

Significance of Corticospinal, Associative and Inter-Hemispheric Tracts for the Development of Posttraumatic Hemiparesis

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For citation: Eduard L. Pogosbekian, Elena V. Sharova, L. M. Fadeeva, Marina V. Shtern, Evgenia V. Aleksandrova, N. E. Zakharova, Igor N. Pronin. Significance of Corticospinal, Associative and Inter-Hemispheric Tracts for the Development of Posttraumatic Hemiparesis. *Obshchaya Reanimatologiya = General Reanimatology*. 2023; 19 (6): 25–38. <https://doi.org/10.15360/1813-9779-2023-6-25-38> [In Russ. and Engl.]

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Summary

Motor disorders are among the most common consequences of severe craniocerebral injury (traumatic brain injury — TBI). Deeper insight into pathophysiological mechanisms of these disorders is important both from a theoretical point of view and in terms of improving neurorehabilitation approaches.

The aim of the study was to investigate the correlation of right-sided posttraumatic hemiparesis severity with composite characteristics of fractional anisotropy (FA) in the segments of the corpus callosum (CC), corticospinal tract (CST) and the inferior fronto-occipital fasciculus (IFO) at different stages of traumatic disease (acute, subacute and long-term periods).

Material and methods. Cases of 43 patients with TBI were analyzed (28 men and 15 women aged 13 to 59 years, mean age 28±9 years). Forty patients were diagnosed with severe TBI with diffuse axonal damage, three patients had moderate severity TBI. Long-term follow up included continuous clinical and neurological examination with evaluation of patient's level of consciousness using the CRS-R scale, and the degree of motor deficits in right-sided hemiparesis using a five-point scale. During three post-TBI periods (up to 1 month, from 1 to 6 months, and from 6 to 12 months), patients were examined using diffusion tensor MRI (DTI), tractography and FA. Motor, cortico-spinal tracts and IFO were divided by measurement grid, correlations between FA and scores of right-sided hemiparesis were calculated for each segment.

Results. FA correlations ($P < 0.05$) with the severity of hemiparesis were established not only for CST motor-specific segments, but also for some CC and IFO segments. In the early period of TBI significant correlations with hemiparesis severity were found not only in the contralateral CST segments, but also in the ipsilateral ones. Significant differences in FA in the related CC and CST segments were found between the groups with good and limited motor recovery: at all stages after TBI, FA was higher in patients with successful recovery.

Conclusion. The results of the study provide better insight into pathophysiological mechanisms of post-traumatic motor disorders development, therefore favoring optimization of therapeutic strategies.

Keywords: TBI; tractography; hemiparesis; fractional anisotropy

Conflict of interest. The authors declare no conflict of interest.

Financing of the study. The study was conducted within the Ministry of Education and Science of the Russian Federation state assignment for 2021–2023.

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Introduction

Severe traumatic brain injury (TBI), which causes damage to various parts of the brain including the cortex, subcortical structures and neural pathways, is a common type of brain disorder [1, 2]. Approximately 75% of individuals affected by TBI experience motor impairments such as reduced muscle strength (limb paresis), increased muscle tone and coordination problems. Motor deficits are a major contributor to post-traumatic disability [3]. It is therefore important to investigate the underlying mechanisms of motor impairments after brain injury and to develop effective strategies for their

rehabilitation. This research is important both from a scientific perspective and in terms of improving neurorehabilitation approaches.

In a series of previous studies fMRI responses during independent and passive (with the help of another person) performance of clenching-unclenching of the fingers of the hand in healthy people, as well as in patients with different severity of right and left hemiparesis after traumatic brain injury [4–7] were investigated. A stereotyped and reproducible motor fMRI response (mainly related to corticospinal tract activity) was demonstrated when this motor test was performed in healthy subjects, while its

variability increased as the severity of the motor defect (manifested as hemiparesis) worsened. The analysis of the involvement of cortical and subcortical brain structures that are not normally active, matched with the topographical neuroanatomy of the motor system, allowed to formulate the hypothesis that, together with the motor cortex of the hemisphere ipsilateral to the movement [8], non-pyramidal tracts and subcortical structures comprising the extrapyramidal system may act as «functional backup» in post-traumatic hemiparesis [9, 10]. These ideas evolved into the study of fMRI connectivity within the functional motor system, including frontal and motor cortical areas associated with movement, as well as a significant number of subcortical nuclei and the cerebellum as «zones of interest» [11]. It was found that as the severity of hemiparesis increases, functional fMRI connectivity in the corticospinal tract (CST) system weakens [12], but some connectivity in the frontal-motor network increases. The increase in the level of bilateral cortical motor and paleostriatal connections in severe hemiparesis can also be considered as a possible compensatory mechanism for motor impairment [11].

However, all the data presented above are based on the results of the analysis of functional parameters. At the same time, the crucial role of brain pathways, and especially the CCT, in ensuring voluntary human movement is well known [13]. Recent studies using neuroimaging techniques have consistently demonstrated the relationship between the integrity of this tract and the presence and severity of hemiparesis after stroke or severe TBI [14, 15]. Meanwhile, tractography data in recent years have expanded traditional understanding of importance of the corpus callosum (CC) [16, 17] and the inferior frontal-occipital tracts (IFOT) [18, 19] in the execution of voluntary movement in both normal and pathological conditions.

In this regard, this study aims to clarify the importance of CST, CCT and IFOT in the severity of post-traumatic hemiparesis. Considering the current neurophysiological ideas about the evolution of neurotrauma [20] and its phases [3], it is reasonable to evaluate the importance of these tracts at different time points following traumatic injury.

