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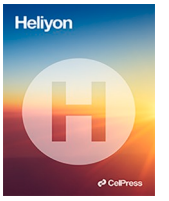

Review article

Psychiatric disorders in post-traumatic brain injury patients: A scoping review

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ABSTRACT

Background: Traumatic Brain Injury (TBI) is an important antecedent in the evaluation of patients with psychiatric disorders. The association between TBI and the subsequent appearance of psychiatric disorders has been documented, however, the findings found in the literature are diverse and controversial.
Objective: To identify the most prevalent psychiatric disorders after head trauma.
Design: An exploratory review (SCOPING) was carried out using the PRISMA extension protocol. Articles published between the years 2010–2022 were used to identify and describe the most prevalent psychiatric disorders after a TBI. Psychiatric disorders were classified according to clinical characteristics in neurotic syndromes, psychotic syndromes, cognitive disorders, among others.
Results: A total of 32 articles were included. In the framework of neurotic syndromes, depression is the most prevalent psychiatric alteration after a TBI, becoming a sequel that shows a higher incidence in the first year after the traumatic event. The findings found in relation to post-traumatic stress disorder are controversial, showing great variability regarding the degree of severity of the injury. The prevalence of psychotic syndromes is relatively low because it is difficult to determine if the psychosis is a direct consequence of a TBI. In the cognitive sphere, it was found that people with TBI presented alterations in cognitive functions.
Conclusions: The findings found in the review respond to the hypothesis initially raised, which assumes that head trauma is an important etiological factor in the appearance of psychiatric disorders.

1. Introduction

The present work exposes two clinical events: traumatic brain injury (TBI) and psychiatric disorders. The development of the latter can also be explained by the presentation of the former. This work presents the association between these two health alterations.

The traumatic brain injury model system defines TBI as an injury to the central nervous system caused by an external mechanical

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force that generates loss of consciousness, a period of post-traumatic amnesia or the presence of neurological findings attributable to cranioencephalic trauma (CeT) during physical or mental examination.

Depending on the mechanism of injury, TBI is classified as a closed (non-penetrating) or open (penetrating) injury. Penetrating head trauma is an injury caused by a foreign body or bone fragment penetrating brain tissue. In contrast, in closed traumatic injury, the brain structures remain intact. Likewise, penetrating trauma is less common than closed head trauma, however, it has a worse prognosis and constitutes the most serious traumatic brain injury [1]. In contrast, mild brain injuries are usually the result of closed brain injuries [2].

On the other hand, in the words of the WHO, normality is a state of complete physical, mental and social well-being. Thus, mental well-being implies the absence of a mental disorder. According to the fourth edition of the diagnostic and statistical manual of mental disorders (DSM-5): "a mental disorder is a behavioral or psychological syndrome or pattern associated with distress or a significantly increased risk of suffering, death, pain or disability, or a significant loss of freedom" [3].

In Colombia, Law 1616 of 2003 defines mental health as a "dynamic state that is expressed through the behavior and interaction of subjects, allowing them to deploy their emotional, cognitive and mental resources to move through daily life, work, establish relationships and contribute to the community" [4].

This research, motivated by the interest of knowing the association between cranioencephalic trauma and psychiatric disorders, which allowed us to identify the prevalence of psychiatric disorders. Health professionals recognize the importance of the anamnesis as a source of information on essential personal and traumatic history in the context of the assessment of patients with psychiatric disorders.

TBI is likely to be linked to the start of psychiatric disorder, which could become a serious public health issue in the future. The etiology of TBI varies by demographic location and age of manifestation in each studied sample. The most common causes are car accidents and falls. Most of the articles evaluated agree that traffic accidents are the leading cause of TBI in young individuals in low- and middle-income countries, while falls constitute the leading cause in older adults. It is believed that 60% of automobile accidents in Cali result in severe brain injuries [5].

Considering a society with high rates of poverty and violence such as Colombia, one must be alert to the increase in violent acts, difficulties in adequate health care and diversity of mental problems. In this sense, it is important to generate actions to reduce mental morbidity and mortality, to prevent subsequent traumatic events from developing greater social problems.

