (right) surfaces. Adapted from Klein A, Tourville J [11]. Available at: https://mindboggle.info/data.

To systematize the data and enable a subsequent comparative analysis, percentage ranges were defined for different levels of change in the morphometric parameters of the frontal lobe structures. Changes of ⩽10% were classified as mild, from 10% to 30% as moderate, and >30% as pronounced. Symmetry was assessed per the following criteria: a difference of ⩽10% between the contralateral structures was considered symmetric, whereas a variation >10% indicated asymmetry.

RESULTS

The structural changes in the frontal lobes were identified during the comparison between the two age groups using MRI morphometry.

Overall alterations in the frontal lobe structures. The mean values of the morphometric parameters of the frontal lobe structures in the children belonging to the two age groups studied are presented in Table 1 and Fig. 2. The percentage change in the mean values of volume (mm^3), surface area (mm^2), and cortical thickness (mm) of the frontal lobe structures between the children of the two age groups is shown in Fig. 3.

Superior frontal gyrus. A marked development of the right superior frontal gyrus compared with the left was observed in terms of volume, surface area, and thickness in both age groups (0–7 and 7–18 years). Both hemispheres demonstrated a symmetric increase in the volumes of the right (26.6%) and left (20.27%) superior frontal gyri. Similarly, the surface area of the right and left superior frontal gyri exhibited a pronounced symmetric enhancement (17.3% and 14.76%, respectively), unlike in the cortical thickness, which was less pronounced (10.61% and 8.89%, respectively).

Middle frontal gyrus. The morphometric parameters (volume, surface area, and thickness) of the right middle frontal gyrus exceeded those of the left middle frontal gyrus in both age groups. The trajectories of the changes in the rostral and caudal parts of the middle frontal gyrus indicated variations in brain development. The rostral part of the middle frontal gyrus was enhanced in volume and surface area, but the caudal part was elevated primarily in volume. The morphometric parameters of volume, surface area, and thickness of the right middle frontal gyrus were greater than those of the left middle frontal gyrus. Both hemispheres exhibited a pronounced symmetric increase in the volume and surface area of the rostral part of the right (23.25% and 22.37%, respectively) and left (15.54% and 18.72%, respectively) middle frontal gyri. However, the thickness enhanced only slightly (3.52% and 2.33%, respectively). In both hemispheres, a pronounced symmetric elevation in the volume of the caudal part of the right (21.37%) and left (20.49%) middle frontal gyri was observed in the two age groups. However, the surface area (8.34% and 10.67%, respectively) and thickness (13.65% and 7.39%, respectively) demonstrated a less pronounced symmetric increase, respectively.

Inferior frontal gyrus. The study demonstrated a significant development of the right inferior frontal gyrus compared with the left, as reflected by increases in volume, surface area, and thickness. The alterations in volume and surface area of the inferior frontal gyrus indicated a symmetric pattern between the right and left hemispheres.

