DOI: https://doi.org/10.23868/gc568311

Изучение структурных атипий головного мозга у детей с акушерским параличом плечевого сплетения: воксель-базированная морфометрия

Д.В. Кадиева[1], Ф. Галло[1], М.А. Уланов[1], А.Н. Шестакова[1], В.В. Моисеева[1], А.М. Ходоровская[2], О.Е. Агранович[2]

[1] Национальный исследовательский университет «Высшая школа экономики», Москва, Российская Федерация;

[2] Национальный медицинский исследовательский центр детской травматологии и ортопедии имени Г.И. Турнера, Санкт-Петербург, Российская Федерация

АННОТАЦИЯ

Обоснование. Акушерский паралич плечевого сплетения — заболевание новорождённых, обычно возникающее в результате разрыва нерва во время трудных вагинальных родов, приводящее к параличу одной из верхних конечностей. Несмотря на то, что современные методы лечения могут гарантировать почти полную реиннервацию конечности, у некоторых пациентов все ещё наблюдается плохая двигательная функция. Одной из причин этого несоответствия может быть чередование в мозге, возникающее в результате ограниченного использования конечности с рождения.

Цель исследования — сравнить объёмы серого вещества у детей с акушерским параличом и здоровых.

Методы. Используя метод воксельной морфометрии в SPM12 (Statistical Parametric Mapping) в MATLAB R2019b, мы проанализировали 46 структурных МРТ 24 детей с акушерским параличом (средний возраст — 10,20 года), из них 12 девочек, и 22 здоровых детей контрольной группы соответствующего возраста (средний возраст — 9,63 года), из них 10 девочек.

Результаты. Мы обнаружили объёмные различия между пациентами и здоровыми участниками, которые выдержали поправку на множественную проверку гипотез (FWE, p <0,005). Результаты показали, что у детей с акушерским параличом были значительно меньшие объёмы левого миндалевидного тела, гиппокампа и правой энторинальной области.

Заключение. Принимая во внимание предыдущие исследования этих областей мозга, мы можем предположить, что комплекс миндалевидное тело–гиппокамп–энторинальная кора может играть значительную роль в моторном поведении.

Ключевые слова: моторные нарушения; объём серого вещества; акушерский паралич плечевого сплетения.

Как цитировать:
Кадиева Д.В., Галло Ф., Уланов М.А., Шестакова А.Н., Моисеева В.В., Ходоровская А.М., Агранович О.Е. Изучение структурных атипий головного мозга у детей с акушерским параличом плечевого сплетения: воксель-базированная морфометрия // Гены и клетки. 2023. Т. 18, № 4. С. 331–339. DOI: https://doi.org/10.23868/gc568311

Рукопись получена: 12.08.2023 **Рукопись одобрена:** 24.10.2023 **Опубликована online:** 13.11.2023

DOI: https://doi.org/10.23868/gc568311

Exploring structural brain changes in children with neonatal brachial plexus palsy: a voxel-based morphometry analysis

Dzerassa V. Kadieva[1], Federico Gallo[1], Maxim A. Ulanov[1], Anna N. Shestakova[1], Victoria V. Moiseeva[1], Alina M. Hodorovskaya[2], Olga E. Agranovich[2]

[1] National Research University Higher School of Economics, Moscow, Russian Federation;

[2] Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Saint Petersburg, Russian Federation

ABSTRACT

BACKGROUND: Obstetric brachial plexus palsy (OBPP) is paralysis of the upper limb resulting from nerve injury during vaginal delivery. Although current treatment approaches frequently lead to complete reinnervation of the limb, some patients show long-term motor deficits. These impairments may result from upper limb disuse that causes structural brain changes.

AIM: This study aimed to compare deep gray matter volumes between children with OBPP and healthy controls.

METHODS: We analyzed the structural magnetic resonance imaging results of 46 children with OBPP (*n*=24, mean age — 10.20, of whom 12 were girls) and healthy age-matched controls (*n*=22, mean age — 9.63, of whom 10 were girls) using a voxel-based morphometry technique in SPM12 package (Statistical Parametric Mapping) in MATLAB R2019b. To minimize false discoveries, we used a stringent procedure to control the family-wise error rate.

RESULTS: We found volumetric brain differences between children with OBPP and healthy controls (all FWE-corrected p <0.005). Children with OBPP had significantly lower gray matter volumes in the left amygdala, bilateral hippocampus, and right entorhinal cortex.

CONCLUSION: Integrating our findings with previous work, we speculate that the amygdala–hippocampus–entorhinal cortex complex might play a significant role in motor disorders.

Keywords: motor disorder; gray matter; obstetric brachial plexus palsy.

To cite this article:
Kadieva DV, Gallo F, Ulanov MA, Shestakova AN, Moiseeva VV, Hodorovskaya AM, Agranovich OE. Exploring structural brain changes in children with neonatal brachial plexus palsy: a voxel-based morphometry analysis. *Genes & cells.* 2023;18(4):331–339. DOI: https://doi.org/10.23868/gc568311

Received: 12.08.2023 **Accepted:** 24.10.2023 **Published online:** 13.11.2023

INTRODUCTION

Obstetric brachial plexus palsy (OBPP) is an injury-related disease in newborns, usually originating from nerve tearing during a difficult vaginal delivery, leading to paralysis of one of the upper limbs [1]. The prevalence of OBPP ranges from 1.6 to 5.1 per 1000 births [2, 3]. Prognosis is generally favorable, with almost half of patients spontaneously recovering upper limb motor functioning. However, in 20–30% of children, severe OBPP can cause persistent hand dysfunction, skeletal deformity, cosmetic deformity, and limitations in activities of daily living, such as feeding, grooming, and dressing [4, 5]. Treatment is based on clinical severity and may include physical therapy, microsurgical nerve reconstruction, shoulder reconstruction, and tendon transfers [6].