Literature analysis reveals various approaches to assessing the state of these tracts. It is possible to estimate average FA values [21], referred to as tractometry in some publications. Sometimes researchers examine FA values in individual manually labeled white matter regions [22]. A more accurate assessment of white matter status can be obtained by estimating FA profiles along tracts [23, 24] or by using the TBSS algorithm [25] and similar methods [26], where tracts are projected onto the white matter «skeleton» and then voxel-wise statistics are calculated for the groups studied. We believe that the method of estimating

profiles along tracts is not suitable for studying the CC, since this structure has numerous branches in different parts of the brain, and the concepts of «beginning» and «end» do not apply to it. The TBSS voxel-wise method is not appropriate for measuring patients with severe traumatic brain injury because they often have serious brain deformities due to surgery, hydrocephalus, and increased intracranial pressure. Edema, hemorrhage, diffuse axonal damage — all of these make it impossible to construct a correct white matter «skeleton» in TBI patients and to perform further group analysis.

The authors [27] created a mask for each patient that excluded areas of post-stroke edema when analyzed with the TBSS method. This approach might allow group analysis of patients with severe TBI, but it would exclude the most damaged white matter regions of interest from the statistics.

Therefore, in this study, we decided to use a non-standard, original, patent-pending algorithm for segmentation of the tracts under study and their subsequent analysis.

The aim of the study was to reveal the correlation between the severity of right post-traumatic hemiparesis and the fractional anisotropy characteristics of CCT, CST and IFOT segments during different phases (acute, subacute and chronic) of traumatic disease.

Materials and Methods

The study was conducted in the Department of Radiology and Radioisotope Diagnostic Methods of the Burdenko Neurosurgical Center of the Ministry of Health of the Russian Federation.

It was an observational and retrospective study, analyzing data collected from September 2011 to January 2020. Patients were studied in the acute (up to 1 month), subacute (1 to 6 months), and chronic (6 to 12 months) phase after TBI.

The main observation group consisted of 43 patients with TBI (28 males and 15 females, aged 13 to 59 years, mean age 28 ± 9 years).

All patients had suffered a TBI with variable brain damage and were treated in the Neurotraumatology department of the Burdenko Neurosurgical Center of the Ministry of Health of the Russian Federation. Among them, 40 patients were diagnosed with severe brain injury with diffuse axonal damage (DAD), while the remaining three had moderate closed TBI. For more information on specific traumatic injuries, see Table 1.

On admission to the hospital, the severity of the disease was assessed using the Glasgow Coma Scale (GCS) [28] (Table 2).

The Glasgow Outcome Scale (GOS) [29] was used to assess the success of recovery six months after the injury: 10 patients received a score of 5 points, 11 patients were assessed 4 points, 11 patients

Table 1. Injuries in traumatic brain injury.

Injury	Number of patients
DAI	25
DAI+SDH	9
DAI+focal contusion	6
Traumatic brain injury without MRI-visible brain damage	3

Note. DAI — diffuse axonal injury; SDH — subdural hematoma.

had 3 points, 10 patients scored 2 points, and one patient received a score of 1 point.

Each patient underwent a thorough repeated clinical and neurological examination, including an assessment of current level of consciousness using the CRS-R scale [30] and the severity of movement impairment using the five-point hemiparesis scale [31], where the most severe hemiparesis corresponds to low points (1–2) and its absence to 5.

The study included patients who either had no hemiparesis or had right hemiparesis following a traumatic injury, which can greatly influence a person's future quality of life.

Exclusion criteria:

- 1) Refusal of the patient or his/her legal representative to sign an informed consent for participation in the study,
- 2) Inability to undergo an MRI study due to the presence of implants, intracranial pressure sensors, braces, clips, etc,
- 3) Serious condition including hemodynamic instability, elevated blood pressure, decompensated heart failure, acute infection, etc.
- 4) Patient's death occurring within one year of the traumatic injury.

Table 3 displays data pertaining to the severity of right hemiparesis throughout the follow-up period.

Magnetic resonance diffusion tensor imaging (DTI) was conducted on all patients with traumatic injuries. In the acute phase, 28 patients underwent the procedure once. In the subacute phase, 22 patients were included, with 4 of them being examined twice. The time interval between examinations ranged from 8 to 77 days. In the chronic phase, 20 patients were scanned, with 7 of them being scanned twice and one being scanned three times.

Table 2. Severity of patients with traumatic brain injury on admission.

Parameter	Values														
GCS score, points	3	4	5	6	7	8	9	10	11	12	13	14	15		
Number of patients	1	6	3	6	4	1	5	0	1	0	0	0	3		

Table 3. Severity of right hemiparesis at different follow-up time points.

Severity, points	Number of tests in different phases		
	Acute	Subacute	Chronic
1	14	3	4
2	2	9	3
3	2	4	4
4	2	3	4
5	7	5	12

Note. The severity of hemiparesis according to manual muscle testing system [31]: 5 — full range of movement and almost normal strength with maximal resistance; 4 — mild hemiparesis; 3 — moderate hemiparesis; 2 — severe hemiparesis; 1 — gross hemiparesis (barely noticeable muscle contractions).

The time intervals between scans ranged from 120 to 511 days. Among the patients, 8 were scanned at least once in each of the acute, subacute, and chronic phases. There were 4 patients who were scanned in the acute and subacute phases only, 6 patients scanned in the subacute and chronic phases only, and 3 patients scanned in the acute and chronic phases only. Furthermore, 14 patients were scanned in the acute phase only, 5 patients were scanned in the subacute phase only, and 4 patients were scanned in the chronic phase only.

The control group for the DTI patients consisted of data from a similar study involving 22 healthy volunteers (14 men and 8 women) with ages ranging from 21 to 55 years, and a mean age of 30 ± 10 years.

The scans were conducted using a 3.0 Tesla magnetic field strength tomograph (3.0 T Signa HDxt, General Electric USA) with an eight-channel head coil utilizing a diffusion tensor MRI (DTI) protocol. The protocol included routine MR imaging in T1, T2, T2 FLAIR (T2 with water signal suppression), gradient echo (T2*, 2D, 3D, or SWAN), and diffusion-weighted imaging (DWI) modes to diagnose traumatic lesions or intracranial hemorrhage. The diffusion tensor MRI in the DTI protocol was performed using a spin echo — echo planar imaging (SE EPI) sequence with the following parameters: TR=8000 ms, $TE_{min}=96$ ms, 33 diffusion gradient directions, diffusion weight $b=0$, 1000 s/mm², two repetitions, reconstruction matrix 256×256; slice thickness/gap 4/0 mm, field of view 240 mm, voxel size 1.9×1.9×4 mm³, and a scan duration of 3 minutes and 40 seconds in one projection.