Table 1. A comparison of the morphometric parameters of the frontal lobes

Structure	Parameter	Group 1 (0–7 years, *n* = 17)	Group 2 (7–18 years, *n* = 32)	Δ*P*, %	*U*	*p*
Right superior frontal gyrus	Volume, mm^3	27985 ± 10527	35430 ± 3058	26,60	142	0,006*
	Surface area, mm^2	8712 ± 2415	10219 ± 836	17.30	144	0.007*
	Thickness, mm	2.64 ± 0.435	2.92 ± 0.116	10.61	186	0.073
Left superior frontal gyrus	Volume, mm^3	26302 ± 9138	31633 ± 3247	20.27	188	0.079
	Surface area, mm^2	7764 ± 2093	8910 ± 877	14.76	179	0.051
	Thickness, mm	2.70 ± 0.414	2.94 ± 0.143	8.89	189	0.083
Rostral part of the right middle frontal gyrus	Volume, mm^3	12571 ± 5191	15494 ± 2172	23.25	173	0.038*
	Surface area, mm^2	3970 ± 1439	4858 ± 739	22.37	154	0.013*
	Thickness, mm	2.56 ± 0.381	2.65 ± 0.133	3.52	271	0.983
Rostral part of the left middle frontal gyrus	Volume, mm^3	12873 ± 4894	14873 ± 2060	15.54	217	0.255
	Surface area, mm^2	3872 ± 1274	4597 ± 679	18.72	143	0.006*
	Thickness, mm	2.58 ± 0.414	2.64 ± 0.130	2.33	248	0.622
Caudal part of the right middle frontal gyrus	Volume, mm^3	6274 ± 2470	7615 ± 1813	21.37	190	0.087
	Surface area, mm^2	2205 ± 754	2389 ± 500	8.34	239	0.499
	Thickness, mm	2.53 ± 0.439	2.80 ± 0.157	10.67	185	0.068
Caudal part of the left middle frontal gyrus	Volume, mm^3	6914 ± 2386	8331 ± 1336	20.49	176	0.044*
	Surface area, mm^2	2345 ± 706	2665 ± 429	13.65	185	0.069
	Thickness, mm	2.57 ± 0.346	2.76 ± 0.119	7.39	200	0.134
Orbital part of the right inferior frontal gyrus	Volume, mm^3	2514 ± 908	3058 ± 423	21.64	163	0.023*
	Surface area, mm^2	713 ± 220	837 ± 118	17.39	174	0.040*
	Thickness, mm	2.78 ± 0.443	2.91 ± 0.133	4.68	264	0.875
Orbital part of the left inferior frontal gyrus	Volume, mm^3	2499 ± 731	2891 ± 398	15.69	180	0.054
	Surface area, mm^2	709 ± 158	818 ± 96	15.37	152	0.012*
	Thickness, mm	2.75 ± 0.425	2.85 ± 0.159	3.64	268	0.933
Triangular part of the right inferior frontal gyrus	Volume, mm^3	4304 ± 1828	5542 ± 853	28.76	149	0.009*
	Surface area, mm^2	1476 ± 468	1734 ± 292	17.48	175	0.043*
	Thickness, mm	2.51 ± 0.454	2.73 ± 0.138	8.76	232	0.407
Triangular part of the left inferior frontal gyrus	Volume, mm^3	4392 ± 1826	5827 ± 906	32.67	143	0.006*
	Surface area, mm^2	1596 ± 451	1851 ± 303	15.98	156	0.014*
	Thickness, mm	2.37 ± 0.518	2.70 ± 0.128	13.92	182	0.060
Opercular part of the right inferior frontal gyrus	Volume, mm^3	4505 ± 1524	5643 ± 798	25.26	129	0.002*
	Surface area, mm^2	1575 ± 424	1747 ± 230	10.92	184	0.066
	Thickness, mm	2.54 ± 0.430	2.85 ± 0.124	12.20	154	0.014*
Opercular part of the left inferior frontal gyrus	Volume, mm^3	4557 ± 1996	5529 ± 1081	21.33	153	0.012*
	Surface area, mm^2	1523 ± 494	1702 ± 315	11.75	187	0.076
	Thickness, mm	2.52 ± 0.522	2.82 ± 0.123	11.90	156	0.015*
The lateral part of the right orbitofrontal cortex	Volume, mm^3	9444 ± 4147	10593 ± 1175	12.17	196	0.113
	Surface area, mm^2	2820 ± 1208	3305 ± 383	17.20	153	0.012*
	Thickness, mm	2.76 ± 0.444	2.75 ± 0.166	–0.36	191	0.091
The lateral part of the left orbitofrontal cortex	Volume, mm^3	9072 ± 2841	10650 ± 1149	17.39	167	0.027*
	Surface area, mm^2	2585 ± 703	3377 ± 281	30.64	68	< 0.001*
	Thickness, mm	2.84 ± 0.355	2.72 ± 0.195	–4.23	143	0.007*
Medial part of the right orbitofrontal cortex	Volume, mm^3	4597 ± 1700	5382 ± 492	17.08	229	0.376
	Surface area, mm^2	1397 ± 402	1695 ± 128	21.33	111	< 0.001*
	Thickness, mm	2.62 ± 0.394	2.62 ± 0.146	0.00	212	0.211
Medial part of the left orbitofrontal cortex	Volume, mm^3	4804 ± 1477	5493 ± 553	14.34	207	0.177
	Surface area, mm^2	1429 ± 332	1782 ± 163	24.70	73	< 0.001*
	Thickness, mm	2.64 ± 0.361	2.57 ± 0.165	–2.65	169	0.031*
Right precentral gyrus	Volume, mm^3	12725 ± 3838	14869 ± 1492	16.85	171	0.034*
	Surface area, mm^2	4884 ± 1222	4953 ± 473	1.41	254	0.716
	Thickness, mm	2.38 ± 0.377	2.70 ± 0.160	13.45	124	0.001*
Left precentral gyrus	Volume, mm^3	12357 ± 3855	15265 ± 1797	23.53	121	0.001*
	Surface area, mm^2	4797 ± 1086	5113 ± 569	6.59	244	0.567
	Thickness, mm	2.37 ± 0.356	2.70 ± 0.166	13.92	108	< 0.001*