Variations in clinical outcomes of OBPP across individuals may arise from alterations in the brain structure and function that results from a restricted use of the upper limb since birth [7–9]. Previous investigations demonstrate that despite muscle reinnervation, some patients show long-term motor deficits and developmental apraxia [9–11]. These suggest that following injury, neuroplastic changes result in unique adaptations in sensory and motor cerebral circuits early in development. While most studies focus on the treatment and repair of peripheral nerves, few have investigated the cerebral sequelae of OBPP. To develop successful rehabilitation strategies, it is crucial to understand the structural and functional differences in the brain of patients with lifelong OBPP when compared to healthy and recovered individuals.

In the present study, we investigate brain changes in children with OBPP. We aimed to explore gray matter volumetric differences between patients and healthy children. While cortical changes in OBPP has been previously reported [9, 12], this is the first report of deep brain structural alterations in OBPP.

METHODS

Participants

Forty-six age-matched children participated in this study: 24 patients (2–17 years old, mean age — 10.20, of whom 12 females), and 22 healthy controls (2–17 years old, mean age — 9.63, of whom 10 females). All healthy participants were right-handed. The hand dominance in the clinical group varied depending on the side of the palsy. Patients with OBPP were recruited and assessed at the Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery (Saint Petersburg, Russia). Patients from different parts of the country were assessed before reconstructive surgery. Participants in the control group were recruited and assessed at the National Research Institute of Emergency Children's Surgery and Traumatology (Moscow, Russia). The study protocol was approved by the local ethics committee of the National Research University Higher School of Economics (N 19–3 dated 09 December 2019). Written informed consent was obtained from the participants' guardians.

Only healthy participants without a history of neuropsychological or orthopedic disease were included in the control group. All patients with OBPP group reported signs and symptoms related to the disease, including upper limb contractures, flaccid palsy, and muscle hypoplasia or aplasia. Patients with any residual brain structural anomalies, such as hydrocephalus, were excluded.

Magnetic resonance imaging data collection

T1-weighted 3D images were collected using two Philips Ingenia Elition X 3.0T magnetic resonance scanners in both study sites. The following parameters were set for magnetic resonance imaging (MRI) data acquisition: voxel size — 1.0×1.0×1.0 mm^3, repetition time — 8.5 ms, echo time — 3.7 ms, 180 slices, slice thickness — 1 mm, acquisition matrix — 256×256, field of view — 256×256 mm, and flip angle — 8°.

Magnetic resonance imaging data preprocessing

Images were visually inspected for movement artifacts and other abnormalities. Images were uniformly aligned to the anterior commissure–posterior commissure line. Images were then spatially normalized and segmented into gray matter (GM), white matter, and cerebrospinal fluid using SPM12 (Statistical Parametric Mapping, https://www.fil.ion.ucl.ac.uk/spm/) in MATLAB R2019b. Total intracranial volumes (TIV) were also automatically acquired. The normalized maps were modulated with the resulting Jacobian determinant maps to preserve GM volumes of native space and smoothed with an 8-mm FWHM Gaussian kernel. Voxel-based morphometry in CAT12 (Computational Anatomy Toolbox, https://neuro-jena.github.io/cat/) within SPM12 was used to compare whole-brain GM density in patients and controls. Maximum tissue probability labels derived from the Neuromorphometrics Atlas (http://www.neuromorphometrics.com/) were used to identify brain regions which showed significant volumetric differences between groups.

Statistical analysis

Voxel-based morphometry analysis was performed in CAT12 using a generalized linear model. The smoothed GM images of both groups were tested by a voxel-based two-sample t-test. TIV, age, and sex were set as covariates to account for differences in individual brain size.

RESULTS

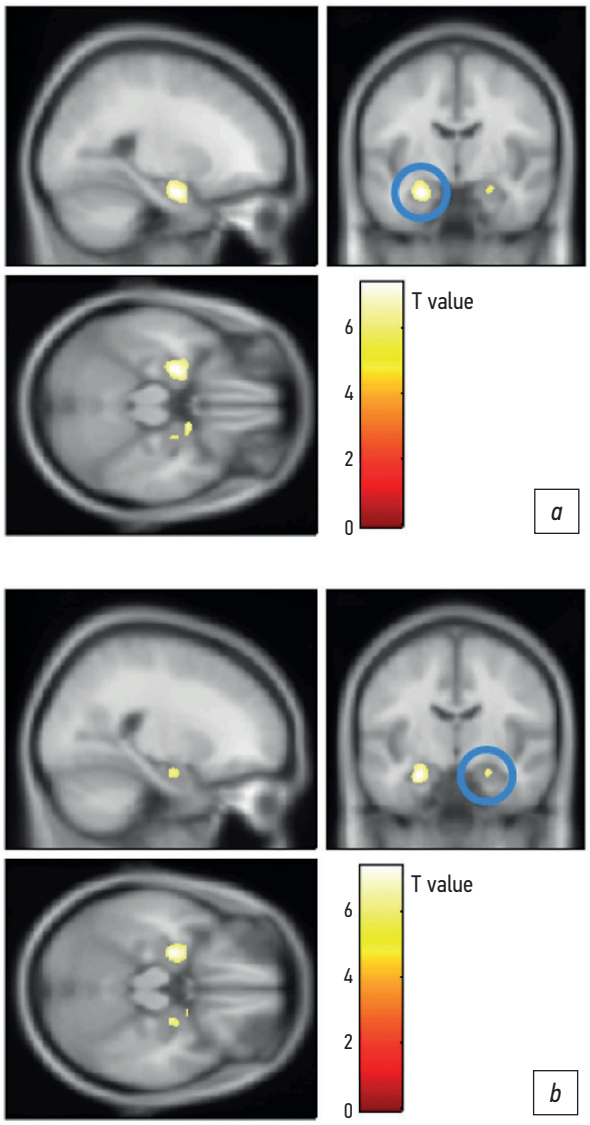
Gray matter volumes comparison, controlled for TIV, age, gender and corrected for multiple comparisons,

