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RESEARCH ARTICLE

Cognitive disorder in brain concussion

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Abstract **This paper presented original study results concerning the prevalence and clinical characteristics of cognitive impairment associated with brain concussion. The cognitive functions of 80 consecutive patients (mean age = 37.40±11.74 years; 50 men and 30 women) admitted to the hospital with brain concussions were evaluated. Their cognitive scores were compared with 40 age- and education-matched healthy volunteers without history of cranial trauma. Cognitive impairment without dementia was found in 93% of the patients. Cognitive impairment in brain concussion was also characterized by prominent cognitive slowness (bradyphrenia), concentration decrease, free recall insufficiency, and visual-spatial dysfunction. Age and severity of anxiety significantly influence the cognitive performance of patients.**

Keywords brain concussion, cognitive impairment

Introduction

Cranial trauma (CT) is one of the most common neurological disorders because of its great prevalence, high level of mortality and disability, and primary failure of many active young and middle-aged individuals (Fearnside et al., 1993; Navratil et al., 2006). According to the World Health Organization (WHO), the frequency of CT increases approximately by 2% annually because of technical progress, increase in the number of automobiles, and urbanization. For instance, approximately 600000 new CT cases are registered in Russia every year. Overall mortality associated with CT ranges from 5% to 10%; in severe cases, mortality can reach 41% to 85%. Thus, approximately 50000 individuals with CT die, and more than 50000 become disabled annually (Konovalov et al., 1998; Levin and Sliscova, 2005; Boyko et al., 2007). At the end of the 20th century, the number of disabled persons because of cranial trauma exceeds 2 million in Russia, 3 million in the US, and 100 million worldwide. According to the Russian Ministry of Health and Social Development, the medical costs of CT accounted for 2.6% of the gross domestic product of Russia in 2008 (www.gks.ru). Furthermore, economic damage because of CT in Russia constitutes 495 billion rubles according to the National Research Institute of Human Health (Konovalov et al., 1998; Levin and Sliscova, 2005).

In routine classification, CT is divided into mild, moderate, and severe categories. Brain concussion (BC) and mild cerebral contusion (MCC) are considered as mild CT; moderate cerebral contusion (ModCC) is considered as moderate; severe cerebral contusion, diffuse axonal damage, and brain compression are considered severe. The majority of cranial trauma victims (up to 80% to 85%) suffer from mild or moderate injuries (Adamovich et al., 1985; Boyko et al., 2007).

Cognitive disorder is observed in CT with different severities and prevalence of 70% to 100% (Kurako and Volanskij,1980; Ropacki and Elias, 2003; Pullela et al., 2006; Visilo and Vlasova, 2006). CT can cause different neurological abnormalities, but cognitive impairment is one of the most consistent and disabling effects that significantly lower the quality of patient life (Pedanchenko et al., 1991; Gitkina et al., 1992; Cossa and Fabiani,1999; Dobrochotova et al., 2002; Zakharov and Yakhno, 2003). Several problems in attention, reaction time, and memory have been observed in patients with acute CT. Furthermore, local neuropsychological symptoms are observed in cases of severe trauma. In many

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cases, cognitive impairment is the only neurological (neuropsychiatric) disorder after trauma occurs. However, this problem is often underestimated. Clinical observations have also revealed that post-traumatic cognitive impairment after mild trauma occurs can significantly interfere with professional activities of patients for a long time (Frankowski et al., 1985; Gonser, 1992; Cicerone, 1996; Binder,1997; Navratil et al., 2006).

Our research aimed to estimate the cognitive state in the acute stage of BC.

Patients and methods

We examined 80 young and middle-aged consecutive patients (50 men and 30 women) with BCadmitted in the Traumatology and Neurosurgery Department of City Clinical Hospital No. 13, Nizhny Novgorod. Inclusion criteria were listed as follows: age from 20 years old to 60 years old; BC within 24 h before admission; clear consciousness at the point of clinical assessment; and informed consent.

The patients with pre-traumatic cognitive complaints or objective evidence of pre-traumatic cognitive decline, diagnosed or retrospectively estimated, were excluded. Pre-traumatic cognitive state was retrospectively assessed with Informant Questionnaire on Cognitive Decline in Elderly (Jorm, 2004). Other exclusion criteria were listed as follows: coexistent vascular, degenerative, or any other organic brain disease; mental diseases (depression, schizophrenia, alcohol or drug abuse, etc.); systemic metabolic disorder that could affect cognitive functions; and pre-traumatic dependence in daily living.