DOI: https://doi.org/10.17816/rmmar660874

Continuation of Table 1

Structure	Parameter	Group 1 (0–7 years, n = 17)	Group 2 (7–18 years, n = 32)	ΔP, %	U	p
Right paracentral lobule	Volume, mm^3	4340 ± 1481	5263 ± 533	21.27	114	< 0.001*
	Surface area, mm^2	1616 ± 376	1776 ± 198	9.90	194	0.104
	Thickness, mm	2.42 ± 0.448	2.70 ± 0.146	11.57	172	0.036*
Left paracentral lobule	Volume, mm^3	4594 ± 1376	5537 ± 706	20.53	146	0.007*
	Surface area, mm^2	1676 ± 372	1857 ± 218	10.80	193	0.097
	Thickness, mm	2.42 ± 0.335	2.69 ± 0.146	11.16	128	0.002*

Note. Values of volume (mm^3), surface area (mm^2), and thickness (mm) are expressed as means ± SD for each age group; ΔP: percent change; Mann–Whitney *U* test; $^*p < 0.05$.

Orbital part of the inferior frontal gyrus. Both hemispheres showed a remarkable symmetric enhancement in the volume and surface area of the orbital part of the right (21.64% and 17.39%, respectively) and left (15.69% and 15.37%, respectively) inferior frontal gyri in the two age groups. In contrast, the thickness increased to a lesser extent (4.68% and 3.64%, respectively).

Triangular part of the inferior frontal gyrus. Both hemispheres exhibited a marked symmetric increase in the volume and surface area of the triangular part of the right (28.76% and 17.48%, respectively) and left (32.67% and 15.98%, respectively) inferior frontal gyri in the two age groups. However, the thickness enhanced less markedly (8.76% and 13.92%, respectively).

Opercular part of the inferior frontal gyrus. Both hemispheres revealed a pronounced symmetric elevation in the volume and surface area of the opercular part of the right (25.26% and 10.92%, respectively) and left (21.33% and 11.75%, respectively) inferior frontal gyri of the two age groups. However, the thickness increased to a lesser extent (12.20% and 11.90%, respectively).

Lateral and medial parts of the orbitofrontal cortex. Both hemispheres showed a marked symmetric increase in the volumes of the lateral part of the right (12.17%) and left (17.39%) orbitofrontal cortex of the two age groups. However, the surface area demonstrated a pronounced asymmetric elevation in the lateral part of the right (17.20%) and a considerably greater enhancement in the left (30.64%) orbitofrontal cortex. The thickness of the former decreased slightly (0.36%), whereas it was more pronounced in the left (4.23%). Both hemispheres demonstrated a marked symmetric increase in the volume and surface area of the medial part of the right (17.08% and 21.33%, respectively) and left (14.34% and 24.70%, respectively) orbitofrontal cortex in the two age groups. In contrast, the thickness of the medial part of the right orbitofrontal cortex remained unaltered (0%), whereas the left showed a decline (2.65%).

Precentral gyrus. A more pronounced development was observed in the left precentral gyrus compared with the right, manifested by increases in volume, surface area, and thickness in the two age groups. Both hemispheres demonstrated a symmetric increase in the volume of the right (16.85%) and left (23.53%) precentral gyri. The surface area of the former and latter showed a mild symmetric increase (1.41% and 6.59%, respectively). However, the thickness of the former and latter enhanced symmetrically and more markedly (13.45% and 13.92%, respectively).