It is known that most people recover from mild traumatic brain injury, however, a percentage of individuals experience cognitive, physical, and psychological symptoms beyond the recovery period. Therefore, it is important to recognize the relationship between TBI and the appearance of post-TBI psychiatric disorders. Also, it is convenient to know data such as the age of the subjects, considering that progress after a head injury depends, in part, on the brain's ability to recover based on neuroplasticity processes.

A scoping review was conducted to identify and describe the most prevalent psychiatric disorders that occur after traumatic brain injury. Thus, a bibliographic review was carried out aimed at defining concepts or variables relevant to the topic of interest, to analyze the positions found and expand existing knowledge on the subject. This is expected to contribute to a better understanding and further emphasis on research involving the study of TBI and psychiatric disorders.

This review allowed us to establish a close relationship between psychiatric disorders and TBI. As will be shown later, various studies report that depressive syndrome is one of the most prevalent post-TBI psychiatric disorders, while cases of anxiety disorders increase after TBI. Furthermore, the articles reviewed showed a degree of controversy between PTSD and the degree of traumatic brain injury. Likewise, a series of difficulties will be evidenced to determine if a psychotic condition could be assumed as a direct consequence of the TBI.

In this sense, if there is a causal relationship between the appearance of a psychiatric disorder after a traumatic brain injury, the following questions could be raised: What are the most prevalent post-TBI psychiatric disorders? Can a cranial trauma cause psychiatric syndromes? Can a cranial trauma cause neurotic, psychotic and cognitive disorders? What position do the various studies suggest regarding post-TBI psychiatric disorders? What are the factors that contribute to the appearance of post-TBI psychiatric disorders? Can previous psychiatric alterations increase exposure to a traumatic brain injury? Is the severity of the traumatic brain injury related to the appearance of a psychiatric disorder? What is the time of onset of the psychiatric alteration after a head trauma?

This review aimed to systematically map the research carried out in this area, compare the findings found in each literature review, identify each of the psychiatric disorders resulting from head trauma, as well as provide a contribution to the knowledge about the occurrence of psychiatric disorders post-TBI.

2. Theoretical framework

2.1. Neurotic syndromes

Neurosis is understood as a disorder in which the analysis of reality and the organization of the personality remain intact, while the subject presents problems derived from the presence of various disturbing symptoms [6].

2.1.1. -Depressive disorder

According to the DSM 5, major depression is characterized by: Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is 1- depressed mood or 2- loss of interest or pleasure. 3- Clinically significant weight loss or gain; 4- Insomnia or hypersomnia; 5- Psychomotor agitation or retardation; 6- Fatigue or loss of energy; 7- Feelings of worthlessness or excessive or inappropriate guilt; 8- Decreased ability to think or

concentrate, or to make decisions; 9- Recurrent thoughts of death or suicidal ideation [7].

The etiology is multifactorial, it is believed that it arises from the interaction of genetic factors, adverse events in childhood, environmental factors, underlying diseases and stressors associated with daily life [8].

2.1.2. -Anxious syndrome

Anxiety is defined as a subjective sensation of fear that can present signs such as tension, tachycardia and dyspnea, as a defensive manifestation associated with fight or flight responses. This may be related to cognitive impairment because of the psychological trauma of the injury or be associated with disorders such as depression [9].

Anxiety syndrome includes post-traumatic stress disorder (PTSD), phobic disorders, obsessive-compulsive disorder (OCD) and generalized anxiety disorder (GAD) [10].

2.1.3. -Post-traumatic stress disorder (PTSD)

PTSD develops through nonconscious encoding of affective and sensory experiences associated with the traumatic event, conscious encoding of some aspects of the event, and of memories of the circumstances surrounding the trauma. It manifests as an initially adaptive "flight or fight" survival response that is later assumed to be maladaptive when sustained after the threat is removed [11].

Clinically, it manifests with dysphoria, nightmares, intrusive thoughts, behavioral avoidance of trauma reminders, anhedonia, sleep disturbances, hypervigilance (associated with concern for one's own physical integrity), or decreased concentration [11].

2.2. Psychotic syndromes

Psychosis is defined as the alteration of reality, where subjects do not accurately evaluate their perceptions and thoughts, establishing incorrect deductions about external reality. It is characterized by a deterioration of social functionality and the inability to perform normal domestic and work functions [6].

