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Features of cognitive impairments in different mechanisms of mild traumatic brain injury: a literature review

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Abstract: *in wartime, a significant number of military personnel and civilians experience mild traumatic brain injuries, which negatively affect their quality of life, social adaptation, and recovery rates. Functional limitations caused by mild traumatic brain injuries impact cognitive, motor, communicative, and social domains. This review aims to explore the impact of mild traumatic brain injury on the development of cognitive dysfunctions through a biblio-systematic analysis of scientific literature. The study utilizes data from PubMed, Scopus, and Web of Science to investigate the effects of mild traumatic brain injury on cognitive impairments. The article analyzes various mechanisms of mild traumatic brain injuries and their impact on cognitive functions. It characterizes the types of cognitive and behavioral impairments resulting from mild traumatic brain injuries, such as decreased attention, memory deficits, impaired executive functions, and reduced processing speed. Special attention is given to blast-induced trauma, which amplifies the consequences of mild traumatic brain injuries through the primary effects of the blast wave. The literature analysis identified pathophysiological mechanisms, including metabolic cascades, structural brain damage, and neurotransmitter imbalances. A decrease in prefrontal cortex activity and disruptions in connectivity with other brain regions were observed. The study found that recovery dynamics in mild traumatic brain injuries patients vary depending on factors such as age, recurrent injuries, and psychological conditions. Comorbidities like depression, sleep disturbances, and chronic pain can exacerbate recovery outcomes, while the level of education serves as an important predictor of cognitive recovery. The effectiveness of diagnosis and rehabilitation during wartime relies on the implementation of a comprehensive approach, including screening tests, neuroimaging methods, and rehabilitation programs. The article provides an in-depth review of tests for memory, attention, and executive functions, such as the Psychomotor Vigilance Test, Rey Auditory Verbal Learning Test, and Stroop Test, as well as modern gamified rehabilitation programs like FitMi Home Therapy Program and ImPACT, which combine physical and cognitive exercises. Future research should focus on the development and improvement of methods for monitoring the condition of patients after mild traumatic brain injury, as well as the creation and adaptation of cognitive testing scales and programs for Ukraine. The primary aim is to enhance the quality of life of military personnel, facilitate their social adaptation, accelerate recovery after injury, and develop individualized rehabilitation programs.*

Keywords: Cognitive Dysfunction; Brain Concussion; Military Personnel; Neurological Rehabilitation; Explosions.

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Introduction

The consequences of war-related injuries include the development of functional limitations in military personnel, which, according to the International Classification of Functioning, Disability, and Health (ICF), manifest in six domains: cognitive, motor, self-care, interpersonal interactions and relationships, life activities, and participation in community life. The most significant impact has been observed in functional status cognitive (memory and concentration), communication, social, and life aspects [1,2]. Military personnel members with mild traumatic brain injury (mTBI) and blast injury (BI) more frequently report experiencing more pronounced cognitive impairments. These may persist significantly longer than in cases of impact-related mTBI that occurs due to direct mechanical contact of the head with an object [3,4].

Aim

To investigate the impact of mTBI on the development of cognitive impairments through a comprehensive review of the scientific literature.

Materials and Methods

A systematic search was conducted in the PubMed, Scopus, and Web of Science databases. Identify scientific articles, systematic reviews, and randomized controlled trials related to the effects of mTBI on cognitive functions. Special attention was given to sources published within the last 5-10 years.

Review and discussion

mTBI can cause long-term physical, cognitive, behavioral, and emotional disorders [5].

Some studies suggest that trauma-induced impairments do not significantly differ based on whether they result from BI or other mechanisms. However, other research indicates that the primary blast component may play a crucial role in the development of cognitive and neuropsychological impairments [6].

Memory impairments can be persistent and may last up to four years after mTBI. Episodic memory deficits are characterized by slower learning rates, slowed cognitive processing, accelerated forgetting, impaired concentration, inconsistent and disorganized learning, diminished capacity for active or visual information encoding, and difficulty with multitasking (divided attention). Notably, phasic alertness (defined as short-term readiness to respond) remains intact; however, memory, and attention span are often impaired. Additionally, mTBI can impact prospective memory, which is essential for an individual's ability to plan and execute future actions. It encompasses the ability to recall tasks or events that must be completed. Individuals with mTBI may encounter challenges in retrieving autobiographical memories, spatio-temporal information, and both fundamental and cultural knowledge, which may correspond to changes in executive function performance [7].

Acetylcholine is essential for the regulation of cognitive functions, such as learning, memory, and attentional processes. Cholinergic signals directed to the medial prefrontal cortex facilitate the modulation of attention processes, while projections to the hippocampus play a critical role in memory consolidation. In mTBI, as in neurodegenerative diseases, cholinergic system dysregulation occurs. In the first hours after injury, there is a massive release of acetylcholine, which is subsequently followed by a persistently decreased level. Additionally, there is a loss of cholinergic nuclei in the medial septal nucleus, the nucleus of the diagonal band of Broca, and the nucleus basalis of Meynert [8].