The original diffusion MR image analysis algorithm used is illustrated in Fig. 1.

Importantly, clinical and DTI correlations took into account the level of localization of the tract segment corresponding to the determined correlation coefficient value, i.e. brainstem, subcortical nuclei, and cortex (Fig. 2). Correlations of 0.6 and higher were considered to be the most interesting.

We used the Wilcoxon test and ROC analysis in Matlab to perform a nonparametric group comparison of FA values for individual tract segment localizations. The severity of right hemiparesis at

the end of treatment was used to divide patients into two groups. Patients with a score of two points or less were assigned to the first group («non-recovered»), while the remainder were assigned to the second group («recovered»).

DTI data from the control group were used at various stages of the study, including template creation and statistical analysis of parameters.

A box-and-whisker plot was generated for selected tract segments that showed a significant cor-

relation between fractional anisotropy (FA) and hemiparesis severity. This plot showed the distribution of FA values between the «recovery» and «non-recovery» patient groups during the chronic phase of TBI. In addition, the plot showed the distribution of FA values in the corresponding tract (or its segment) in a group of healthy volunteers. Using ROC analysis, we determined and plotted the optimal FA value that could discriminate between the «recovered» and «non-recovered» patient groups.

Results

During the visual matching, the tracts analyzed in all patients and healthy volunteers closely aligned with the template image used to mark the measurement areas. Consequently, no subjects were excluded from the study due to errors in the data acquisition algorithm.

Table 4 shows the highest correlation values between the severity of right hemiparesis and FA of the tract segments studied in acute TBI. The correlation coefficient (r) values for different segments of the left corticospinal tract (responsible for voluntary motor activity in the right hand) ranged from 0.61 to 0.64, indicating a moderate level of congruency between these parameters. Furthermore, these segments included both cortical (paracentral lobule) and subcortical (thalamus and caudate nu-

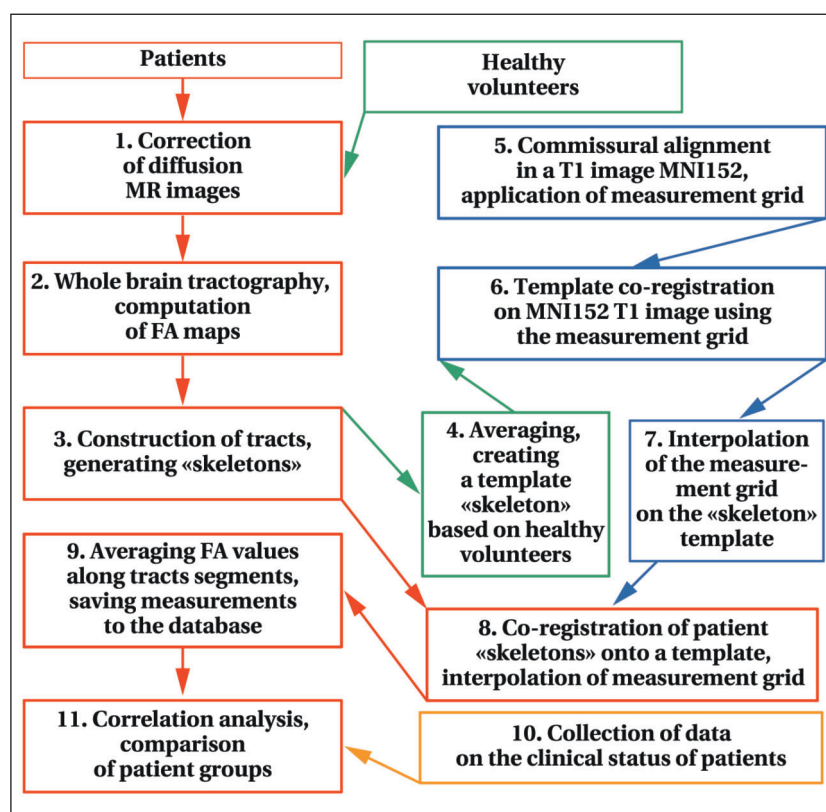


Fig. 1. Stages of DTI data analysis.

Note. The red color indicates steps using patient MRI data, the green color indicates steps using healthy volunteer MRI data only, the blue color indicates MNI152 template only, and the orange color indicates patient clinical assessment data. Step explanations:

1. Diffusion image correction included removing Gibbs artifacts and thermal noise, and correcting eddy current artifacts with FSL eddy (<http://fmrib.ox.ac.uk/fsl/>) and Mrtrix3 (<https://www.mrtrix.org/>) software.

2. Whole brain tracts were calculated in Mrtrix3 using the HARDI CSD method [32] with default settings and a stopping criterion of 10 million fibers. Mrtrix3 was also used to compute metric fractional anisotropy maps.

3. Construction of corticospinal (CST), inferior fronto-occipital (IFOT), and corpus callosum (CCT) tracts for each subject in TrackVis (<http://trackvis.org/>). The combination of these tracts was dubbed the «skeleton», with the tracts connecting the brain's margins in three orthogonal directions: interhemispheric, frontal-occipital, and cortical-brainstem. Based on the findings of previous studies [33, 34], seven leads were conventionally identified in the CCT.

4. The averaged «skeleton» was built using the ANTs software package's script `antsMultivariateTemplateConstruction2` (<http://stnava.github.io/ANTs/>).

5. In MNI152 space, the template T1 image was rotated so that the anterior and posterior commissures were on the same section in axial projection.