Paracentral lobule. The study showed a pronounced development of the paracentral lobules in terms of volume, surface area, and thickness in both age groups. The volume and surface area were enhanced symmetrically in the right (21.27% and 9.90%, respectively) and left (20.53% and 10.80%, respectively) lobules. The thickness elevated more markedly and symmetrically (11.57% and 11.16%, respectively).

Sex differences. A comparative analysis of sex-related differences in the morphometric parameters of the frontal lobe structures, adjusted for the percentage of these parameters relative to total intracranial volume, revealed no statistically significant variations between the studied age groups ($p < 0.05$). However, the morphometric parameters of the frontal lobe structures were relatively larger in boys compared with girls, although statistically insignificant.

DISCUSSION

Morphometric parameters of volume, surface area, and cortical thickness of the frontal lobe structures varied considerably among children in different age groups. These differences reflect brain maturation processes such as myelination, synaptogenesis, growth, and differentiation of nerve cells. The rate of nervous system development is especially high during the first 3 months of life. Differentiation of nerve cells is achieved by 3 years of age, and the cerebral cortex structurally resembles that of an adult by 8 years. The first period (0–7 years) encompasses early childhood, when intensive brain development occurs, associated with the active formation of neuronal connections and structural organization of the cerebral cortex. The second period (7–18 years) covers adolescence, when significant changes in brain

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Fig. 2. Values of volume (mm³; left), surface area (mm²; center), and thickness (mm; right) of the frontal lobe structures in children of the age groups 0–7 years (upper bars) and 7–18 years (lower bars). Vertical lines indicate the medians. The left and right borders of the boxes represent the lower and upper quartiles, respectively.

neuroanatomy and functionality take place. This duration is characterized by active learning and socialization, which also influence the morphometric parameters. Comparing these two groups allows the identification of the key changes in frontal lobe morphometry that result from natural development and environmental influences.

The results of our study are consistent with the findings reported previously [14]. In particular, a tendency

DOI: https://doi.org/10.17816/rmmar660874

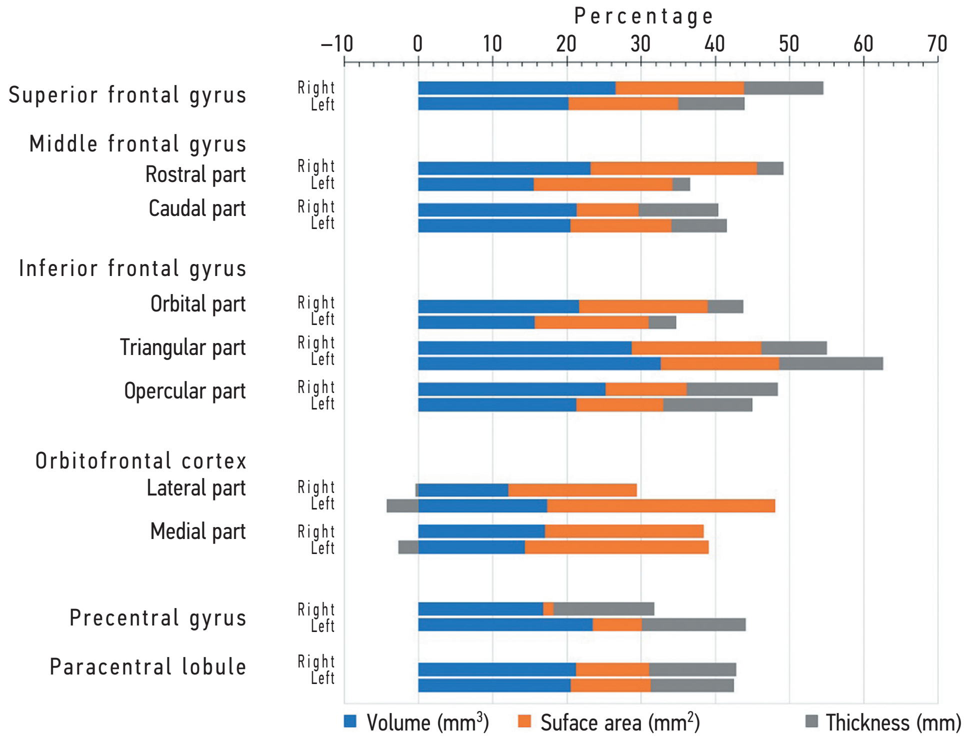

Fig. 3. Percentage change in the mean values of volume (mm^3), surface area (mm^2), and thickness (mm) of the structures between age groups 0–7 and 7–18 years.