A total of 40 healthy age- and education-matched volunteers (20 men and 20 women from 20 years old to 60 years old) constitute the control group (Table 1). The inclusion criteria of the control group were listed as follows: age from 20 years to 60 years; no history of cranial trauma; and informed consent. The exclusion criteria were the same as in the study group: no previous history of cognitive decline, vascular, degenerative or any other organic brain disease; mental diseases (depression, schizophrenia, alcohol or drug abuse or other); systemic metabolic disorder that could affect cognitive functions; and pre-traumatic dependence in daily living.

Table 1 Comparison of studied groups: general characteristics

Descriptions	Control group	Patients with BC
Number	40	80
Mean age (year)	39.18±12.50	37.40±11.74
Mean education-time (year)	12.62±2.75	11.45±3.43

Study and control groups did not differ significantly in terms of age, sex, and educational level. The study groups also showed a similar profile of concomitant diseases, namely, mild arterial hypertension, chronic gastro-intestinal diseases, chronic lungs diseases, chronic back pain, and others.

In the patient group, 48 individuals were employed (60%), 5 were students (6.25%), 11 were retired (13.75%), and 16 were unemployed (20%). In the control group, 26 individuals were employed (65%), 2 were students (5%), 7 were retired (17.5%), and 5 were unemployed (12.5%). No significant difference was found between the groups in terms of socio-occupational state.

In the study group, neurological and neuropsychological evaluation was performed twice: at 2 d to 7 d after BC and at the end of the third month after BC. Cognitive assessment was performed only if the patient exhibited clear consciousness and normal vital signs.

Neuropsychological evaluation included the following tests: literal and category fluency; mini-mental state examination (MMSE); frontal assessment battery (FAB); clock drawing test; judgment of line orientation test; free and cued recall of 12 words; visual memory ("6 objects" by A. R. Luria); modified Boston's naming test; recognition of unfinished pictures (A. R. Luria); and parts A and B of the trail making test(Lezak,1983; 17).

The emotional state of the patients and the control subjects, specifically the presence and severity of anxiety and depression symptoms, were estimated using Hamilton depression scale and Spilberger questionnaire (Hamilton, 1960; Spielberger et al., 1983).

Data were statistically analyzed using SPSS 17.

Results

The clinical image of BC of the studied patients was characterized by short-term loss of consciousness (100% patients) that lasted several seconds to 10 min, severe headache with nausea and/or vomiting (98.2% patients), and memory gap during the peri-traumatic period (62% patients). Retrograde amnesia was observed in 10 patients (12.5%), and anterograde amnesia was observed in 12 (15%) patients with BC.

At the time of the first cognitive evaluation (2 d to 7 d after concussion), complaints of headache with various severity were reported by 69% of the patients; 29% of the patients also suffered from dizziness or vertigo. Furthermore, several patients complained of fatigue, vision impairment (flashing in eyes), tearfulness, hearing loss, and tinnitus. The most common signs were unsteadiness in Romberg's test and horizontal nystagmus. Among the 80 patients, 11 (13.75%) developed acute transient vestibular ataxia. Local motor and sensory deficit, reflex asymmetry, and muscle tone asymmetry were not present in patients with BC. In the control group, complaints and local neurological deficit were absent.

At the end of the third month after BC occurred, 73.75% of the patients did not complain. Nevertheless, 14 patients

(17.5%) complained of excessive fatigue, 11 patients (13.75%) complained of intermittent headache, and 4 patients (5%) manifested early insomnia. All of the patients did not exhibit objective neurological signs.

Cognitive assessment

On the first evaluation (2 d to 7 d) and on the second evaluation (end of third month), the majority of the patients did not have memory or cognitive complaints. However, neuropsychological evaluation at 2 d to 7 d after trauma revealed abnormalities in 93.25% of patients. Cognitive impairment in all of the patients did not satisfy the diagnostic criteria of dementia.

At the end of the third month after trauma, the prevalence of cognitive disorder decreased from 93.25% to 82.5%. Similar to the results of the first evaluation, follow-up assessment did not detect dementia in any of the patients.

The cognitive scores of patients with BC at 2 d to 7 d and at the end of the third month are presented in Table 2.