Psychotic Disorder Due to TBI is the current DSM-5 diagnosis given to those who develop a psychosis after a traumatic brain injury. Diagnostic criteria include: 1) presence of hallucinations or delusions; 2) evidence that psychosis is a direct physiological consequence of TBI; 3) the psychosis is not better explained by another mental disorder; and 4) psychosis does not occur exclusively during a delusional state [3].

2.3. Cognitive disorders

Cognitive reserve decreases throughout life through the normal aging process or accumulated insults from disease or external stressors such as trauma [12]. Three types of cognitive disorders are described: dementia, delirium, and amnestic disorders, which are characterized by cognition disturbances involving impairments in memory, language, orientation, judgment, interpersonal relationships, praxis, and problem solving triggered by a biological compromise that it is accompanied by behavioral disorganization [6].

2.3.1. -Alterations in sleep pattern

Sleep disturbances are classified as insomnia, hypersomnia, and excessive daytime sleepiness. These alterations are clinically relevant because they compromise the patient's recovery and generate a negative impact at a physical, cognitive and behavioral level [13].

On the one hand, fatigue is defined as the "unconscious decrease in the ability to perform a physical or mental activity as a result of an imbalance in the availability, use or recovery of the physiological or psychological resources necessary to carry out said activity" [14].

Two types of fatigue are defined: psychological fatigue, characterized as "a state of caution related to demotivation, prolonged mental fatigue or boredom" associated with stress, anxiety and depression. Physical fatigue described as "the result of excessive energy consumption, a decrease in certain hormones or neurotransmitters, or a decreased ability of muscle cells to contract" [14].

In relation to fatigue, this should be understood as a subjective motivational state that arises because of the integration of a wide variety of indicators related to physical effort. It allows to regulate the level of effort and protect the organism [15].

Various scales have been developed which allow evaluating the perception of fatigue, among them, the most used are:

- RPE (Rating of Perceived Effort): It allows subjectively estimating the intensity of the physical effort perceived by the practitioner when performing a physical activity [15].
- VAS fatigue (Visual Analogue Scale-fatigue): The subject indicates his perception of his level of fatigue, marking the point on the scale that he believes represents the state of fatigue at that moment. It consists of a scale of ten degrees. The number 0 represents the minimum personal perception of fatigue (no fatigue), and the number 10 represents the maximum feeling of fatigue (maximum fatigue) [15].
- SEES scale (Subjective Exercise Experiences Scale): It shows a multidimensional evaluation represented in 12 items (Very well, fatal, exhausted, lively, dejected, strong, discouraged, very tired, formidable, disgusted, and tired) that reflect the variations in three dimensions: psychological well-being, negative stress or psycho-distress and the feeling of fatigue. It is given a rating from 1 (not at all) to 7 (completely). Higher scores correspond to higher degrees of perception of the dimension evaluated [15].

- POMS (Profile of Mood State): It is used to assess mood. It is assessed using a scale that contains 58 items represented in 6 dimensions of mood: tension, depression, anger, vigor, fatigue, confusion. A rating of 0 (meaning nothing) to 4 (meaning a lot) is given. Lower values imply a better general state of mind [15].

Next, the methodology that guided this review is described, for the sake of the search for rigor on said procedure.

3. Methodology

3.1. Study design

As already mentioned, this research is categorized as a SCOPING-type review, which consists of a systematic review that allows the compilation and subsequent synthesis of the scientific evidence documented in various articles and publications that respond to a specific health topic [16].

The approach was based on the phased methodological framework proposed by Arksey and O'Malley: 1) Elaboration of the question: What are the most prevalent psychiatric disorders after cranioencephalic trauma? 2) Establishment of inclusion and exclusion criteria and systematic search, 3) Review and selection of studies, 4) Data extraction, 5) Analysis and reporting of results.

3.2. Study protocol

A protocol based on the PRISMA extension was developed for scope reviews that allowed directing the order for the literature search to select, classify and synthesize the advances and knowledge existing to date.

3.3. Eligibility criteria

The selection criteria of the bibliographic search were:

- Articles published between the years 2010–2022.
- Literature in Spanish and English.
- Articles that respond to the theme of this review: Post-cranioencephalic trauma psychiatric disorders.
- Reports published in any demographic area.