Table 1. Cluster level and peak level voxel-based morphometry differences

Таблица 1. Статистически значимые результаты воксель-базированной морфометрии на уровне кластеров и пиковом уровне

Region	Cluster level		Peak level	
	$p_{FWE-corr}$	K_c	$p_{FWE-corr}$	mm mm mm
Left hippocampus	0.0001	1899	0.0001	–24 –7 –22
Right entorhinal area	0.002	185	0.004	27 1 –15
Left amygdala	0.002	192	0.007	–24 0 –21
Right hippocampus	0.002	174	0.01	23 –10 –19

revealed significant differences between patients with OBPP and healthy controls in several regions. Patients showed significantly lower GM volume than controls in clusters whose peaks were located in the left amygdala and hippocampus (p <0.0001 family wise error (FWE)-corrected cluster level), right entorhinal area (p <0.002 FWE-corrected cluster level), and right hippocampus (p <0.002 FWE-corrected cluster level). The results are shown in Table 1 and Fig. 1. No regions showed greater GM volume in the OBPP group compared to controls. We did not observe differences in GM volume in the motor cortex between the groups.



DISCUSSION

In this explorative study, we compared the brain structures of young patients with OBPP and age-matched healthy controls. Our findings corroborate previous work suggesting that neonatal injury to a peripheral nerve can lead to the reorganization in the brain [9, 13]. We found volumetric differences between patients and healthy controls using a stringent procedure to control the family-wise error rate. Below, we discuss our results by individual brain region.

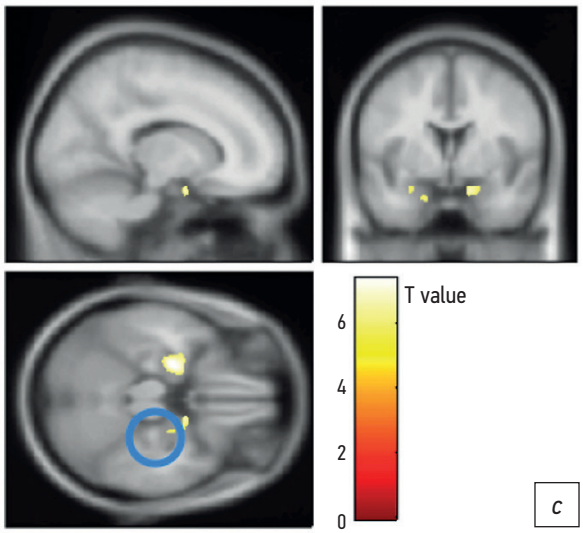


Fig. 1. Regional differences in gray matter volume between children with OBPP and healthy controls groups based on voxel-based morphometry analyses: *a* — left amygdala and hippocampus; *b* — right entorhinal area; *c* — right hippocampus.

Рис. 1. Области, демонстрирующие значительные различия в объёме серого вещества между пациентами и здоровыми участниками на основе воксельной морфометрии: *a* — левая миндалина и гиппокамп; *b* — правая энторинальная область; *c* — правый гиппокамп.

Amygdala

The amygdala is most known for its role in emotions, reward processing, context-appropriate social behaviors, and modulation of memory [14–16]. However, the role of the amygdala in goal-directed movement is supported by its projections to the premotor and primary motor cortices [17, 18]. Notably, reduced volumes in the amygdala have been reported in patients with neurodegenerative motor diseases, such as Huntington's disease and amyotrophic lateral sclerosis [19, 20]. Further investigations of the motor contributions of the amygdala are required to further characterize alterations beyond GM volumes.

Hippocampus

Aligned with its well-established role in memory [21, 22], the hippocampus has a documented motor function, especially during motor sequence learning [23–25]. In addition, the hippocampus has been implicated in theta wave generation during spatial navigation, which improves motor performance [26]. Hippocampal projections to the sensorimotor cortex have been shown to be activated during repetitive and learned-paced movements [27]. This finding suggests that the hippocampus may contribute to volitional finger movements, even in the absence of motor learning. Taken together, our results on reduced hippocampal volume in a motor disease highlights the potential role of the hippocampus in voluntary movement.

Entorhinal area

A recent study by de Brouwer et al. [28] reported that higher entorhinal cortex volumes were associated with better during error and reinforcement motor learning. In support of this, our results revealed higher entorhinal cortical volumes in healthy children compared to those with OBPP.

Moreover, the entorhinal cortex has strong connections with the hippocampus and amygdala. Projections between the entorhinal cortex and hippocampus play a role in spatial navigation and memory in humans and animals [29–32]. Projections from the amygdala to both hippocampus and entorhinal cortex govern reward-driven modulation of memory processes [33]. Moreover, both structures have functional connections with medial prefrontal cortex (mPFC) and anterior cingulate cortex, which support synaptic plasticity-mediated memory consolidation [34]. Our results suggest that volumetric differences due to neonatal injury have manifold functional consequences, which include sensorimotor function, as well as higher-order cognitive functions, such as learning and episodic memory.

