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CHANGES IN REGIONAL CEREBRAL BLOOD FLOW, COGNITIVE FUNCTIONS AND EMOTIONAL STATUS IN PATIENTS AFTER MILD TRAUMATIC BRAIN INJURY – RETROSPECTIVE EVALUATION

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Abstract. The aim of the study was to estimate rCBF in patients after mild traumatic brain injury (mTBI) and to compare the results of neuropsychological examinations. The study was conducted in a group of 17 males aged 19-25 years (average age 22.1) after mTBI. The SPECT examination carried out early after the trauma, showed in 16 patients numerous foci of the decreased perfusion mostly in the frontal and temporal areas and, less frequently, in the parietal areas of brain; the foci were localised predominantly in the left hemisphere. One year after the injury, both the magnitude and the intensity of rCBF alterations were in 7 patients less pronounced than shortly after the trauma, and in 3 patients reduction of changes was very significant. Abnormal concentration and attention divisibility level was found in 9 (52.9%) patients in early period after mTBI. In five of them, and another one (35.3%) with previous normal result of Couve test, abnormalities were found a year after TBI as well. Short-term memory was weak directly after mTBI in 11 (64.7%) subjects. High anxiety level coexisted in patients with abnormalities described above in early period and a year after trauma. Depression was diagnosed in 5 patients a year after TBI. It was consistent with their complaints found in other psychological examinations. All above-mentioned abnormal results were found in patients with high level of neuroticism. Multifocal rCBF changes revealed in acute phase and a year after trauma did not correlated with psychological patient status. Our survey did not revealed any relationship between the results of SPECT examination and the development or sort of posttraumatic cognitive abnormalities found in neuropsychological tests.

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Key words: Postconcussion syndrome - Regional cerebral blood flow - Mild traumatic brain injury - Cognitive disturbances

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Introduction

Mild traumatic brain injury (mTBI) is one of the most common neurological disorders, with only migraine and herpes zoster having a higher incidences and only migraine having a higher prevalence [2]. Sport, recreation and communication injuries are the most often causes of head trauma [4]. Most patients with mild TBI recover within weeks to months without specific intervention, but a year after injury approximately 15% of patients still have disabling symptoms – constituting postconcussion syndrome (PCS) [20].

PCS is a cluster of symptoms, resistant to current treatments, that includes complaints of memory difficulty, headache, vertigo, depression, anxiety, concentration difficulty, blurred vision, fatigue, irritability, photophobia and hyperacoutism [3,21,29]. It is thought that the primary cause of PCS is cerebral dysfunction, as a result of complex pathophysiological processes occurring in the brain at the cellular level, which end up in necrosis and/or apoptosis of the nerve cells [5,12]. Exposure to the linear acceleration forces brings about the most pronounced changes in the deep structures of the brain whereas angular acceleration damages mainly the cerebral cortex, particularly frontal and temporal lobes [30]. This pattern may be responsible for the eventual predominance of attentional and "executive" deficits in even the mildly impaired [2].

The development of new diagnostic method, such as the single photon emission computerized tomography (SPECT) has provided an opportunity to more thoroughly analyse the underlying pathological processes and hence to more precisely assess the patients' conditions.

Elsewhere it has been argued that although PCS may initially have an organic basis it persists because of psychological factors or is primarily psychogenic in origin [18]. It is thought that assessment of neuropsychological status can assist physicians in determining safe return-to-play for athletes who sustain mTBI [9,17,23].

The aim of the study was to estimate rCBF in patients after mTBI and to compare the results with psychological examinations. The protocol of the study was approved by the Ethical Committee of Polish Air Force Institute of Aviation Medicine (PAFIAM).

Materials and Methods

The study was conducted in a group of 17 males aged 19-25 years (average age 22.1 y) who were admitted to the Dept. of Neurology, PAFIAM because of mTBI accompanied by the consecutive brain commotion. TBI occurred as a result of professional activity, sports exercises, and car accidents. The diagnosis was based on

history, physical examination, and the CT analysis. Written consent was obtained from all the subjects allotted to the study.