toward cortical thinning with age was observed in most regions examined. The morphometric characteristics of the frontal lobes influence cognitive function, emotional regulation, and social behavior. The tendency observed for a greater increase in the morphometric parameters of the frontal lobe structures in boys compared with girls highlights the need for further investigation into sex-associated variations using MRI morphometry. Our findings were consistent with the data published on sexual dimorphism in the brain morphometric parameters; notably, that boys have a larger total brain volume compared to girls [15]. The brain structure and size may serve as a valuable tool for the early detection of developmental abnormalities [14, 16]. Our findings are comparable with the results of the MRI-based morphometric studies on neurodegenerative diseases, particularly epilepsy [17], which highlights the significance of research in this direction.

The challenges associated with brain studies in clinically healthy children are well known in the scientific community. The limited number of participants is largely due to a scarcity of brain imaging studies in children without neurologic symptoms, difficulty in obtaining parental consent, and the challenge of ensuring immobility in children during the examination to acquire high-quality images free of any movement-induced artifacts. Nevertheless, the results of such studies may contribute to a better understanding of brain development and to the diagnosis of neurologic disorders in children.

CONCLUSION

MRI morphometry revealed age- and sex-related changes in the volume, surface area, and cortical thickness of the various frontal lobe structures in children, supporting its potential as a method for studying neurodegenerative diseases in this population. Overall, the morphometric parameters of the frontal lobe structures were greater in boys than in girls. To further investigate these sex-associated differences, we plan to expand the study by including a larger sample size and additional age groups.

ADDITIONAL INFO

Author contributions: All authors made substantial contributions to the conceptualization, investigation and manuscript preparation, and reviewed and approved the final version prior to publication. Personal contribution of each author: N.N. Semibratov: conceptualization and methodology, data analysis and interpretation, writing—original draft, preparation, creation of the published work; V.A. Fokin: supervision of the research stages execution, approval of the final version; G.E. Trufanov: advisory assistance at all stages of the work, editing of the final version; A.Yu. Efimtsev: advisory assistance at all stages of the work, data processing, writing—review & editing; K.B. Abramov, G.V. Kondratiev: data collection and processing, writing—review & editing; A.G. Levchuk: data collection and processing, image processing.

Funding sources: The authors declare no external funding was received for the study.

Ethics approval: The research was conducted as part of a dissertation thesis approved by the Local Ethics Committee of the Federal State Budgetary

Institution Almazov National Medical Research Center, Abstract No. 29 of Local Ethics Committee Protocol, dated February 12, 2018. All study participants provided a written informed consent before being included in the study, which was approved by the Local Ethics Committee as part of the study protocol.

Disclosure of interests: The authors declare no potential conflict of interest to be disclosed in this article.

Statement of originality: No previously published material (text, images, or data), except for frontal lobe images (Fig. 1), which were adapted from Klein A. and Tourville J. [11] (distributed under CC-BY 3.0 license), was used in this study.

Data availability statement: Access to the data obtained in this study is restricted due to confidentiality reasons.

Generative AI: No generative artificial intelligence technologies were used to prepare this article.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Вклад каждого автора: Н.Н. Семибратов — концепция и дизайн исследования, анализ и интерпретация полученных данных, написание текста, подготовка, создание опубликованной работы; В.А. Фокин — контроль выполнения всех этапов исследовательской работы, утверждение окончательного варианта статьи; Г.Е. Труфанов — консультативная помощь на всех этапах выполнения работы, итоговый вариант редактирования текста работы; А.Ю. Ефимцев — консультативная помощь на всех этапах выполнения работы, обработка результатов, редактирование текста работы; К.Б. Абрамов, Г.В. Кондратьев — сбор и обработка данных, редактирование текста работы; А.Г. Левчук — сбор и обработка данных, обработка изображения.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Этическая экспертиза. Исследование проводилось в рамках диссертационной работы, одобренной локальным этическим комитетом (ЛЭК) ФГБУ «НМИЦ им. В.А. Алмазова», выписка № 29 из протокола заседания ЛЭК от 12.02.2018 г. Все участники исследования до включения в исследование добровольно подписали форму информированного согласия, утвержденную в составе протокола исследования этическим комитетом.