Motor cortex

We found no changes in GM volume in the primary motor cortex in OBPP. This result is consistent with previous studies that reported no differences in motor cortical volumes between patients with OBPP and controls [35, 36]. From healthy adult studies, acquisition and execution of motor skills is supported by distributed neural networks that include the premotor cortex, parieto-occipital area, subcortical structures, cerebellum, and hippocampus [37–42]. Moreover, the roles of the primary motor cortex and other motor structures during motor learning and execution are unequal, depending on the stage and type of motor skill [43]. Finally, developmental studies show that the peak of plastic changes in the sensorimotor cortical areas occurs early in the first year of life [44]. This suggests that further acquisition of motor skills later in development recruits other motor areas. Therefore, we propose that OBPP children might rely on compensatory strategies in motor learning and functioning in systems beyond the primary cortex that develop later in development. These structures and networks govern motor programming, sensorimotor transformation, and spatial navigation. These circuits might support motor adaptations used by OBPP children to overcome their motor deficits.

Altogether, our present study provides a basis for a fascinating novel involvement of deep brain structures, such as the amygdala, hippocampus, and entorhinal area, in motor-related behavior. Our next step will be to conduct a surface-based analysis comparing the cortical properties in the brains of patients with OBPP and healthy controls.

CONCLUSION

One third of children with obstetric brachial plexus palsy never recover their motor abilities even after complete restoration of limb innervation. Current literature focus on peripheral nerve rehabilitation. Less attention has been given to central nervous system changes due to limb disuse and its negative effects in successful recovery. We compared structural brain changes in children with obstetric brachial plexus and healthy controls to understand how this restrictions in movement can affect the cerebral organization. We found the obstetric brachial plexus, gray matter volumes were reduced in the left amygdala, bilateral hippocampus, and right entorhinal cortex. We hypothesize that these subcortical regions might play a significant role in motor function. However, further investigations on the anatomical and functional changes in these deep brain structures are warranted to support their role in motor circuits and motor disease.

ADDITIONAL INFORMATION

Funding source. This work is an output of a research project supported by the grant N 20-68-47038.
Competing interests. The authors declare that they have no competing interests.
Authors' contribution. D.V. Kadieva — data collection and processing, analysis, preparation of the text of the article;

F. Gallo — editing of the article, literature review; M.A. Ulanov — editing of the article, literature review; A.N. Shestakova and A.M. Hodorovkaya — MRI collection; O.E. Agranovich — surgical treatment of the patient, assistance with collecting MRI data; V.V. Moiseeva — editing of the article.All authors confirm that their authorship meets the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research and preparation of the article, read and approved the final version before publication).

ДОПОЛНИТЕЛЬНО

Источник финансирования. Научное исследование проведено при поддержке гранта № 20-68-47038.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Вклад авторов. Д.В. Кадиева — сбор и обработка данных, анализ, подготовка текста статьи; Ф. Галло — редактирование статьи, обзор литературы; М.А. Уланов — редактирование статьи, обзор литературы; А.Н. Шестакова и А.М. Ходоровская — сбор данных МРТ; О.Е. Агранович — хирургическое лечение пациента, помощь с сборе данных МРТ; В.В. Моисеева — редактирование статьи. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

REFERENCES

1. Walle T, Hartikainen-Sorri A-L. Obstetric shoulder injury: associated risk factors, prediction and prognosis. *Acta Obstet Gynecol Scand*. 1993;72(6):450–454. doi: 10.3109/00016349309021133

2. Hoeksma AF, ter Steeg AM, Nelissen RG, et al. Neurological recovery in obstetric brachial plexus injuries: an historical cohort study. *Dev Med Child Neurol*. 2007;46(2):76–83. doi: 10.1111/j.1469-8749.2004.tb00455.x

3. Coroneos CJ, Voineskos SH, Coroneos MK, et al. Primary nerve repair for obstetrical brachial plexus injury: a meta-analysis. *Plast Reconstr Surg*. 2015;136(4):765–779. doi: 10.1097/prs.0000000000001629

4. Pondaag W, Malessy MJ, van Dijk JG, Thomeer RT. Natural history of obstetric brachial plexus palsy: a systematic review. *Dev Med Child Neurol*. 2004;46(02):138–144. doi: 10.1017/s0012162204000258

5. Anguelova GV, Malessy MJ, Buitenhuis SM, et al. Impaired automatic arm movements in obstetric brachial plexus palsy suggest a central disorder. *J Child Neurol*. 2016;31(8):1005–1009. doi: 10.1177/0883073816635746

6. Hale HB, Bae DS, Waters PM. Current concepts in the management of brachial plexus birth palsy. *J Hand Surg Am*. 2010;35(2):322–331. doi: 10.1016/j.jhsa.2009.11.026

7. Smania N, Gandolfi M, Paolucci S, et al. Reduced-intensity modified constraint-induced movement therapy versus conventional therapy for upper extremity rehabilitation after stroke. *Neurorehabil Neural Repair*. 2012;26(9):1035–1045. doi: 10.1177/1545968312446003

8. Bhat DI, Indira Devi B, Bharti K, Panda R. Cortical plasticity after brachial plexus injury and repair: a resting-state functional MRI study. *Neurosurg Focus*. 2017;42(3):E14. doi: 10.3171/2016.12.focus16430

9. Longo E, Nishiyori R, Cruz T, et al. Obstetric brachial plexus palsy: can a unilateral birth onset peripheral injury significantly affect brain development? *Dev Neurorehabil*. 2020;23(6):375–382. doi: 10.1080/17518423.2019.1689437

10. Scarfone H, McComas AJ, Pape K, Newberry R. Denervation and reinnervation in congenital brachial palsy. *Muscle Nerve*. 1999;22(5):600–607. doi: 10.1002/(sici)1097-4598(199905)22:5<600::aid-mus8>3.0.co;2-b

11. Blagovechtchenski E, Koriakina M, Bredikhin D, et al. Similar cognitive skill impairment in children with upper limb motor disorders due to arthrogryposis multiplex congenita and obstetrical brachial plexus palsy. *Int J Environ Res Public Health*. 2023;20(3):1841. doi: 10.3390/ijerph20031841