Selection of the patients for the study was based on the following criteria: skull and brain injuries with brain commotion experienced for the first time shortly before the study (i.e., 24 - 96 hours before hospitalisation), 19-41 years of age, male, and no detectable mental disorders, somatic diseases or other physical abnormalities. In addition, no past history of abnormal EEG recordings and no family history of epilepsy were required.

The injuries were evaluated using the Glasgow Coma Scale (GCS). Accordingly, the total score (ranging from 3 points for the most serious condition to 15 points for the least serious one) obtained after the assessment of the eye-opening capacity and the verbal and motor responses were used to divide the patients into the following 3 groups: a) minor (scaled 13-15), b) moderate (scaled 8-12), and c) heavy head trauma (scaled 3-7).

During the first 24 hours after the admission, CT with no contrasting medium was performed. Normal images of the brain and the cerebellum with no detectable dislocations in the ventricular system were required for the inclusion of a patient in the study. All the CT images were examined by one and the same physician.

Beginning from the 10th to 14th day after the injury, regional cerebral blood flow (rCBF) was examined using SPECT methodology (examinations were performed in the Dept. of Nuclear Medicine of Central Clinical Hospital of Military Medical Academy in Warsaw). Brain imaging by SPECT was done using the rotating Elscint Apex-SP-6 gamma camera with a single detection head, equipped with a highly distributive collimator for low energy. Acquisition of the data started 15 min after the i.v. administration of 740 MBq (20mCi) of the ^{99m}Tc-HMPAO complex. The head rotated by every 6° in a circular 360° orbit. The computer-processed results were presented as a qualitative report. Brain perfusion was evaluated using visual and semi-quantitative method. As indicated by Gray *et al.* [13] ^{99m}Tc-HMPAO distributes symmetrically in the grey matter of healthy subjects with the tendency for the marker to accumulate in central parts of the occipital lobes and the cerebellar cortex. The results of the investigations by these authors were used as controls for the purpose of the present study.

From 10th to 14th day after TBI patients underwent assessment by applying psychological test with special attention to the following symptoms: ability of concentration and divisibility of attention (Couve test), short term memory (STM) (repetition of numbers from Wechsler Adult Intelligence Scale - Revised, WAIS-R), emotional status (level of anxiety and depression from Zung tests) and individual hypersensitivity (neuroticism level in Eysenck personality Questionnaire - Revised, EPQ-R).

During the immediate post-traumatic period the patients were not allowed to take any drugs or use condiments that could significantly affect bioelectric activity of the

brain. The only medicine administered to the patients at that time was Aescine (3 tablets twice a day), a tightener of the capillary walls and inhibitor of the capillary permeability (the drug does not affect brain bioelectric activity).

One year after the TBI SPECT- HMPAO, and psychological examinations were repeated in all the patients.

Results

Based on the anamnesis, information was obtained about the causes of the experienced skull-brain injury, and the character and duration of the disturbance of consciousness. The causes of the trauma included: beating (11 cases), road accidents (4 cases), and tumbling (2 cases). The post-traumatic shock and loss of consciousness occurred in all the patients but the duration of the unconsciousness varied from several seconds in 7 patients to 1-20 min in 6 patients to 30-60 min in 5 patients. The several minute-retroactive amnesia was reported by all the subjects. The post-traumatic amnesia (PTA), which in the extreme case lasted almost 6 hours, was also reported by all the patients.

According to the CGS, 12 patients were scored 15 points and 5 patients were scored 14 points. In the latter group, one point was subtracted from the highest score because the patients were able to open their eyes on demand.