On the first evaluation, the scores of the screening express-tests (MMSE, FAB) of the patients slightly but significantly differed from those of the control group. These patients also exhibited significantly lower literal and category fluency than the control subjects. The difference in category fluency was significant but lower than that in literal fluency. Verbal and visual memory impairment was also detected. Visual memory test ("6 objects") results revealed that the patients with BC exhibited a significantly lower performance than the control subjects. In the 12-word test, no significant differencewas found in cued recall between patient and control groups. However, a significant difference was observed in both immediate and delayed free recall. Mildtomoderate visual-spatial impairment was detected at 2 d to 7 d in patients with BC in terms of their judgments of line orientation and recognition of unfinished pictures. The performance of the patients in the clock drawing test was slightly but significantly lower than that of the healthy subjects. Remarkable differences between patients and control groups were also obtained in terms of attention and executive functions tests (trail making test, parts A and B). For instance, significant slowing was observed in both parts of the trail making test. The time at which parts A and B of the test was performed increased proportionally in the patient group showing lack of concentration rather than set-shifting difficulties; this result indicated an impaired performance. No significant abnormality in object recognition was found in modified Boston test in the patient group. Nevertheless, the patients significantly needed more frequent literal cues.

The age of patients significantly influenced memory scores. Elderly patients (40 years old to 60 years old) performed poorly in verbal and visual memory tests ($p < 0.01$) compared with younger patients (20 years old to 40 years old; Table 3). No association was found between age and other cognitive scores. Gender and educational level did not also influence cognitive performance.

At the end of the third month after trauma, cognitive test results were improved; attention, memory, and visual-spatial and executive functions tests ("12 words,""6 subjects," judgment of line orientation, recognition of unfinished pictures, and trail making test) were also normalized. However, literal and category fluency and modified Boston's naming test results of the patient group remained significantly less than those in the control group.

Table 2 Cognitive scoresin brain concussion (BC) in comparison with healthy subjects

Test	2d–7d after BC	End of 3 month of BC	Control
Mini-mental state examination, score	28.51±1.34*	28.78±1.60	29.60±0.67
Frontal assessment battery, score	17.63±0.62	17.72±0.48	17.85±0.36
Literal fluency, score	13.15±3.18*	14.20±3.38*^	18.33±1.67
Category fluency, score	16.74±2.72*	17.67±2.29*^	19.88±0.46
"12 words," immediate free recall, score	6.78±1.48*	7.59±1.64	8.25±1.17
"12 words," immediate cued recall, score	11.61±0.85	11.59±0.68	11.80±0.52
"12 words," delayed free recall, score	7.21±1.98*	8.40±1.50^	8.85±1.46
"12 words," delayed cued recall, score	11.41±1.05	11.67±0.83	11.85±0.53
Visual memory ("6 objects"), score	19.28±3.61*	21.27±2.46^	21.13±3.53
Judgment of line orientation, score	25.19±2.34*	28.13±2.01^	29.21±0.90
Recognition of not-finished pictures, score	9.39±1.86*	10.80±1.01^	11.35±0.70
Clock drawing test, score	9.86±0.44	9.86±0.39	10.0±0.00
Trail making test, part A, seconds	45.16±13.99*	38.27±10.75^	35.43±10.40
Trail making test, part B, seconds	104.47±37.32*	82.93±22.70^	77.50±17.79
Modified Boston naming test, number of category cues	0.19±0.58	0.20±0.29	0.00±0.00
Modified Boston naming test, number of literal cues	3.46±2.18*	1.73±1.7*^	0.48±0.88

* $p < 0.001$ in comparison with healthy subjects.
^ $p < 0.01$ in comparison with 2–7 days.

Table 3 Memory scores in brain concussion (2 d–7 d after trauma) in patients of different age groups

	20–40 years	40–60 years
Verbalmemory (12 words) immediatefreerecall	7.09±1.49	6.42±1.39*
Verbalmemory (12 words) immediatecuedrecall	11.73±0.73	11.47±0.95
Verbalmemory (12 words) delayedfreerecall	7.73±1.96	6.63±1.85*
Verbalmemory (12 words) delayedcuedrecall	11.59±0.83	11.21±1.23
Visualmemory (6 designs), 3 immediateand 1 delayedrecall, sum	20.19±3.52	18.26±3.48*

* $p < 0.01$.

Behavioral assessment

At the time of the first evaluation, depressive symptoms were significantly higher in patients than in the control subjects according to Hamilton's depression rating scale. We also detected a remarkable increase in personal and reactive anxiety in patients with recent trauma according to Spielberger's questionnaire (Figs. 1 and 2).

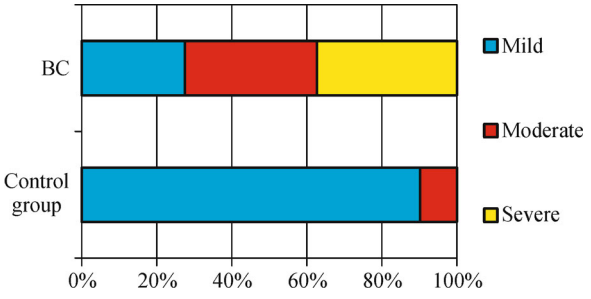

Figure 1 % of patients with mild, moderate and severe personal anxiety according to Speilberger questionnaire in brain concussion (BC) and control group.