6, 7, 8. The averaged skeleton was co-registered to the template T1 image using affine and nonlinear transformations with the ANTs software package's `antsRegistrationSyN.sh` utility. The same utility was used to co-register the patient «skeletons» to the image averaged over the group of healthy volunteers. The measurement grid used to divide the tracts into segments was made up of $18 \times 18 \times 18$ mm³ cells. If one of the CCT's seven leads was analyzed, the central part of the CCT, delimited by a parallelepiped of $5 \times 2 \times 3$ cells, was counted as one measurement block.

9, 11. The average FA values for each tract segment were collected and saved, and statistical analysis was carried out using Matlab R2018b software (<http://www.mathworks.com/>). For each tract segment, two value vectors were saved, including the average FA values of that tract segment for each patient and the assessment of right hemiparesis. These vectors were used to compute the Spearman rank correlation. In the table of final correlations, only values with a multiple value-adjusted significance level of $P < 0.05$ were included. The total number of segments analyzed for each tract (approximately 100) was included in the correction. On the template T1 image, the cells of the tract segments with statistically significant correlations were displayed.

Table 4. Correlation of right hemiparesis severity with fractional anisotropy for segments of different tracts in the acute traumatic brain injury.

Tract	FA (min-max- average)	Hemisphere	Level	<i>r</i> (<i>p</i>)	95% CI of the correlation (min-max)	Adjacent anatomical structure
Splenium of CC	0.22–0.54 0.37±0.09	left	Subcortical nuclei	0.86 (2×10 ⁻⁷)	0.68–0.93	Superior temporal gyrus. Lateral ventricle. Gyrus supramarginalis
CC	0.22–0.54 0.37±0.09	left	Subcortical nuclei	0.86 (4×10 ⁻⁷)	0.67–0.93	Superior temporal gyrus. Lateral ventricle
CC	0.16–0.39 0.31±0.05	left	Cortex	0.69 (0.00014)	0.33–0.85	Posterior middle frontal gyrus. Superior frontal gyrus.
Anterior CC	0.16–0.40 0.31±0.05	left	Cortex	0.68 (0.00018)	0.32–0.85	Posterior middle frontal gyrus. Superior frontal gyrus
Splenium of CC	0.27–0.54 0.37±0.08	right	Subcortical nuclei	0.66 (0.0005)	0.24–0.87	Superior temporal gyrus. Lateral ventricle. Inferior parietal gyrus
Left CST	0.32–0.63 0.45±0.08	left	Cortex	0.64 (0.0020)	0.21–0.84	Paracentral lobule. Posterior cingulate gyrus
Left CST	0.36–0.69 0.58±0.09	left	Subcortical nuclei	0.62 (0.0009)	0.27–0.82	Thalamus
Left CST	0.31–0.6 0.47±0.08	left	Cortex	0.61 (0.0010)	0.23–0.81	Lateral ventricle. Caudate nucleus
Right CST	0.30–0.67 0.53±0.10	right	Subcortical nuclei	0.60 (0.0012)	0.24–0.82	Amygdala. Ventral intermediate medulla. Hippocampus

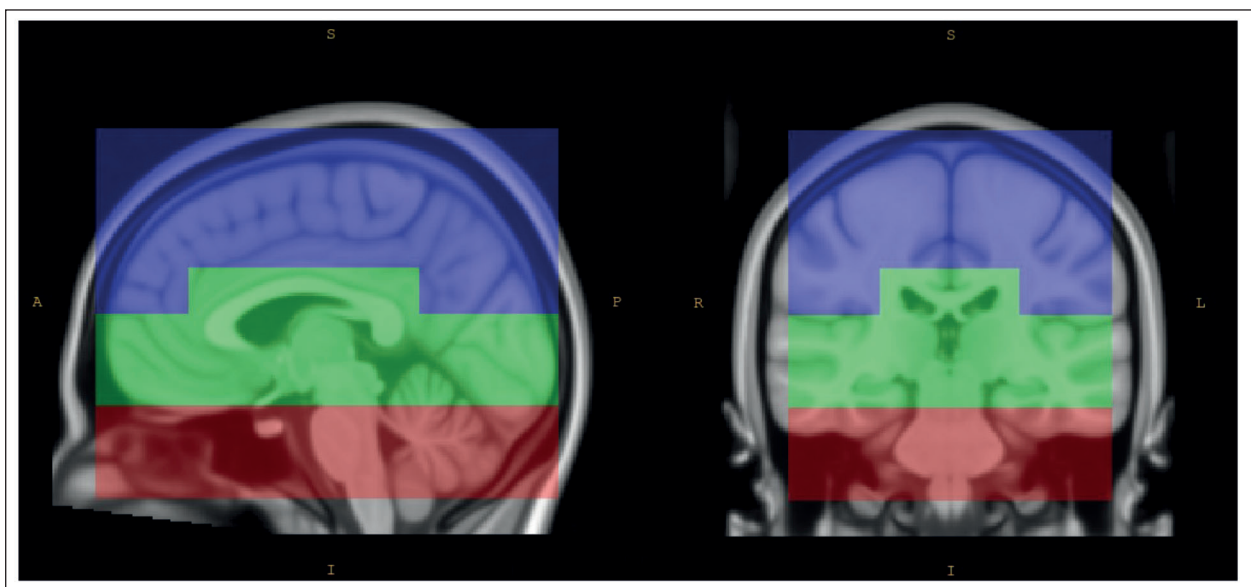
cleus) components of the left corticospinal tract (Fig. 3, I).

However, more significant correlations with hemiparesis severity (ranging from 0.66 to 0.86) were found both for the CC as a whole and for its individual segments (Table 4). Relatively low *r* values were found for the right part of the splenium of the CC (lateral ventricle and inferior parietal gyrus, *r*=0.66) and the left anterior CC (superior frontal gyrus, *r*=0.68). The most significant correlation (0.86) was found for the left part of the splenium of

the CC located near the lateral ventricle and superior supramarginal gyrus. The highest *r* values were associated with subcortical CC areas.

Moreover, we observed a correlation of approximately 0.6 between the severity of right hemiparesis and the fractional anisotropy (FA) of subcortical segments of the right corticospinal tract (CST) ipsilateral to the hemiparesis (Table 4, Fig. 3, III).