12. Björkman A, Weibull A, Svensson H, Dahlin L. Cerebral reorganization in patients with brachial plexus birth injury and residual shoulder problems. *Front Neurol*. 2016;7. doi: 10.3389/fneur.2016.00240

13. Kislay K, Devi BI, Bhat DI, et al. Novel findings in obstetric brachial plexus palsy: a study of corpus callosum volumetry and resting-state functional magnetic resonance imaging of Sensorimotor Network. *Neurosurgery*. 2018;83(5):905–914. doi: 10.1093/neuros/nyx495

14. Roozendaal B, McGaugh JL. Memory modulation. *Behav Neurosci*. 2011;125(6):797–824. doi: 10.1037/a0026187

15. Baxter MG, Croxson PL. Facing the role of the amygdala in emotional information processing. *Proc Natl Acad Sci U S A*. 2012;109(52):21180–21181. doi: 10.1073/pnas.1219167110

16. Adolphs R. What does the amygdala contribute to social cognition? *Ann N Y Acad Sci*. 2010;1191(1):42–61. doi: 10.1111/j.1749-6632.2010.05445.x

17. Grèzes J, Valabrègue R, Gholipour B, Chevallier C. A direct amygdala-motor pathway for emotional displays to influence action: a diffusion tensor imaging study. *Hum Brain Mapp*. 2014;35(12):5974–5983. doi: 10.1002/hbm.22598

18. Dum RP, Strick PL. Frontal lobe inputs to the digit representations of the motor areas on the lateral surface of the hemisphere. *J Neurosci*. 2005;25(6):1375–1386. doi: 10.1523/jneurosci.3902-04.2005

19. Ahveninen LM, Stout JC, Georgiou-Karistianis N, et al. Reduced amygdala volumes are related to motor and cognitive signs in Huntington's disease: the image-HD study. *Neuroimage Clin*. 2018;18:881–887. doi: 10.1016/j.nicl.2018.03.027

20. Chipika RH, Christidi F, Finegan E, et al. Amygdala pathology in amyotrophic lateral sclerosis and primary lateral sclerosis. *J Neurol Sci*. 2020;417:117039. doi: 10.1016/j.jns.2020.117039

21. Fernández-Seara MA, Aznárez-Sanado M, Mengual E, et al. Continuous performance of a novel motor sequence leads to highly correlated striatal and hippocampal perfusion increases. *Neuroimage*. 2009;47(4):1797–1808. doi: 10.1016/j.neuroimage.2009.05.061

22. Gheysen F, Van Opstal F, Roggeman C, et al. The neural basis of implicit perceptual sequence learning. *Front Hum Neurosci*. 2011;5:137. doi: 10.3389/fnhum.2011.00137

23. Kelemen E, Fenton AA. Dynamic grouping of hippocampal neural activity during cognitive control of two spatial frames. *PLoS Biol*. 2010;8(6):e1000403. Corrected and republished from: *PLoS Biol*. 2015;13(3):e1002100. doi: 10.1371/journal.pbio.1000403
24. Rudner M, Rönnberg J. The role of the episodic buffer in working memory for language processing. ***Cogn Process.*** 2007;9(1):19–28. doi: 10.1007/s10339-007-0183-x
25. Rose M, Haider H, Salari N, Büchel C. Functional dissociation of hippocampal mechanism during implicit learning based on the domain of associations. *J Neurosci*. 2011;31(39):13739–13745. doi: 10.1523/jneurosci.3020-11.2011
26. Hoffmann LC, Cicchese JJ, Berry SD. Harnessing the power of theta: Natural manipulations of cognitive performance during hippocampal theta-contingent eyeblink conditioning. *Front Syst Neurosci*. 2015;9:50. doi: 10.3389/fnsys.2015.00050
27. Burman DD. Hippocampal connectivity with sensorimotor cortex during volitional finger movements: laterality and relationship to motor learning. *PLoS One*. 2019;14(9):e0222064. doi: 0.1371/journal.pone.0222064
28. de Brouwer AJ, Areshenkoff CN, Rashid MR, et al. Human variation in error-based and reinforcement motor learning is associated with entorhinal volume. *Cereb Cortex*. 2022;32(16):3423–3440. doi: 10.1093/cercor/bhab424
29. Quirk GJ, Muller RU, Kubie JL, Ranck JB Jr. The positional firing properties of medial entorhinal neurons: description and comparison with hippocampal place cells. *J Neurosci*. 1992;12(5):1945–1963. doi: 10.1523/jneurosci.12-05-01945.1992
30. Tukker JJ, Beed P, Brecht M, et al. Microcircuits for spatial coding in the medial entorhinal cortex. *Physiol Rev*. 2022;102(2):653–688. doi: 10.1152/physrev.00042.2020
31. Epstein RA, Patai EZ, Julian JB, Spiers HJ. The cognitive map in humans: spatial navigation and beyond. *Nat Neurosci*. 2017;20(11):1504–1513. doi: 10.1038/nn.4656
32. Howard LR, Javadi AH, Yu Y, et al. The hippocampus and entorhinal cortex encode the path and euclidean distances to goals during navigation. *Curr Biol*. 2014;24(12):1331–1340. doi: 10.1016/j.cub.2014.05.001
33. Pratt WE, Mizumori SJ. Characteristics of basolateral amygdala neuronal firing on a spatial memory task involving differential reward. *Behav Neurosci*. 1998;112(3):554–570. doi: 10.1037/0735-7044.112.3.554
34. Takehara-Nishiuchi K. Entorhinal cortex and consolidated memory. *Neurosci Res*. 2014;84:27–33. doi: 10.1016/j.neures.2014.02.012
35. Lu Y, Liu H, Hua X, et al. Attenuation of brain grey matter volume in brachial plexus injury patients. *Neurol Sci*. 2016;37(1):51–56. doi: 10.1007/s10072-015-2356-1
36. Fraiman D, Miranda MF, Erthal F, et al. Reduced functional connectivity within the primary motor cortex of patients with brachial plexus injury. *Neuroimage Clin*. 2016;12:277–284. doi: 10.1016/j.nicl.2016.07.008
37. Pearson K. Motor systems. *Curr Opin Neurobiol*. 2000;10(5):649–654. doi: 10.1016/s0959-4388(00)00130-6
38. Lang EJ, Apps R, Bengtsson F, et al. The roles of the Olivocerebellar pathway in motor learning and motor control. A consensus paper. *Cerebellum*. 2016;16(1):230–252. doi: 10.1007/s12311-016-0787-8
39. Doyon J, Gabitov E, Vahdat S, et al. Current issues related to motor sequence learning in humans. *Curr Opin Behav Sci*. 2018;20:89–97. doi: 10.1016/j.cobeha.2017.11.012
40. Krakauer JW, Hadjiosif AM, Xu J, et al. Motor learning. *Compr Physiol*. 2019;9(2):613–663. Corrected and republished from: *Compr Physiol*. 2019;9(3):1279. doi: 10.1002/cphy.c170043
41. Dhawale AK, Wolff SBE, Ko R, Ölveczky BP. The basal ganglia control the detailed kinematics of learned motor skills. *Nat Neurosci*. 2021;24(9):1256–1269. doi: 10.1038/s41593-021-00889-3
42. Rossi C, Bastian AJ, Therrien AS. Mechanisms of proprioceptive realignment in human motor learning. *Curr Opin Physiol*. 2021;20:186–197. doi: 10.1016/j.cophys.2021.01.011
43. Taubert M, Draganski B, Anwander A, et al. Dynamic properties of human brain structure: learning-related changes in cortical areas and associated fiber connections. *J Neurosci*. 2010;30(35):11670–11677. doi: 10.1523/jneurosci.2567-10.2010
44. Casey BJ, Tottenham N, Liston C, Durston S. Imaging the developing brain: what have we learned about cognitive development? *Trends Cogn Sci*. 2005;9(3):104–110. doi: 10.1016/j.tics.2005.01.011