The SPECT examination carried out early after the trauma, showed in 16 patients numerous foci of the decreased perfusion mostly in the frontal and temporal areas and, less frequently, in the parietal areas of the brain; the foci were localised predominantly in the left hemisphere (Table 1). Eleven of the 16 patients exhibited similar changes also one year after the trauma. In 5 subjects, the SPECT imaging carried out one year after the injury did not reveal any differences compared to the initial examination. One year after the injury, both the magnitude and the intensity of rCBF alterations were in 7 patients less pronounced than shortly after the trauma, and in 3 patients reduction of changes was very significant. In one patient, the magnitude of the rCBF disturbances recorded one year after the injury was greater than during the initial examination. In one case, hyperperfusion foci detected during the early period after the trauma transformed into a hypoperfusion foci one year later. In addition, in one patient the focus of a decreased perfusion changed its localisation one year after the trauma. Finally in one patient the results of the two examinations separated by one year were similar and revealed no brain abnormalities.

Abnormal concentration and attention dividity level was found in 9 (52.9%) patients in early period after mTBI. In five of them, and another one (35.3%) with previous normal result of Couve test, abnormalities were found a year after TBI as well.

Table 1
Regional cerebral blood flow abnormalities in mTBI patients a year after trauma

Patient N^o	Frontal region		Temporal region		Parietal region		Occipital region	
	left	right	left	right	left	right	left	right
1.	X	X	X		X	X		
2.		X	X				X	
3.	X		X		X	X		
4.	X	X	X		X			
5.	X		X		X			
6.	X		X		X		X	X
7.	X		X	X	X			
8.			X		X			
9.	X	X						
10.	X	X	X				X	X
11.		X	X	X				
12.	X	X		X			X	
13.	X	X	X		X	X		
14.								
15.		X		X		X		
16.	X		X				X	
17.			X		X	X		

Short-term memory was weak directly after mTBI in 11 (64.7%) subjects. In six of them abnormalities still existed a year after TBI, and in 4 other patients (58.8%) with normal results in acute phase.

High anxiety level coexisted in patients with abnormalities described above in early period and a year after trauma (Table 2).

Depression was diagnosed in 5 patients a year after TBI. It was consistent with their complaints found in other psychological examinations.

What was interesting all abnormal above-mentioned results were found in patients with high level of neuroticism.

Multifocal rCBF changes revealed in acute phase and a year after trauma did not correlated with psychological patient status, except one finding. In four (23.5%) from five patients with abnormal results in all psychological tests rCBF changes were also found in right frontal lobe.

Table 2
Psychological assessment results

Patient N^o	Concentration and attention dividity (Couve test) N: ≥ 21 pt.		Short term memory (Wechsler test) N: ≥ 10 pt.		Anxiety level (Zung test) N: ≤ 35 pt.		Depression (Zung test) N: ≤ 39 pt.		Personality (Eysenck test) N: ≤ 18 pt.
	Acute period	A year after TBI	Acute period	A year after TBI	Acute period	A year after TBI	Acute period	A year after TBI	
1.	13	20	8	9	38	28	25	34	11
2.	35	40	10	9	20	28	20	25	9
3.	24	37	10	9	37	23	35	26	10
4.	18	24	9	10	38	35	34	34	16
5.	20	24	8	10	31	33	31	37	18
6.	27	24	11	8	30	29	35	30	17
7.	25	40	9	10	27	25	35	28	13
8.	27	40	10	10	28	29	26	32	9
9.	20	20	9	8	42	40	42	40	21
10.	16	18	8	7	35	51	29	41	22
11.	19	18	9	8	42	40	39	40	23
12.	16	17	8	8	30	45	34	45	24
13.	32	37	11	12	26	20	25	21	8
14.	26	23	9	8	39	29	42	39	21
15.	19	21	9	10	28	29	23	25	9
16.	20	31	9	10	43	28	34	34	15
17.	27	18	10	8	42	51	53	62	23
Deterioration	9 (52.9%)	6 (35.3%)	11 (64.7%)	10 (58.8%)	8 (47.1%)	5 (29.4%)	3 (17.6%)	5 (29.4%)	6 (35.3%)