In subacute TBI, the number of correlations of hemiparesis severity with DTI data exceeding 0.6 (Table 5) was significantly lower than in the acute

**Fig. 2. Three levels of anatomical location of clinical-DTI correlations: brainstem (red), subcortical nuclei (green), and cortex (blue).**

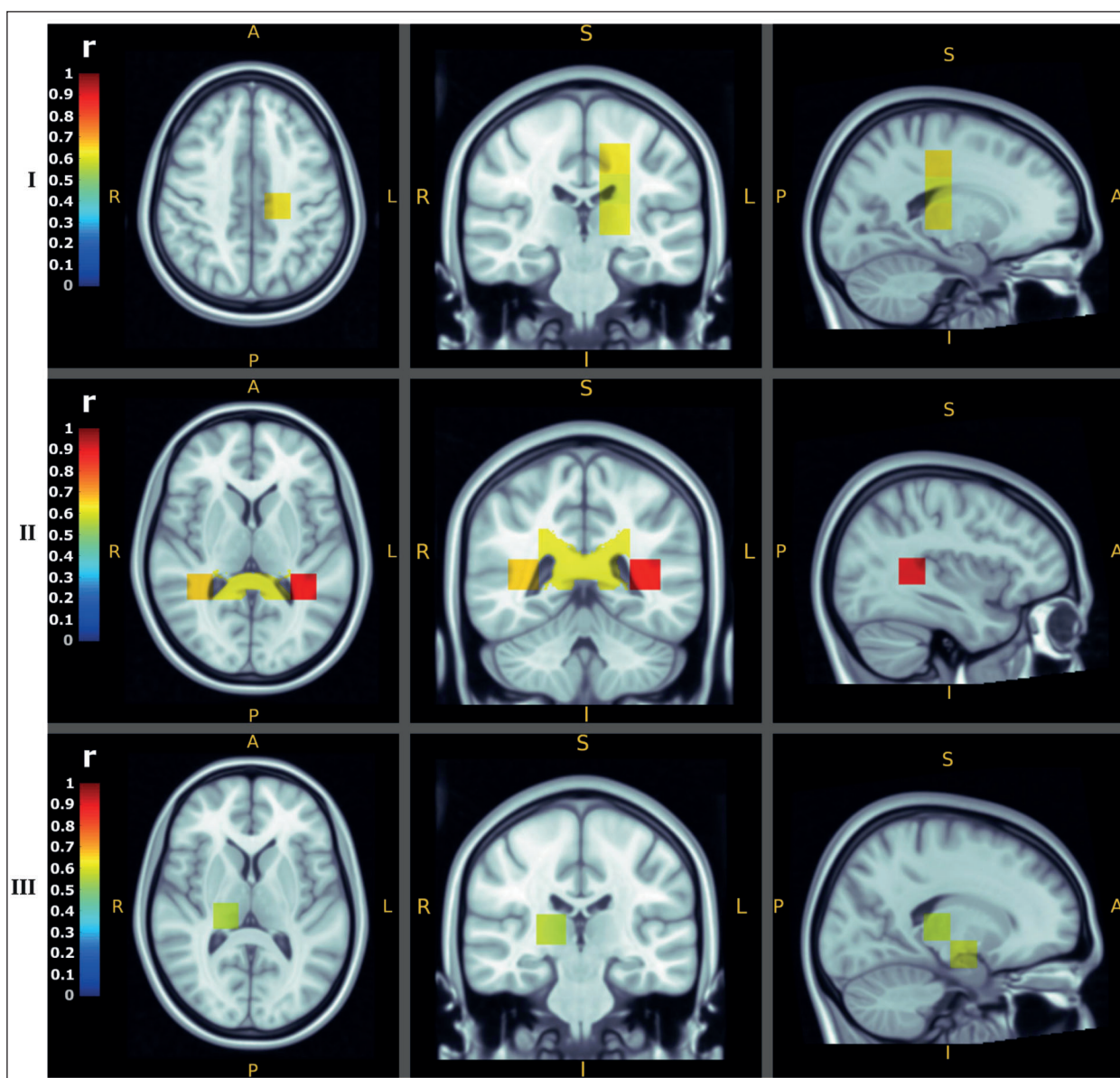


Fig. 3. Zones of correlation between severity of right hemiparesis and fractional anisotropy of segments of left CST (I), splenium of corpus callosum (II), and right CST (III) in acute TBI.

Note. In Figures 3–5, the color scale on the left reflects the values of the correlation coefficient.

phase (Table 4); their values ranged from 0.6 to 0.71. Meanwhile, only one parameter was related to the cortical segment of the left CST (Fig. 4, I), while the other two were associated with the subcortical segments of the anterior part and especially with the splenium of the CC. Together with them, we revealed the previously missing correlation between the severity of hemiparesis and the status of the central segment of the left inferior fronto-occipital tract adjacent to the hippocampus (Fig. 4, II).

In chronic TBI, the correlation of hemiparesis severity with the status of conduction pathways was less strong, with maximum r values not exceeding 0.68 and mainly ranging from 0.53 to 0.58 (Table 6). The CSTs of both hemispheres were absent among the tracts with significant correlations. However, the «representation» of cortical projections of the

corpus callosum (mainly its right anterior part) was preserved (Fig. 5, I). In addition, we found a correlation with FA for the central segment of the right IFOT, but not for the left one (Fig. 5, II).

The important directions of this study included the impact of FA of the tracts correlating with hemiparesis severity at different phases of traumatic disease on the recovery of motor function in the chronic phase.

Fig. 6 shows the plots of FA for splenium of CC in acute TBI (Fig. 3, II), the cortical segment of the left CST in subacute phase (Fig. 4, I), and for the FA of anterior CC in the chronic phase (Fig. 5, I).