СПИСОК ЛИТЕРАТУРЫ

1. Walle T., Hartikainen-Sorri A.L. Obstetric shoulder injury. Associated risk factors, prediction and prognosis // Acta Obstet Gynecol Scand. 1993. Vol. 72, N 6. P. 450–454. doi: 10.3109/00016349309021133
2. Hoeksma A.F., ter Steeg A.M., Nelissen R.G., et al. Neurological recovery in obstetric brachial plexus injuries: an historical cohort study // Dev Med Child Neurol. 2007. Vol. 46, N 2. P. 76–83. doi: 10.1111/j.1469-8749.2004.tb00455.x
3. Coroneos C.J., Voineskos S.H., Coroneos M.K., et al. Primary nerve repair for obstetrical brachial plexus injury: a meta-analysis // Plast Reconstr Surg. 2015. Vol. 136, N 4. P. 765–779. doi: 10.1097/prs.0000000000001629
4. Pondaag W., Malessy M.J., van Dijk J.G., Thomeer R.T. Natural history of obstetric brachial plexus palsy: a systematic review // Dev Med Child Neurol. 2004. Vol. 46, N 2. P. 138–144. doi: 10.1017/s0012162204000258
5. Anguelova G.V., Malessy M.J., Buitenhuis S.M., et al. Impaired automatic arm movements in obstetric brachial plexus palsy suggest a central disorder // J Child Neurol. 2016. Vol. 31, N 8. P. 1005–1009. doi: 10.1177/0883073816635746
6. Hale H.B., Bae D.S., Waters P.M. Current concepts in the management of brachial plexus birth palsy // J Hand Surg Am. 2010. Vol. 35, N 2. P. 322–331. doi: 10.1016/j.jhsa.2009.11.026
7. Smania N., Gandolfi M., Paolucci S., et al. Reduced-intensity modified constraint-induced movement therapy versus conventional therapy for upper extremity rehabilitation after stroke // Neurorehabil Neural Repair. 2012. Vol. 26, N 9. P. 1035–1045. doi: 10.1177/1545968312446003
8. Bhat D.I., Indira Devi B., Bharti K., Panda R. Cortical plasticity after brachial plexus injury and repair: a resting-state functional MRI study // Neurosurg Focus. 2017. Vol. 42, N 3. P. E14. doi: 10.3171/2016.12.focus16430
9. Longo E., Nishiyori R., Cruz T., et al. Obstetric brachial plexus palsy: can a unilateral birth onset peripheral injury significantly affect brain development? // Dev Neurorehabil. 2020. Vol. 23, N 6. P. 375–382. doi: 10.1080/17518423.2019.1689437