Discussion

Traumatic brain injury (TBI) is found in many sports. A mild TBI (mTBI) is found in more than 80%, mainly in sports with contact to others. Especially affected by death are air sports, horse riding and cycling, whereby brain damage often is the leading injury. According to the gravitational scale of cerebral concussion, an adequate sports break should be kept. Postcommotional symptoms prove sports inability. A chronic brain damage is rarely found in some combative sports. In this case the injury may result in a traumatic encephalopathia with the evaluation of dementia and in some cases also Parkinson's disease is observed. [28]. However most patients with mild TBI recover within weeks to months without specific intervention, but a year after injury approximately 15% of patients still have disabling symptoms – constituting postconcussion syndrome (PCS) [2,20].

It is thought that the primary cause of PCS is cerebral dysfunction, as a result of complex pathophysiological processes occurring in the brain at the cellular level, which end up in necrosis and/or apoptosis of the nerve cells [5,12]. The primary neuropathology of TBI is diffuse axonal injury (DAI) caused by shearing forces generated in the brain by sudden deceleration. These shearing forces disrupt fragile structures running in the long axis of the brain, primarily axons and small vessels. Axonal injury causes localized transport failures in the axon, leading to swelling and often lysis of the axon with wallerian degeneration [6,10]. Vascular injury can disrupt small veins, producing petechial hemorrhages or local or focal oedema [25]. The primary distribution of injury seems to be parasagittal white matter spreading from cortex to brainstem. Exposure to the linear acceleration forces brings about the most pronounced changes in the deep structures of the brain whereas angular acceleration damages mainly the cerebral cortex, particularly of frontal and temporal lobes [30]. Frontal and temporal lobes, as part of systems covering many cortical and subcortical structures, are involved in memory, attention and emotional processes [11,15]. That’s why we can expect that changes occurring in these CNS elements result in memory, attention and emotional disturbances.

Wallesch *et al.* [27] evaluated the neuropsychological symptoms in the early posttraumatic period following blunt head injury and their correlation to routine imaging data in a consecutive series of 135 TBI patients. The presence of DAI was correlated with behavioral and cognitive symptoms of frontal lobe dysfunction. The presence of local frontal or temporal traumatic lesions was associated with deficits in concept formation, fluency tasks and behavioral symptoms, but not with increased interference. Patients with frontal contusions were impaired in a task of visuomotor planning and performance. Authors’ data indicate that both traumatic DAI and focal lesions result in frontal lobe symptoms.

SPECT has provided an opportunity to more thoroughly analyse the underlying pathological processes and hence to more precisely assess the patients' conditions.

Mild TBI causes changes of rCBF in about 60-88%% of the subjects [13]. Abu Judeh *et al.* [1] presented SPECT brain perfusion findings in 32 patients who suffered mild traumatic brain injury without loss of consciousness and normal computed tomography. The results showed that 19 (59%) were abnormal (13 studies performed within 3 months of the date of injury and six studies performed more than 3 months post-injury). In the 17 abnormal studies with focal lesions, the following regions were involved in descending frequency: frontal lobes 58%, basal ganglia and thalami 47%, temporal lobes 26% and parietal lobes 16%.

Such changes in the rCBF do not necessarily result from the direct damage to nervous tissue but instead may be a manifestation of deterioration in the blood-brain barrier function or of a local tissue oedema [16]. In a half of cases such rCBF abnormalities disappear after a few weeks and they are not found in repeated SPECT examination. In other subjects failing rCBF is recognized even 12 months after brain concussion [6]. The changes may explain a neurological component of the patient's symptoms in the absence of morphological abnormalities using other imaging modalities.