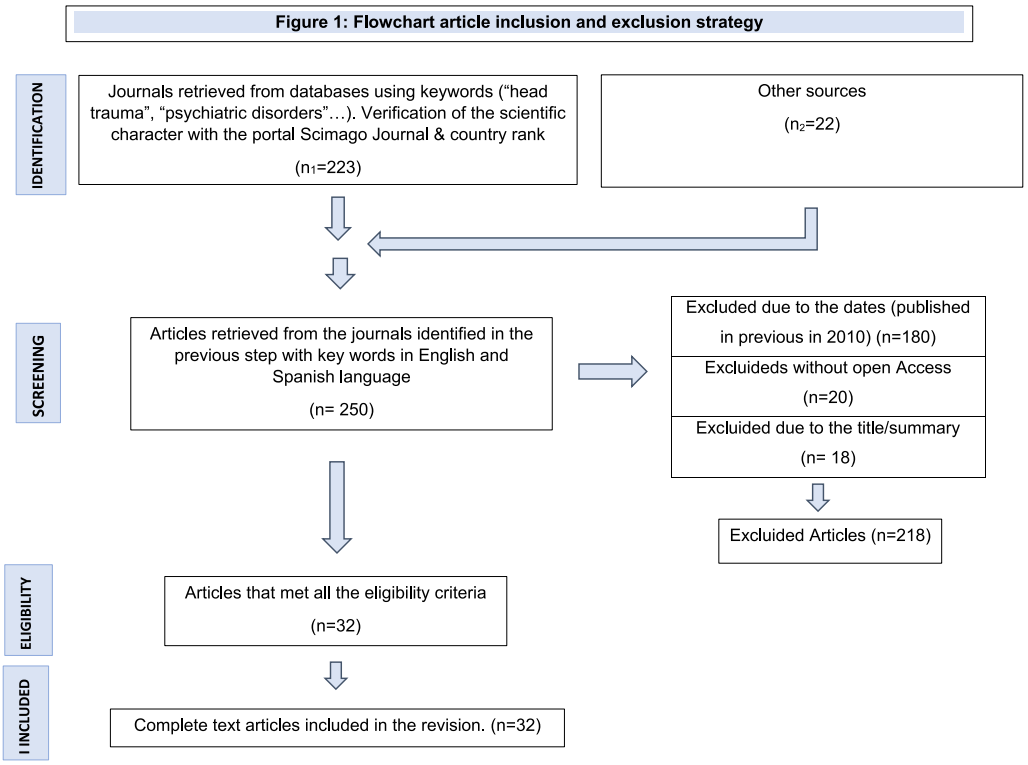

Fig. 1. Flowchart article inclusion and exclusion strategy.

- Clinical case reports.
- Open access

The exclusion criteria used during the review were:

- Articles with a publication prior to the year 2010.
- All the literature to be reviewed should maintain a close relationship with the expressions psychiatric disorder and cranioencephalic trauma.
- Articles that did not have open access.

3.4. Information sources and literature search

The literature search process was carried out in the following databases: "PubMed", "DOAJ", "Dialnet", "Taylor&Francis", "Scopus", "Scielo", "MEDLINE", "PsycInfo" and " ScienceDirect".

A filter search was carried out based on keywords in Spanish and English, such as: ("Cerebral injury" or "Brain injury" or "Cranioencephalic trauma" or "Traumatic brain injury" or "Cranial trauma" or "Traumatic Brain Injury" or " head trauma", "Psychiatric disorders") and ("Psychiatric disorders" or "Psychiatric disorder", "Psychiatric disorders" or "Psychiatric disturbances" or "Posttraumatic stress disorder" or "Posttraumatic Stress Disorder").

3.5. Study selection process

The articles that responded to the main objective of this research and that met the previously defined eligibility criteria were reviewed and selected. The main reason for excluding articles was non-compliance with the criteria based on the date between the period 2010–2022 (see Fig. 1).

3.6. Data elements and data abstraction process

The reviewed articles were placed in a systematization grid which allowed a schematic view that facilitated their understanding and comparison. Within the grid, the following aspects were included: name of the article, year of publication, journal and corresponding quartile, keywords, objective, methodology, results, and differences and similarities found with the other articles.

The data extraction was carried out from the exhaustive analysis of each of the selected articles, verifying the answer to the questions raised. Through these rigorous procedures, it was intended to document some type of causal relationship between the appearance of a psychiatric disorder and a traumatic brain injury based on the classification of psychiatric disorders as: neurotic, psychotic and cognitive.