According to this correlation, the vast majority of FA parameters for different tracts were lower than normal in the examined patients at all stages of the study. The magnitude of the reduction was

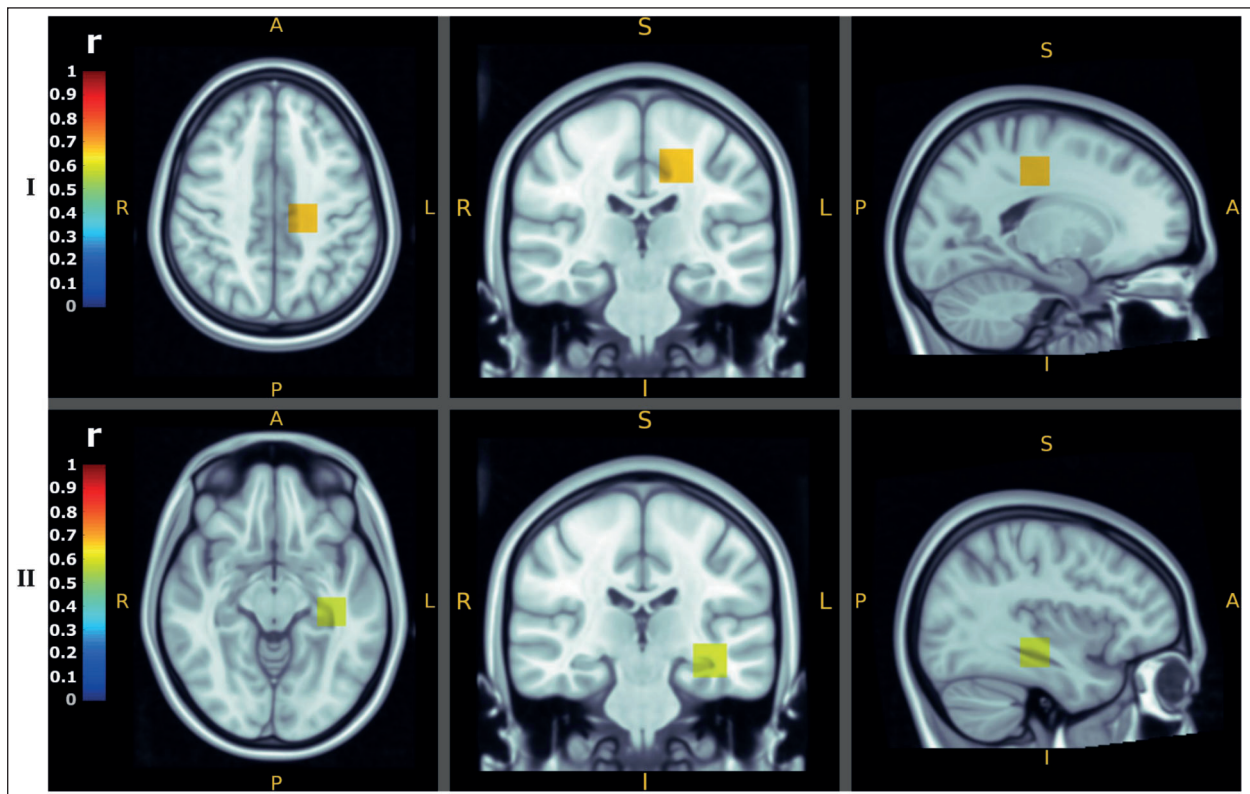


Fig. 4. Zones of correlation between the severity of right hemiparesis and fractional anisotropy of segments of the left CST (I) and left IFOT (II) in subacute traumatic brain injury.

Table 5. Correlations of severity of right hemiparesis with fractional anisotropy of segments of different tracts in chronic TBI.

Tract	Hemisphere	Level	<i>r</i>	Adjacent anatomical structures
CCT	Right	Cortex	0.68	Superior frontal gyrus Posterior middle frontal gyrus Posterior cingulate gyrus
Anterior CCT	—	Subcortical nuclei	0.58	Anterior cingulate cortex
Middle CCT	Right	Cortex	0.58	Anterior cingulate gyrus Superior frontal gyrus Posterior middle frontal gyrus
Right IFOT	Right	Subcortical nuclei	0.56	Inferior lateral ventricle Amygdala Putamen Insula Hippocampus
Anterior CCT	Right	Cortex	0.56	Anterior cingulate gyrus Superior frontal gyrus Posterior middle frontal gyrus
Middle CCT	—	Subcortical nuclei	0.53	Anterior cingulate gyrus

directly related to the severity and persistence of the motor deficits.

Figures 6 B and C show typical variants of FA values distribution in the study groups. Thus, in patients with subacute TBI (from 1 to 6 months), FA values for the cortical segment of the left CST less than 0.4 were associated with no further reduction of right hemiparesis, whereas higher values of this parameter were associated with further regression of this motor defect (nonparametric Wilcoxon test, $P=0.02$). DTIs performed in the chronic phase show similar FA ratios for the right anterior

segment of the corpus callosum ($P=0.03$ when comparing groups using the Wilcoxon test) (Fig. 6, C). The selective comparison of parameters in the study groups revealed that the average FA values in «non-recovery» patients were 68-78% of the normal values of the specific segment at all stages of the study.

In «recovery» patients, the tracts with segmental FA values within or above the normal range were found only in the acute phase. These tracts included subcortical segment of splenium of CC (Fig. 6, A), as well as cortical and subcortical parts of the left corticospinal tract.