Changes of rCBF in early period and a year after trauma were found in all but one subjects of the estimated group. Changes localisation was similar to that found in previous surveys. There was no correlation between the nature and localisation of rCBF deterioration shown in SPECT and the type or duration time of the psychological abnormalities in examined patients. These results are similar to those exhibited by Hoffman *et al.* [14] who examined 21 patients after mTBI. They underwent MR, SPECT HMPAO examinations and neurocognitive assessment within 5 days after injury. Neurocognitive follow-up was conducted 2 and 6 months after injury, and MR imaging was repeated after 6 months. The association between hypoperfusion seen on acute SPECT and brain atrophy after 6 months suggested the possibility of (secondary) ischemic brain damage. There was only a weak correlation between neuroimaging findings and neurocognitive outcome.

Although PCS may initially have an organic basis, it persists because of psychological factors or is primarily psychogenic in origin [7,10,18]. Mittenberg *et al.* [22] indicated that the relative incidence of postconcussion symptoms reported by head trauma patients correlated substantially with the relative frequency of postconcussion symptoms anticipated by uninjured controls. This study suggested another common denominator: the anticipation, widely held by individuals who have had no opportunity to observe or experience postconcussive symptoms, that PCS will occur following mild head injury. Moreover the tendency was indicated for patients with head injuries to attribute premorbid symptoms to head trauma. The incidence of PCS was higher when patient received no explanation of their symptoms and were not provided treatment or encouragement [22].

The aetiological role of expectations may also explain why persistent PCS is uncommon following mTBI sustained by children and athletic competition [8,24].

Participants in boxing, football, and other contact sports are repeatedly observed to sustain mTBI without obvious persistent ill effects. Being "knocked out" or "dazed" in the context of an athletic event is therefore less likely to elicit anticipations of persistent PCS than identical experiences that occur in the context of a motor vehicle accident [22].

In estimated group of patients authors found correlation between intensity and persistent character of attention, STM disturbation and neuroticism. This suggests that organic changes occurring after TBI could be responsible for PCS but personality abnormalities can help to create chronic PCS.

According to results found in our survey and opinion of other investigators [9,17,19,23] neuropsychological testing seems to be an effective way to obtain useful data on the short-term and long-term effects of mTBI. Moreover, knowledge of the various definitions and management strategies, as well as the utility of neuropsychological testing, is essential for those involved in decision-making with athletes with mild traumatic brain injuries.

References

1. Abu-Judeh H.H., R.Parker, M.Singh et al. (1999) SPECT brain perfusion imaging in mild traumatic brain injury without loss of consciousness and normal computed tomography. *J.Nucl.Med.Commun.* 20:505-510

2. Alexander M.P. (1995) Mild traumatic brain injury: Pathophysiology, natural history, and clinical management. *Neurology* 45:1253-1260

3. Alves W.M., A.R.Colohan, T.J.O'Leary et al. (1986) Understanding post-traumatic symptoms after minor head injury. *J.Head Trauma Rehab.* 1:1–12

4. Annegers I.F., J.D.Grabow., L.T.Kurland (1980) The incidence, causes and secular trends of head trauma in Olmsted County, Minnesota 1935-74. *Neurology* 30:912-919

5. Binder L.M. (1986) Persisting symptoms after mild head injury: A review of the postconcussive syndrome. *J.Clin.Exper.Neurpsychol.* 8:323-346

6. Brown S.J., S.R.Fann, I.Grant (1994) Postconcussional disorder: time to acknowledge a common source of neurobehavioral morbidity. *J.Neuropsychiatry* 6:15-22

7. Bryant R.A., A.G.Harvey (1999) Postconcussive symptoms and posttraumatic stress disorder after mild traumatic brain injury. *J.Nerv.Ment.Dis.* 187:302-305

8. Casey R., S.Ludwig, M.S.McCormick (1986) Morbidity following minor head trauma in children. *Paediatrics* 78:497-502

9. Echemendia R.J., L.J.Julian (2001) Mild traumatic brain injury in sports: neuropsychology's contribution to a developing field. *Neuropsychol.Rev.* 11:69-88

10. Feinstein A., D.Ouchterlony, J.Somerville, A.Jardine (2001) The effects of litigation on symptom expression: a prospective study following mild traumatic brain injury. *J.Med.Sci.Law* 41:116-121