3.7. Risk of bias assessment

To ensure the reliability of the journals from which the reviewed articles came, the SCImago Journal & Country Rank portal was used, which contributed to the verification of their scientific nature.

3.8. Summary of results

Once the systematization grid was carried out, where the articles that met the inclusion criteria were included, the content of each of them was analyzed, and subsequently the psychiatric disorders (most prevalent post-TBI) found in the literature were described grouping them by syndromes as follows:

- Neurotic syndromes including depressive disorder, anxiety disorders, OCD (obsessive compulsive disorder) and PTSD (post traumatic stress disorder).
- Psychotic syndromes that include manic syndrome, schizophreniform syndrome and schizophrenia.
- Cognitive disorders including delirium, dementia and amnestic disorders.
- Other associated disorders such as problem behaviors: anger and aggression (sociopathy and psychopathy), sleep disturbances and addictive behaviors.

Finally, the discussion was carried out based on the findings found in the literature considering the respective limitations found, and finally conclusions and final recommendations were included.

The previously exposed methodology allowed us to describe, synthesize and expand the existing scientific evidence that relates psychiatric disorders in post-traumatic brain injury patients. In addition, new research questions emerged from this review, which may lead to new studies and contribute to the enrichment of this dimension of knowledge.

4. Results

4.1. Selection of studies and characteristics of included papers

The present scoping review included a total of 32 articles. Following the definition of the key words that framed the study's purpose, the procedure of identifying the articles was successful. 14 publications were also acquired in addition to these documents to widen the study's scope in terms of trauma types, age-related impacts, and treatment options. From the title and abstract, several articles that satisfied the inclusion requirements were chosen for screening. In the eligibility phase, papers are chosen that, after a thorough reading, satisfy the requirements and contribute to resolving the key research topics. Fig. 1 shows the flow chart used as a selection strategy for the chosen articles.

The articles selected from the retrieved journals is summarized in Table 1.

4.2. Individual results of the sources of evidence

Based on the review of the literature, this research compiles the most prevalent post-TBI psychiatric disorders in syndromes according to the simultaneity in time of signs and symptoms. The grouping into syndromes allows generating an integrative vision according to the clinical characteristics of psychiatric disorders to support their better understanding. Table 2 shows the classification of psychiatric disorders.

5. Summary of results

5.1. Neurotic syndromes

5.1.1. -Depressive syndrome

The diagnosis of post-TBI depression is complex, in part because the diagnostic tools used in the studies are diverse. In addition, there is overlap between symptoms, such as inability to perform daily activities, ability to cope with stressors, increased irritability, and behavioral problems [9].

Within the manifestations of post-TBI depression, it has been described that subjects experience fatigue, social withdrawal, difficulty concentrating, feelings of helplessness, despair, anxiety and aggressive behavior [9].

Several studies report that depressive syndrome is one of the most prevalent post-TBI psychiatric disorders. A study carried out at the Hospital Universitario del Valle in Cali, Colombia compared 30 subjects with cranial trauma vs. 30 controls, concluding that 76.7% of the patients manifested depressive symptoms at some point [5].

Another investigation carried out with 113,906 Danish subjects, found that the risk of depression increased by 59% after a head injury [18]. Similarly, in Uganda, the neuropsychological results of a traumatic brain injury were compared with non-cranial trauma, observing higher rates of depressive symptoms in the event involving a cranial trauma (43.9% vs. 7.9%) [18]. In one study, 63 patients were evaluated, of whom 18.5% manifested post-TBI depression. Also, 129 patients with mild TBI were evaluated, of which 11.6% showed major depression at 3 months [19].

In addition, various investigations found in the literature show that a large percentage of post-TBI subjects manifest depressive

Table 1
Chosen articles.