10. Scarfone H., McComas A.J., Pape K., Newberry R. Denervation and reinnervation in congenital brachial palsy // Muscle Nerve. 1999. Vol. 22, N 5. P. 600–607. doi: 10.1002/(sici)1097-4598(199905)22:5<600::aid-mus8>3.0.co;2-b
11. Blagovechtchenski E., Koriakina M., Bredikhin D., et al. Similar cognitive skill impairment in children with upper limb motor disorders due to arthrogryposis multiplex congenita and obstetrical brachial plexus palsy // Int J Environ Res Public Health. 2023. Vol. 20, N 3. P. 1841. doi: 10.3390/ijerph20031841
12. Björkman A., Weibull A., Svensson H., Dahlin L. Cerebral reorganization in patients with brachial plexus birth injury and residual shoulder problems // Front Neurol. 2016. Vol. 7. P. 240. doi: 10.3389/fneur.2016.00240
13. Kislay K., Devi B.I., Bhat D.I., et al. Novel findings in obstetric brachial plexus palsy: a study of corpus callosum volumetry and resting-state functional magnetic resonance imaging of Sensorimotor Network // Neurosurgery. 2018. Vol. 83, N 5. P. 905–914. doi: 10.1093/neuros/nyx495
14. Roozendaal B., McGaugh J.L. Memory modulation // Behav Neurosci. 2011. Vol. 125, N 6. P. 797–824. doi: 10.1037/a0026187
15. Baxter M.G., Croxson P.L. Facing the role of the amygdala in emotional information processing // Proc Natl Acad Sci U S A. 2012. Vol. 109, N 52. P. 21180–21181. doi: 10.1073/pnas.1219167110
16. Adolphs R. What does the amygdala contribute to social cognition? // Ann N Y Acad Sci. 2010. Vol. 1191, N 1. P. 42–61. doi: 10.1111/j.1749-6632.2010.05445.x
17. Grèzes J., Valabrègue R., Gholipour B., Chevallier C. A direct amygdala-motor pathway for emotional displays to influence action: a diffusion tensor imaging study // Human Brain Mapp. 2014. Vol. 35, N 12. P. 5974–5983. doi: 10.1002/hbm.22598
18. Dum R.P., Strick P.L. Frontal lobe inputs to the digit representations of the motor areas on the lateral surface of the Hemisphere // J Neurosci. 2005. Vol. 25, N 6. P. 1375–1386. doi: 10.1523/jneurosci.3902-04.2005
19. Ahveninen L.M., Stout J.C., Georgiou-Karistianis N., et al. Reduced amygdala volumes are related to motor and cognitive signs in Huntington's disease: The IMAGE-HD study // Neuroimage Clin. 2018. Vol. 18. P. 881–887. doi: 10.1016/j.nicl.2018.03.027
20. Chipika R.H., Christidi F., Finegan E., et al. Amygdala pathology in amyotrophic lateral sclerosis and primary lateral sclerosis // J Neurol Sci. 2020. Vol. 417. P. 117039. doi: 10.1016/j.jns.2020.117039
21. Fernández-Seara M.A., Aznárez-Sanado M., Mengual E., et al. Continuous performance of a novel motor sequence leads to highly correlated striatal and hippocampal perfusion increases // NeuroImage. 2009. Vol. 47, N 4. P. 1797–1808. doi: 10.1016/j.neuroimage.2009.05.061
22. Gheysen F., Van Opstal F., Roggeman C., et al. The neural basis of implicit perceptual sequence learning // Front Hum Neurosci. 2011. Vol. 5. doi: 10.3389/fnhum.2011.00137
23. Kelemen E., Fenton A.A. Dynamic grouping of hippocampal neural activity during cognitive control of two spatial frames // PLoS Biol. 2010. Vol. 8, N 6. P. e1000403. Corrected and republished from: PLoS Biol. 2015. Vol. 13. P. e1002100. doi: 10.1371/journal.pbio.1000403
24. Rudner M., Rönnberg J. The role of the episodic buffer in working memory for language processing // Cogn Process. 2007. Vol. 9, N 1. P. 19–28. doi: 10.1007/s10339-007-0183-x
25. Rose M., Haider H., Salari N., Büchel C. Functional dissociation of hippocampal mechanism during implicit learning based on the domain of Associations // J Neurosci. 2011. Vol. 31, N 39. P. 13739–13745. doi: 10.1523/jneurosci.3020-11.2011
26. Hoffmann L.C., Cicchese J.J., Berry S.D. Harnessing the power of theta: natural manipulations of cognitive performance during hippocampal theta-contingent eyeblink conditioning // Front Syst Neurosci. 2015. Vol. 9. P. 50. doi: 10.3389/fnsys.2015.00050
27. Burman D.D. Hippocampal connectivity with sensorimotor cortex during volitional finger movements: laterality and relationship to Motor Learning // PLoS One. 2019. Vol. 14, N 9. P. e0222064. doi: 10.1371/journal.pone.0222064
28. de Brouwer A.J., Areshenkoff C.N., Rashid M.R., et al. Human variation in error-based and reinforcement motor learning is associated with entorhinal volume // Cereb Cortex. 2022. Vol. 32, N 16. P. 3423–3440. doi: 10.1093/cercor/bhab424
29. Quirk G.J., Muller R.U., Kubie J.L., Ranck J.B. Jr. The positional firing properties of medial entorhinal neurons: description and comparison with hippocampal place cells // J Neurosci. 1992. Vol. 12, N 5. P. 1945–1963. doi: 10.1523/jneurosci.12-05-01945.1992
30. Tukker J.J., Beed P., Brecht M., et al. Microcircuits for spatial coding in the medial entorhinal cortex // Physiol Rev. 2022. Vol. 102, N 2. P. 653–688. doi: 10.1152/physrev.00042.2020
31. Epstein R.A., Patai E.Z., Julian J.B., Spiers H.J. The cognitive map in humans: spatial navigation and beyond // Nat Neurosci. 2017. Vol. 20, N 11. P. 1504–1513. doi: 10.1038/nn.4656
32. Howard L.R., Javadi A.H., Yu Y., et al. The hippocampus and entorhinal cortex encode the path and euclidean distances to goals during navigation // Curr Biol. 2014. Vol. 24, N 12. P. 1331–1340. doi: 10.1016/j.cub.2014.05.001
33. Pratt W.E., Mizumori S.J. Characteristics of basolateral amygdala neuronal firing on a spatial memory task involving differential reward // Behav Neurosci. 1998. Vol. 112, N 3. P. 554–570. doi: 10.1037/0735-7044.112.3.554
34. Takehara-Nishiuchi K. Entorhinal cortex and consolidated memory // Neurosci Res. 2014. Vol. 84. P. 27–33. doi: 10.1016/j.neures.2014.02.012
35. Lu Y., Liu H., Hua X., et al. Attenuation of brain grey matter volume in brachial plexus injury patients // Neurol Sci. 2015. Vol. 37, N 1. P. 51–56. doi: 10.1007/s10072-015-2356-1
36. Fraiman D., Miranda M.F., Erthal F., et al. Reduced functional connectivity within the primary motor cortex of patients with brachial plexus injury // Neuroimage Clin. 2016. Vol. 12. P. 277–284. doi: 10.1016/j.nicl.2016.07.008
37. Pearson K. Motor systems // Curr Opin Neurobiol. 2000. Vol. 10, N 5. P. 649–654. doi: 10.1016/s0959-4388(00)00130-6
38. Lang E.J., Apps R., Bengtsson F., et al. The roles of the olivocerebellar pathway in motor learning and motor control. A consensus paper // Cerebellum. 2017. Vol. 16, N 1. P. 230–252. doi: 10.1007/s12311-016-0787-8
39. Doyon J., Gabitov E., Vahdat S., et al. Current issues related to motor sequence learning in humans // Curr Opin Behav Sci. 2018. Vol. 20. P. 89–97. doi: 10.1016/j.cobeha.2017.11.012
40. Krakauer J.W., Hadjiosif A.M., Xu J., et al. Motor learning // Compr Physiol. 2019. Vol. 9, N 2. P. 613–663. Corrected and republished from: Compr Physiol. 2019. Vol. 9, N 3. P. 1279. doi: 10.1002/cphy.c170043
41. Dhawale A.K., Wolff S.B.E., Ko R., Ölveczky B.P. The basal ganglia control the detailed kinematics of learned mo-