11. Grabowska A. (1997) Visual perception and its analogies in comparison to other forms of perception. In: T.Górska, A.Grabowska, J.Zagrodzka (eds.) Brain and Behaviour PWN, Warsaw, pp. 147-183

12. Graham D.I., T.K.McIntosh (1996) Neuropathology of brain injury. In: R.W.Evans (ed.) Neurology and Trauma. W.B.Saunders Co., Philadelphia, pp. 53-90

13. Gray B.G., M.Ischise, D-G.Chung et al. (1992) Technetium-99m-HMPAO SPECT in the evaluation of patients with a remote. History of traumatic brain injury: A comparison with X-ray computed tomography. *J.Nucl.Med.* 33:52-59

14. Hofman P.A., S.Z.Stapert, M.J. van Kroonenburgh et al. (2001) MR imaging, single-photon emission CT, and neurocognitive performance after mild traumatic brain injury. *Am.J.Neuroradiol.* 22:441-449

15. Kowalska D.M. (1997) Anatomical basis of memory. In: T.Górska, A.Grabowska, J.Zagrodzka (eds.) Brain and Behavior. PWN, Warsaw, pp. 298-319

16. Kraus J.F., D.L.McArthur (1996) Epidemiology of brain injury. In: R.W.Evans (ed.) Neurology and Trauma. W.B.Saunders Co., Philadelphia, pp. 3-17

17. Leclerc S., M.Lassonde, J.S.Delaney et al. (2001) Recommendations for grading of concussion in athletes. *Sports Med.* 31:629-636

18. Levin H.S., A.L.Benton, R.G.Grossman (1982) Neurobehavioral consequences of closed head injury. Oxford Press, New York

19. Maroon J.C., M.R.Lovell, J.Norwig (2000) Cerebral concussion in athletes: evaluation and neuropsychological testing. *Neurosurgery* 47:659-669

20. McLean A., N.R.Temkin, S.Dikmen et al. (1983) The behavioral sequelae of head injury. *J.Clin.Neuropsychol.* 5:361-376

21. McMordie W.R. (1988) Twenty-year follow-up of the prevailing opinion on the posttraumatic or postconcussional syndrome. *Clin.Neuropsychologist* 2:198-212

22. Mittenberg W., D.V.DiGullio, S.Perrin, A.E.Bass (1992) Symptoms following mild head injury: expectations as aetiology. *J.Neurol.Neurosurg.Psychiat.* 55:200-204

23. Mrazik M., M.S.Ferrara, C.L.Peterson et al. (2000) Injury severity and neuropsychological and balance outcomes of four college athletes. *Brain Inj.* 14:921-931

24. Pollin R.S., W.M.Alves, J.A.Jane Sr. (1996) Sports and head injuries. In: R.W.Evans (ed.) Neurology and Trauma. W.B.Saunders Co., Philadelphia, pp. 166-185

25. Povlishock J.T. (1979) The morphopathologic substrates of concussion. *Acta Neuropathol.* 47:1-11

26. Povlishok J.T., D.P.Becker, C.L.Y.Cheng et al. (1986) Axonal change in minor head injury. *J.Neuropathol.Exp.Neurol.* 42:225-242

27. Wallesch C.W., N.Curio, I.Galazky et al. (2001) The neuropsychology of blunt head injury in the early postacute stage: effects of focal lesions and diffuse axonal injury. *J.Neurotrauma* 18:11-20

28. Weber J., H.Jaksche (1999) Craniocerebral trauma in sports. With recommendations for prevention. *J.Sportverletz Sportschaden* 13:30-35

29. World Health Organisation (1978) Mental disorders: glossary and guide to their classification in accordance with the 9th revision of the international classification of diseases. WHO, Geneva

30. Yokota H. (1991) Significance of magnetic resonance imaging in acute head injury. *J.Trauma* 31:351-359

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