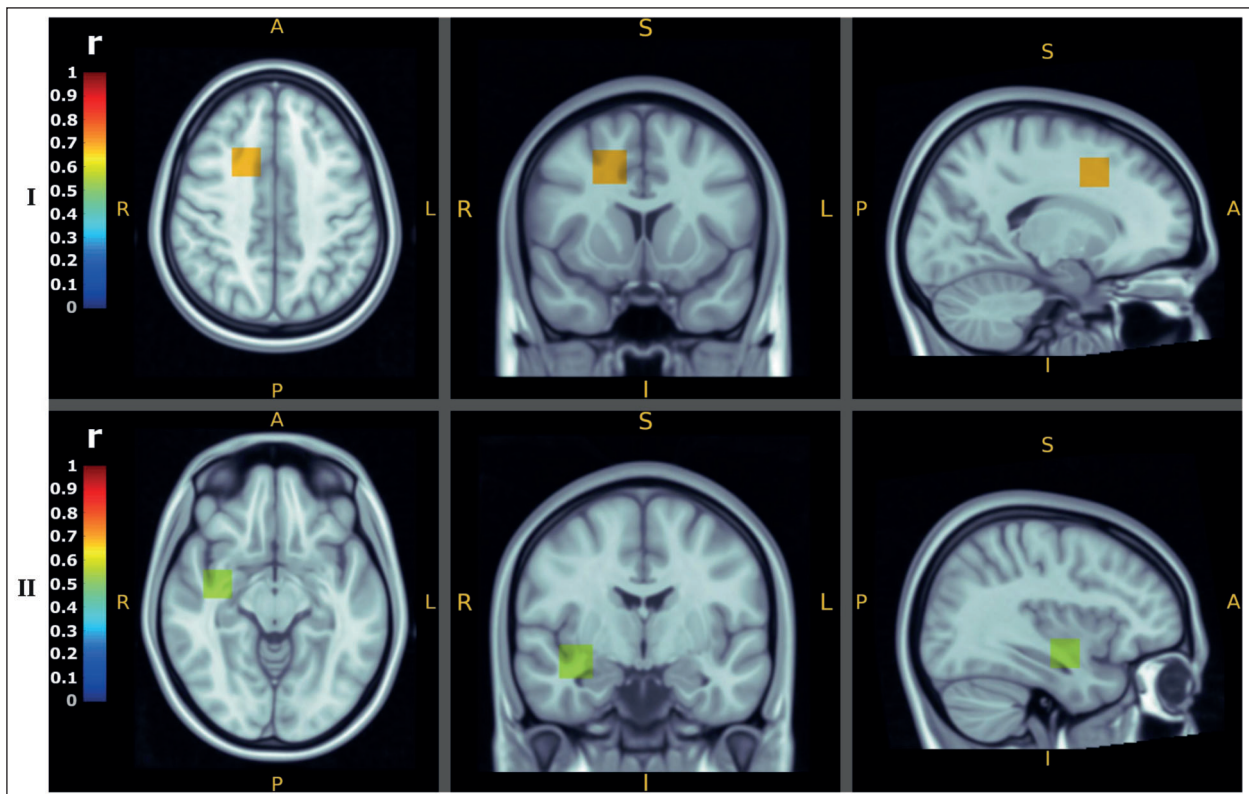


Fig. 5. Zones of correlation between the severity of right hemiparesis and fractional anisotropy of the right anterior CCT segments (I) and right IFOT (II) in the chronic traumatic brain injury.

Table 6. Correlations between right hemiparesis severity and fractional anisotropy of segments of different tracts in the chronic traumatic brain injury.

Tract	FA (min–max– average)	Hemisphere	Level	r (P-value)	95% CI of the correlation (min–max)	Adjacent anatomical structure
CCT	0.15–0.41 0.31±0.08	right	Cortex	0.68 (0.0002)	0.20–0.86	Superior frontal gyrus. Posterior middle frontal gyrus. Posterior cingulate gyrus
Anterior CCT	0.14–0.40 0.32±0.06	—	Subcortical nuclei	0.58 (0.0017)	0.04–0.82	Anterior cingulate gyrus
Middle CCT	0.16–0.45 0.32±0.08	right	Cortex	0.58 (0.003)	0.04–0.85	Anterior cingulate gyrus. Superior frontal gyrus. Posterior middle frontal gyrus
Right IFOT	0.22–0.39 0.33±0.04	right	Subcortical nuclei	0.56 (0.008)	0.10–0.80	Inferior lateral ventricle. Amygdala. Putamen. Insula. Hippocampus
Anterior CCT	0.14–0.43 0.32±0.07	right	Cortex	0.56 (0.005)	0.05–0.80	Anterior cingulate gyrus. Superior frontal gyrus. Posterior middle frontal gyrus
Middle CCT	0.25–0.49 0.36±0.07	—	Subcortical nuclei	0.53 (0.005)	0.07–0.79	Anterior cingulate gyrus

Discussion

We used a non-conventional algorithm to measure cerebral white matter FA in patients with traumatic brain injury. The MR images of some of them showed severe brain damage and signs of cerebral oedema, which made it difficult to mark the measurement zones. The advantage of the al-

gorithm used was its automation, which minimized the dependence of the result on the expertise of the researcher. The successful application of the developed algorithm suggests its usefulness for the other studies.

The results of this study demonstrate a dynamic, time-dependent correlation between the severity of right post-traumatic hemiparesis and FA of the

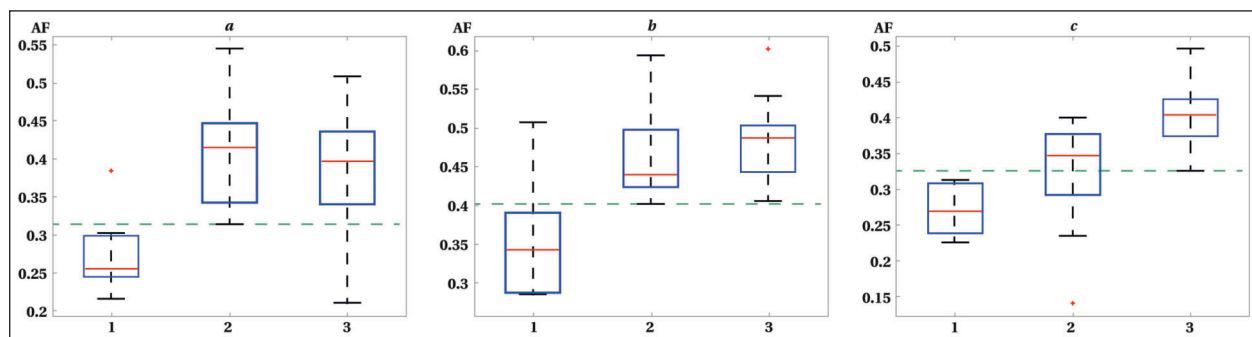


Fig. 6. Fractional anisotropy of segments of individual tracts in patients with different degree of motor function recovery and in healthy subjects.