Раскрытие интересов авторов. Авторы заявляют об отсутствии потенциального конфликта интересов, требующего раскрытия в данной статье.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные), за исключением иллюстрации структур лобной доли (рис. 1), заимствованной и адаптированной из работы Klein A. и Tourville J. [11] (распространяется на условиях лицензии CC-BY 3.0).

Доступ к данным. Доступ к данным, полученным в настоящем исследовании, закрыт по причине конфиденциальности.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

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AUTHORS' INFO

Nikolay N. Semibratov, MD, radiologist; ORCID: 0000-0002-0034-7413; eLibrary SPIN: 9179-7660; e-mail: nsemibr@gmail.com

Vladimir A. Fokin, MD, Dr. Sci. (Medicine), Professor; ORCID: 0000-0001-7885-9024; eLibrary SPIN: 5939-5198; e-mail: vladfokin@mail.ru

Gennady E. Trufanov, MD, Dr. Sci. (Medicine), Professor; ORCID: 0000-0002-1611-5000; eLibrary SPIN: 3139-3581; e-mail: trufanovge@mail.ru

Alexander Yu. Efimtsev, MD, Dr. Sci. (Medicine), Professor of the Department; ORCID: 0000-0003-2249-1405; eLibrary SPIN: 3459-2168; e-mail: atralf@mail.ru

Konstantin B. Abramov, MD, Cand. Sci. (Medicine); ORCID: 0000-0002-1290-3659; eLibrary SPIN: 5615-4624; e-mail: kalyghanin@mail.ru

Gleb V. Kondratiev, MD, Pediatric Oncologist, Assistant Professor of the Department; ORCID: 0000-0002-1462-6907; eLibrary SPIN: 9092-3185; e-mail: spbgvk@mail.ru

***Anatoly G. Levchuk**; address: 2, Akkuratova str., Saint Petersburg, 197341, Russia: ORCID: 0000-0002-8848-3136; eLibrary SPIN: 6214-5934; e-mail: feuerlag999@yandex.ru

* Corresponding author / Автор, ответственный за переписку

ОБ АВТОРАХ

Семибратов Николай Николаевич, врач-рентгенолог; ORCID: 0000-0002-0034-7413; eLibrary SPIN: 9179-7660; e-mail: nsemibr@gmail.com

Фокин Владимир Александрович, докт. мед. наук, профессор; ORCID: 0000-0001-7885-9024; eLibrary SPIN: 5939-5198; e-mail: vladfokin@mail.ru

Труфанов Геннадий Евгеньевич, докт. мед. наук, профессор; ORCID: 0000-0002-1611-5000; eLibrary SPIN: 3139-3581; e-mail: trufanovge@mail.ru

Ефимцев Александр Юрьевич, докт. мед. наук, профессор кафедры; ORCID: 0000-0003-2249-1405; eLibrary SPIN: 3459-2168; e-mail: atralf@mail.ru

Абрамов Константин Борисович, канд. мед. наук; ORCID: 0000-0002-1290-3659; eLibrary SPIN: 5615-4624; e-mail: kalyghanin@mail.ru

Кондратьев Глеб Валентинович, врач — детский онколог, ассистент кафедры; ORCID: 0000-0002-1462-6907; eLibrary SPIN: 9092-3185; e-mail: spbgvk@mail.ru

***Левчук Анатолий Геннадьевич**; адрес: Россия, 197341, Санкт-Петербург, ул. Аккуратова, д. 2; ORCID: 0000-0002-8848-3136; eLibrary SPIN: 6214-5934; e-mail: feuerlag999@yandex.ru