tor skills // Nat Neurosci. 2021. Vol. 24, N 9. P. 1256–1269. doi: 10.1038/s41593-021-00889-3

42. Rossi C., Bastian A.J., Therrien A.S. Mechanisms of proprioceptive realignment in Human Motor Learning // Curr Opin Physiol. 2021. Vol. 20. P. 186–197. doi: 10.1016/j.cophys.2021.01.011

43. Taubert M., Draganski B., Anwander A., et al. Dynamic properties of human brain structure: learning-related changes in cortical areas and associated fiber connections // J Neurosci. 2010. Vol. 30, N 35. P. 11670–11677. doi: 10.1523/jneurosci.2567-10.2010

44. Casey B., Tottenham N., Liston C., Durston S. Imaging the developing brain: what have we learned about cognitive development? // Trends Cogn Sci. 2005. Vol. 9, N 3. P. 104–110. doi: 10.1016/j.tics.2005.01.011

AUTHORS' INFO

*** Dzerassa V. Kadieva;**
address: 20 Myasnitskaya street, 101000 Moscow, Russian Federation;
ORCID: 0009-0006-7848-596X;
eLibrary SPIN: 9563-0254;
e-mail: k.dzerassa.v@gmail.com

Federico Gallo, Cand. Sci. (Psych.);
ORCID: 0000-0002-4343-4664;
e-mail: fedegallo92@hotmail.it

Maxim A. Ulanov, Cand. Sci. (Psych.);
ORCID: 0000-0003-0624-931X;
eLibrary SPIN: 6052-9784;
e-mail: maxim.ulanov.report@gmail.com

Anna N. Shestakova, Cand. Sci. (Biol.);
ORCID: 0000-0001-9374-9878;
eLibrary SPIN: 6010-6538;
e-mail: a.shestakova@hse.ru

Victoria V. Moiseeva, Cand. Sci. (Biol.);
ORCID: 0000-0001-8729-1610;
eLibrary SPIN: 7234-1453;
e-mail: moiseevavictoria@gmail.com

Olga E. Agronovich, MD, Dr. Sci. (Med.);
ORCID: 0000-0002-6655-4108;
eLibrary SPIN: 4393-3694;
e-mail: olga_agranovich@yahoo.com;

Alina M. Hodorovskaya;
ORCID: 0000-0002-2772-6747;
eLibrary SPIN: 3348-8038;
e-mail: alinamyh@gmail.com

* Corresponding author / Автор, ответственный за переписку

ОБ АВТОРАХ

*** Кадиева Дзерасса Викторовна;**
адрес: Российская Федерация, 101000, Москва, ул. Мясницкая, д. 20;
ORCID: 0009-0006-7848-596X;
eLibrary SPIN: 9563-0254;
e-mail: k.dzerassa.v@gmail.com

Галло Федерико, к.псих.н.;
ORCID: 0000-0002-4343-4664;
e-mail: fedegallo92@hotmail.it

Уланов Максим Александрович, к.псих.н.;
ORCID: 0000-0003-0624-931X;
eLibrary SPIN: 6052-9784;
e-mail: maxim.ulanov.report@gmail.com

Шестакова Анна Николаевна, к.б.н.;
ORCID: 0000-0001-9374-9878;
eLibrary SPIN: 6010-6538;
e-mail: a.shestakova@hse.ru

Моисеева Виктория Владимировна, к.б.н.;
ORCID: 0000-0001-8729-1610;
eLibrary SPIN: 7234-1453;
e-mail: moiseevavictoria@gmail.com

Агранович Ольга Евгеньевна, д.м.н.;
ORCID: 0000-0002-6655-4108;
eLibrary SPIN: 4393-3694;
e-mail: olga_agranovich@yahoo.com

Алина Михайловна Ходоровская;
ORCID: 0000-0002-2772-6747;
eLibrary SPIN: 3348-8038;
e-mail: alinamyh@gmail.com