Note. *a* — FA of the subcortical segment of the splenium of CC in the acute phase. *b* — FA of the subcortical segment of the left CST in the subacute phase. *c* — FA of the right anterior CC in chronic traumatic brain injury. 1 — patients with right hemiparesis 1 and 2 points on the manual muscle testing scale [31] in chronic traumatic brain injury («not recovered»); 2 — patients with right hemiparesis 3, 4 and 5 points in chronic traumatic brain injury («recovered»); 3 — healthy subjects. The green dotted line is the optimal threshold value calculated using ROC-analysis and discriminating between groups of patients.

cerebral tracts, supporting the idea of the staged development of traumatic brain disease [3].

FA of the corticospinal tract contralateral to the hemiparesis has been shown to correlate significantly with motor deficits in acute and subacute TBI, which in turn is consistent with classical neuroanatomy [13, 35]. However, even in the acute phase, a similar correlation was found for ipsilateral hemiparesis and the right corticospinal tract. Furthermore, the correlation between the segments of different tracts of this hemisphere and the degree of hemiparesis increased up to the chronic phase of TBI. This suggests that the hemisphere ipsilateral to the defect is likely to be involved in neuroplastic compensatory processes. The active role of the 'healthy' hemisphere in these processes is well known in stroke, which is usually caused by unilateral hemispheric damage [36, 15].

In TBI with diffuse, often bilateral brain damage, our previous studies [10, 5] have shown that the severity of ipsilateral hemiparesis is most evident in mild cases of paresis (4 points), where there is predominantly unilateral hemispheric damage or no damage at all. This significance cannot be ruled out in patients with marked hemiparesis but without focal lesions.

We have found that there is a dynamic relationship between cerebral structures and the severity of hemiparesis that changes over time. In the acute phase of TBI, the correlation is stronger in the deeper (subcortical) parts of the brain, while in the chronic phase it shifts to the cortical areas. The presence of significant correlations in the acute phase, specifically damage to subcortical structures, can be attributed to the continuous functional activity of the extrapyramidal system. This system is responsible for controlling motor functions and muscle tone and is in constant functional interaction with the pyramidal system. These correlations can be considered as an early compensation for motor

disorders during the post-traumatic depression of the functional activity of the corticospinal tract (CST). As the traumatic injury progresses to subacute and chronic stages, the role of subcortical formations decreases, and the activity of cortical areas involved in movement production becomes the main manifestation of neuroplastic mechanisms.

Aside from the well-established importance of movement-specific corticospinal tracts in the acute phase, significant correlations with the severity of hemiparesis have also been discovered for some areas of the corpus callosum, which persist even in chronic TBI. The importance of interhemispheric interaction of the brain sensorimotor areas in providing motor function has previously been demonstrated using both functional methods [37, 12, 38] and DTI data [16, 17]. The hypogenesis of the corpus callosum and the corresponding decrease in FA in children with spastic diplegia have been found to correlate with the severity of motor impairments and to be an accurate indicator of motor deficits [39]. The results of our study directly confirm this fact in TBI.

Furthermore, our study revealed correlations between the severity of right hemiparesis and segments of the inferior fronto-occipital fasciculus (IFOT), with the left segment being significant in the subacute phase and the right segment in the chronic phase. Although this tract is not directly related to motor function, current ideas about multicomponent neural networks supporting different types of activity suggest that it may be involved in the sensorimotor integration required for movement execution. A study [40] found that therapeutic translingual stimulation improved motor functions as well as increased the initially reduced FA of several non-motor brain tracts, including the left inferior frontal-occipital tract, in children with cerebral palsy. The authors believe that the IFOT, a ventral associative pathway that connects the frontal

lobe to the occipital and parietal lobes via the temporal lobe and the insula [41], is involved in mixed sensorimotor integration because of its middle component. Changes in its FA correlated with hemiparesis severity in our study as well, and it is one of the «areas of interest» of neural networks such as DMN, relevance, and speech networks [42]. While the CST's cortical and subcortical segments are part of the sensorimotor neural network, which ensures the direct act of executing a voluntary movement, the DMN, relevance, and speech networks are associated with more sophisticated components of movement organization, such as memory, motivation and behavior integration, sensory integration, spatial navigation, and others.

According to the obtained data, we can assume that the importance of structural and functional interactions of sensorimotor neuronal networks is more obvious in the development of motor disorders in the acute phase, while in the subacute and especially in the chronic phase, the persistence and severity of these disorders depend more on the preservation of anatomical connections of more global (integral) neuronal networks.

In general, the results of our study confirm the literature data on the diagnostic usefulness of tractography (and in particular fractional anisotropy values) in the development and regression of motor

disorders such as hemiparesis, both in stroke [43] and in traumatic brain injury [44]. Moreover, the dynamic changes in the correlations between FA parameters and hemiparesis severity in different phases of TBI can serve as a rationale for the use of DTI in neurorehabilitation, both for diagnostic purposes and for studying the different mechanisms of recovery from motor disorders of different etiologies [45, 46].

Conclusion

We found that post-traumatic right motor dysfunction is associated not only with damage to the left CST, but also with disruption of interhemispheric interaction due to damage to the tracts of the corpus callosum.

In the subacute and especially in the chronic phase of TBI, a correlation has been demonstrated between the severity of right hemiparesis and the topography of the bilateral IFOTs, which are non-specific with respect to motor function. This could indicate the involvement of these tracts, the CST and the ipsilateral hemiparesis in the compensation of the motor defect.

The obtained specific quantitative characteristics of structural and clinical correlations, as well as FA values in cases with different success rates of motor recovery, should be considered in the management of patients with traumatic brain injury.

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Received 17.07.2023
Accepted 23.10.2023