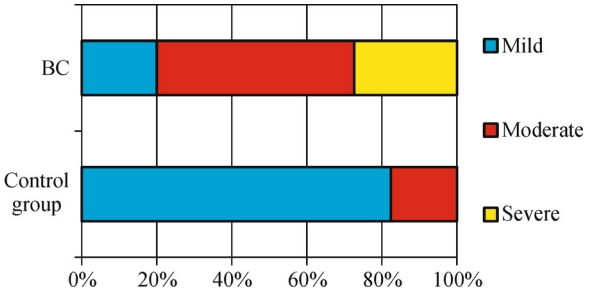

Figure 2 % of patients with mild, moderate and severe reactive anxiety according to Speilberger questionnaire in brain concussion (BC) and control group.

A moderately positive correlation was observed between anxiety and attention deficit (trail making test, parts A (r = 0.48, $p < 0.001$) and B (r = 0.56, $p < 0.001$)) at 2 d to 7 d of BC.

At the end of the third month, Hamilton depression rating score significantly ($p < 0.05$) decreased (5.35±3.5) compared with the result obtained at the time of the first evaluation (3.33±2.06) but remained higher than that in the control group (2.46±2.3).

Discussion

Our study showed that cognitive function impairment is one of the most common and significant neurological disorders in BC. Despite the absence of complaints, cognitive deterioration was found by subjecting > 90% of the patients to neuropsychological tests. Other neurological disturbances were relatively rare or not prominent and did not interfere with daily living. More than half of our patients were working individuals (54.5%); thus, cognitive dysfunction is the most important early consequence of mild CT.

Neuropsychological testing results revealed deterioration in memory, concentration, verbal fluency, visual-spatial recognition, and executive functions. However, "focal" neuropsychological abnormalities, such as aphasia, apraxia, or agnosia, were observed. Memory impairment in patients with BC was characterized predominantly by a deficiency in retrieval with the efficacy of semantic cues. Literal fluency was impaired to a greater extent than category fluency; this result indicated the relative sparing of semantic memory. This pattern of cognitive disorder resembles a"frontal-subcortical type of cognitive impairment" (bradyphrenia, excessive forgetfulness caused by retrieval deficiency, and visual spatial disturbances), and was not linked to any focal injury of the brain because of trauma. We hypothesized that the underlying mechanism of cognitive dysfunction involves diffuse microstructural changes in the brainstem (very slight diffuse axonal damage), thereby leading to a decrease in the effect of ascending activation on the cortex.

The emotional rating of patients with BC showed a high prevalence of anxiety. The prevalence of marked personal and reactive anxiety in the patient group was significantly higher than that in the control group. Depression was not similarly prominent despite average scores on Hamilton's depression rating scale that were slightly higher than that in the control group. Anxiety was moderately correlated with attention deficit; this result could indicate the negative influence of anxiety on cognitive functions in post-traumatic patients. However, emotional disturbances could not be the only reason for cognitive problems because emotional disturbance was correlated only with decline in attention and executive functions. No statistical link was observed between anxiety or depression and memory, verbal fluency, and overall cognitive scores.

The age of patients significantly influenced memory but not other cognitive functions. Elderly patients yielded lower scores in terms of verbal and visual memory. Gender and educational level were not significantly associated with any cognitive score.

The patients were subjected to follow-up observation, and the results showed the general pattern to cognitive improvement within three months after trauma. Nevertheless, the cognitive performance of $> 82\%$ of the patients differed from age-matched subjects without history of trauma. The level of anxiety and depression also remained higher in the patient group than in the control group.

Conclusion

Our study confirmed the high prevalence, clinical, and social significance of cognitive dysfunction in CT, including mild cases. The specific characteristics of cognitive impairment showed that this condition is not the result of focal brain damage. The limitation of the study is the lack of functional neuroimaging (PET, fMRI), which could ascertain the pathophysiology of cognitive impairment after mild CT. Further follow-up observation is also necessary to further evaluate the changes in cognitive functions after BC.

Compliance with ethics guidelines

All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional – University committee of ethical standards in the field of dissertation "Cognitive impairment in mild and moderate cranial trauma," national and with the Helsinki Declaration of 1975 as revised in 2000. Informed consent was obtained from all the patients for being included in the study.

Vladimir Zakharov, Ekaterina Drozdova and Nikolay Yakhno declare that they have no conflict of interest.

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