In cases of mTBI, changes have been noted in the prefrontal and temporal regions. One study found thinning of the prefrontal cortex, a condition that contributes to the development of depression. Notably, the most common cause of mTBI was identified as BI [9]. Military personnel who experience mTBI often suffer from prolonged sympathetic activation and chronic hypoactivity of the prefrontal cortex, which in turn contributes to the development of cognitive and psycho-emotional disorders [10]. Among the leading pathways most frequently affected, 41% of patients exhibited damage to the anterior part of the corona radiata, while 30% had damage to the uncinate fasciculus. The uncinate fasciculus is part of the ventrolateral limbic pathway, which connects the amygdala to the orbitofrontal cortex via the temporal pole. The amygdala is linked to the dorsomedial thalamus, which sends signals to the prefrontal cortex, hypothalamus, and autonomic cranial nerve nuclei, establishing a connection with the autonomic nervous system. The uncinate fasciculus and the anterior limb of the internal capsule play a role in emotional behavior [6]. One study found working memory impairment in patients following mTBI and repeated blast injuries. This cognitive function is associated with the prefrontal and parietal cortices, which in affected individuals show increased activity during the task performance compared to non-injured individuals. The mechanism underlying memory impairments in mTBI involves the formation of pathological connections between these brain regions, as well as hypometabolism of the right parietal lobe [11,12].

In addition, common cognitive impairments following mTBI include attention deficits, reduced information processing speed, impaired fine motor speed, and executive dysfunction [13,14]. One study found that patients with mTBI and BI, based on fractional anisotropy data, exhibited white matter integrity disruptions, which correlated with poorer cognitive performance, particularly in planning, organization, and problem-solving. These functions typically recovered within 90 days, although in some cases, impairments persisted for a longer period [15]. The presence of BI in patients with mTBI was associated with slower information processing speed compared to non-blast-related mTBI [16]. One study noted that increased uptake of fluorodeoxyglucose in the left pallidum could serve as a non-invasive biomarker for identifying BI and associated executive dysfunctions. Studies indicate that cognitive functions did not significantly differ between groups that were exposed to explosions at close range (less than 30 feet) compared to those at greater distances [17,18]. However, several other studies have found that the intensity of the blast wave can significantly exacerbate the negative effects of mTBI, impacting key cognitive functions such as memory, reaction time, executive functions, selective attention, information processing speed, and sleep. Sub-threshold blast exposure (explosions that do not produce clinical mTBI symptoms) can also affect the brain and behavior, although the consequences are less pronounced than those observed in clinical mTBI cases. Specifically, veterans exposed to blasts within 10 meters have exhibited impairments in immediate and delayed recall. Furthermore, the impact of mTBI on performance increases linearly with the intensity of the blast. Significant cognitive impairments following mTBI typically resolve within 3 to 12 months. However, in some cases, persistent attentional dysautonomia deficits and slowed information processing speed may continue for decades after the initial injury [17,19,20]. Explosions occurring within 10 meters have been associated with increased inflammatory responses in the brain, which correlate with neuropsychological impairments. Several key biomarkers have been identified across different pathological processes, including inflammation markers such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and eotaxin-1, as well as a reduction in anti-inflammatory markers; neuronal degeneration markers: amyloid-beta 40/42, neuron-specific enolase, tau protein; axonal injury markers: light neurofilaments; neuroregeneration markers: brain-derived neurotrophic factor (BDNF) [21,22].

Improvement in basic cognitive functions, such as immediate attention and orientation, typically precedes the enhancement of more complex cognitive skills, such as problem-solving and executive functions, following mTBI, regardless of the mechanism of injury. Additionally, comorbid conditions such as depression and dysautonomia can contribute to mental fatigue, negatively affecting test performance. The risk of long-term cognitive impairments is higher in older adults and patients with recurrent mTBI, compared to other population groups. At the same time, level of education is considered the strongest predictor of cognitive function outcomes [7]. National researchers, such as Kurako Y.L., have studied memory function following mTBI and identified short-term memory impairments, particularly in patients aged 50–60 years. These deficits primarily impact the ability to memorize and recall information, with gradual improvement observed by the tenth day, although the recovery of recall processes tends to lag behind memorization [23].

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Assessment of cognitive function in both military personnel and civilians is a widely used method for evaluating the condition following mTBI globally. Cognitive impairment tests are typically classified based on the specific cognitive subdomain they aim to assess [7,24]. Attention is a multidimensional concept, and while phasic alertness (the ability to respond quickly to stimuli) is largely preserved after mTBI, deficits in sustained attention (the ability to maintain prolonged focus) remain a topic of discussion. To evaluate attention, several standardized tests are commonly used: Conners Continuous Performance Test—3rd Edition (Conners CPT 3), which measures sustained attention and response inhibition; the Psychomotor Vigilance Test (PVT) assesses sustained attention; the Digit Span test evaluates auditory attention and working memory; the Test of Variables of Attention (TOVA) analyzes selective attention and reaction time variability; the Stroop Test examines cognitive flexibility; the Letter-Number Sequencing test assesses short-term memory and the ability to repeat information; and Cancellation tests are used to detect attention deficits associated with right hemisphere lesions [7].

Patients with mTBI often experience difficulties in recalling autobiographical episodes and spatiotemporal details, which correlate with executive function test performance. Several tests are commonly used to assess executive functions, including the Wisconsin Card Sorting Test (WCST), which evaluates cognitive flexibility and the ability to switch between tasks; Tower of London Test (TOL), which assesses planning and problem-solving skills; Trail Making Test (TMT), designed to measure cognitive flexibility and information processing speed; Stroop Color and Word Test, which examines cognitive inhibition by requiring participants to name the color of printed words rather than reading the words themselves; Delis-Kaplan Executive Functions System, which provides a comprehensive evaluation of both verbal and non-verbal aspects of executive functions [7].

Halalmeh identified the primary tests for memory assessment, including the Rey Auditory Verbal Learning Test (RAVLT), Hopkins Verbal Learning Test (HVLT), and California Verbal Learning Test (CVLT), which are used to evaluate verbal learning, specifically the ability to memorize and recall word lists; Wechsler Memory Scale (WMS) provides a comprehensive assessment of visual, verbal, and working memory; Brief Visuospatial Memory Test-Revised (BVMT-R) is designed to analyze visual learning and memory, while the Rey-Osterrieth Complex Figure Test (ROCF) assesses visual memory and visuospatial abilities through tasks requiring the reproduction of a complex figure [7].

To assess visuospatial functions, several tests are commonly used, including the Block Design Test, which evaluates a patient's ability to construct figures using cubes; the Facial Recognition Test, designed to analyze the ability to recognize faces and emotions; Visual Form Discrimination Test, which measures the ability to distinguish shapes among similar ones; Benton Visual Retention Test, which assesses visual memory through image reproduction; Rey-Osterrieth Complex Figure Test (ROCF), which analyzes organizational abilities and the ability to reproduce complex figures; Judgment of Line Orientation Test (JLO), aimed at assessing spatial orientation of lines; Visual Object and Space Perception Battery (VOSP), which evaluates the ability to perceive and process spatial information about objects. For the assessment of language functions, the following tests are commonly used: the Boston Naming Test (BNT), which evaluates expressive language and object-naming ability; the Controlled Oral Word Association Test (COWAT), which measures verbal fluency; the Retain-Indiana Aphasia Screening Test, aimed at detecting language deficits such as difficulties in reading, writing, and oral speech; the Word Fluency Test, which analyzes verbal agility through tasks requiring naming words from specific categories; the Multilingual Aphasia Examination, which determines the degree and type of aphasia; the Token Test, which assesses language comprehension and semantic memory; and the Peabody Picture Vocabulary Test (PPVT), which evaluates receptive vocabulary by matching images to spoken words [7].

One of the most commonly used tests in neuropsychological assessment is the Mini-Mental State Examination (MMSE), which evaluates general cognitive functions by assessing orientation, attention, memory, language, and visuospatial abilities. The Wechsler Adult Intelligence Scale (WAIS) is often used to measure the speed of processing new information and is frequently employed to track cognitive functions over time [7,24].

Despite the extensive research on cognitive functions, several programs now allow for screening assessments of cognitive impairments across multiple domains simultaneously. For example, Automated Neuropsychological Assessment Metrics version 4 (ANAM4) is used to assess attention, processing speed and reaction time; BrainCheck is a mobile application that evaluates attention and executive functions through interactive games; Central Nervous System (CNS) Vital is a test designed to measure cognitive flexibility; Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) serves as a screening tool for post-mTBI assessment [7,25].

The Quick ImPACT (QT) test is a shorter version of the ImPACT neurocognitive test, conducted via an iPad app and taking approximately 5–7 minutes to complete. The advantages of this test include its speed, accessibility, and the ability to assess neurocognitive functions without the need for bulky technical equipment. The test battery includes subtests such as Symbol Match, Three Letters, and Attention Tracker, with results presented in percentile ranks adjusted for age and gender. The final score provides percentages for motor speed, attention tracker, and memory. This battery of tests is specifically designed for the assessment of mTBI [26,27].

The gamified rehabilitation platform FitMi Home Therapy Program combines physical and cognitive therapy and serves as a rehabilitation program aimed at improving motor and cognitive outcomes in patients with mTBI. Tasks related to verbal fluency, which involve generating new information, indicate that patients with mTBI typically demonstrate reduced productivity, producing fewer items per minute and showing a tendency toward repetitive and stereotypical responses, reflecting limitations in cognitive flexibility. Furthermore, test results highlight impairments in various aspects of social cognition, such as emotion perception and empathy [7].

Instrumental diagnostic methods are widely used to study cognitive functions after mTBI. Functional magnetic resonance imaging (fMRI) helps detect reduced activity of the prefrontal cortex during cognitive tasks and planning processes [7]. For example, one study found that men and women with post-traumatic stress disorder (PTSD) exhibited increased bilateral amygdala activation in response to images of fearful facial expressions [28]. Diffusion tensor imaging (DTI) and tractography have revealed weakened neural connections between the prefrontal cortex and other brain regions in individuals with mTBI [7]. However, in Ukraine, there is limited data on the use of such tests in military personnel.

Conclusion

In the current wartime conditions, a significant number of military personnel and civilians are experiencing mTBI. However, cognitive function assessment is often overlooked due to time limitations, the large number of affected individuals, and limited experience. This issue leads to a significant reduction in the effectiveness of the rehabilitation process, which in turn negatively impacts the quality of life, social adaptation, and recovery rate. The utilization of modern tools, including neuropsychological tests and assessment programs, can provide more accurate diagnostics and patient monitoring, facilitating the development of personalized rehabilitation programs. Future research should focus on the development and adaptation of cognitive testing scales and programs to better address the specific needs of patients in Ukraine.

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Conflict of interests

None declared.

Consent to publication

Our review article did not involve the use of personal patient data; therefore, obtaining consent for publication was not required.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F– Final approval of article.

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Особливості когнітивних порушень при різних механізмах легкої закритої черепно-мозкової травми: огляд літератури

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Анотація: *в умовах війни значна кількість військовослужбовців та цивільних осіб зазнають легкої закритої черепно-мозкової травми, що негативно впливає на якість життя, соціальну адаптацію та швидкість відновлення. Функціональні обмеження, спричинені легкою закритою черепно-мозковою травмою, впливають на когнітивну, рухову, комунікаційну та соціальну сфери. Метою даного огляду є дослідження впливу легкої закритої черепно-мозкової травми на розвиток когнітивних порушень шляхом проведення бібліосистематичного огляду наукової літератури в базах даних PubMed, Scopus та Web of Science щодо впливу легкої закритої черепно-мозкової травми на розвиток когнітивних порушень. У статті проаналізовано різні механізми виникнення легкої закритої черепно-мозкової травми та їхній вплив на когнітивні функції.*

Охарактеризовано види когнітивних та поведінкових порушень, що виникають внаслідок легкої закритої черепно-мозкової травми, зокрема зниження уваги, порушення пам'яті, виконавчих функцій та швидкості розумових процесів. Особливу увагу приділено ролі мінно-вибухової травми, яка підсилює наслідки легкої закритої черепно-мозкової травми шляхом первинного впливу вибухової хвилі. Під час аналізу літературних джерел встановлено, що патофізіологічні механізми включають метаболічний каскад, структурні пошкодження мозку та дисбаланс нейротрансмітерів. Спостерігається зниження активності префронтальної кори, порушення зв'язків між нею та іншими ділянками мозку. Визначено, що пацієнти із легкою закритою черепно-мозковою травмою мають різну динаміку відновлення, яка залежить від супутніх факторів, таких як вік, повторні травми та психологічний стан. Супутні стани, такі як депресія, порушення сну та хронічний біль, можуть погіршувати результати відновлення, а рівень освіти є важливим предиктором когнітивного відновлення. Ефективність діагностики та реабілітації під час війни залежить від застосування комплексного підходу, який включає використання скринінгових тестів, нейровізуалізаційних методів та реабілітаційних програм. В статті детально розглянуті тести на пам'ять, увагу та виконавчі функції, зокрема Psychomotor Vigilance Test, Rey Auditory Verbal Learning Test та Stroop Test, а також сучасні гейміфіковані реабілітаційні програми, такі як FitMi Home Therapy Program та ImPACT, які поєднують фізичні та когнітивні вправи. Подальші дослідження мають бути спрямовані на розробку та вдосконалення моніторингу стану пацієнтів після легкої закритої черепно-мозкової травми, адаптацію шкал, програм когнітивного тестування для України з метою покращення якості життя військовослужбовців, поліпшення їх соціальної адаптації та прискорення відновлення після травми.

Ключові слова: когнітивні порушення, легка закрита черепно-мозкова травма, військовослужбовці, нейрореабілітація, мінно-вибухова травма