Magazine	Quartile	Articles	Country
Am. J. Psychiatry	Q1	2	Denmark- Australia
J. Neuropsychiatry Clin. Neurosci.	Q2	5	EE.UU.
Brain Inj.	Q2	3	EE.UU.
BMC Neurol.	Q2	2	Canada - Africa
J Can Acad Child Adolesc Psychiatry	Q2	1	Canada
J. Pediatr. Rehabil. Med.	Q2	1	EE.UU.
J. Athl. Train.	Q1	1	EE.UU.
Rev Colomb Psiquiatr.	Q4	1	Colombia
Rev. Asoc. Esp. Neuropsiquiatr		1	Spain
J. Head Trauma Rehabil.	Q1	2	EE.UU.
JAMA	Q1	2	EE.UU.
EBioMedicine	Q1	1	EE.UU.
Surg Clin North Am	Q1	1	EE.UU.
Lancet Neurol.	Q1	1	EE.UU.
J. Neurol.	Q1	2	EE.UU.
Nat. Rev. Neurol.	Q1	1	EE.UU.
J. Neurosurg.	Q1	1	EE.UU.
Cell Transplant.	Q2	2	EE.UU.
Neurochem Int.	Q2	1	U.K
Pediatric Critical Care Medicine	Q1	1	EE.UU.
	n	32	

Table 2
Classification of psychiatric disorders.

Neurotic syndromes	Psychotic syndromes	Cognitive disorders	Other associated disorders
Depressive disorder	Manic syndrome	Delirium	Problem behaviors: anger and aggression (sociopathy and psychopathy)
Anxiety disorder	Schizophreniform syndrome	Dementia	Sleep disturbances
OCD (obsessive compulsive disorders)	Schizophrenia	Amnestic disorders	Addictive behaviors
PTSD (post-traumatic stress disorder)			

symptoms at any time in their lives and most meet the DSM-5 criteria for major depressive disorder.

For example, in the United States, a study was carried out with 559 adults diagnosed with TBI, a follow-up was carried out for one year in which 53% of the patients met the criteria for major depressive disorder. Of the percentage described, it was reported that the strongest predictor for the diagnosis of post-TBI major depressive disorder was in those subjects with a history of major depressive disorder at the time of the trauma. In the same study, the percentage of people with major depressive disorder after TBI (53.1%) was compared to the expected percentage of new cases in subjects without TBI (6.7%) [20].

5.1.2. -Anxious syndrome

It is currently known that after suffering a TBI the incidence of anxious symptoms increases [20]. A study conducted in Texas with pediatric patients 6 months after a TBI reviewed the prevalence of anxiety disorders in subjects diagnosed before the traumatic event vs post-TBI anxiety disorder. This study included a sample of 141 subjects aged 5–14 years. Of the total, 12 of the patients (8.5%) had an anxiety disorder prior to TBI and 24 of the subjects (17%) had an anxiety disorder post-TBI. The latter was related to younger age and other associated disorders such as depression [10].

Likewise, there was a distinction in the prevalence of the disorder according to the severity of the injury, since of the 70 patients with mild TBI, 8 (11%) were already diagnosed with anxiety disorder and 14 of the patients (20%) developed an anxiety disorder secondary to TBI. On the other hand, of the 17 patients with moderate TBI, no patient had a previous diagnosis of anxiety disorder, and 4 patients (24%) manifested post-TBI anxiety disorder. Of the 54 patients with severe TBI, 4 (7%) had an anxiety disorder already defined and 6 subjects (11%) were attributed anxiety disorder after the traumatic event [10].

5.1.3. -Obsessive compulsive disorder (OCD)

The incidence of post-TBI OCD is poorly documented, and in the studies carried out the incidence is minimal. One study shown that OCD affects less than 10% of the population after a TBI [9]. In another investigation carried out with a pediatric population, it was found that within the anxiety syndromes of recent post-TBI, no child turned out to present OCD [10]. Another study reported high rates of anxiety disorders, with obsessive-compulsive disorder having a prevalence of 15% [12].

5.1.4. -Post-traumatic stress disorder (PTSD)

The reviewed articles present controversy regarding the degree of traumatic brain injury and the appearance of PTSD. Some studies suggest that various events such as severe brain injury, altered consciousness and impaired memory after a TBI could act as protective factors for PTSD [21]. Likewise, another study links the development of PTSD with a shorter period of post-traumatic amnesia with respect to the event [11].

In contrast, another study suggests that in the case of mild TBI and the absence of prolonged loss of consciousness, alterations in mental status may negatively affect the encoding of trauma memory, generating difficulties in controlled memory retrieval [11].

Among the various investigations reporting PTSD after a TBI, one study evaluated 95 children, of which 13% developed PTSD one year after the injury, of which 71% experienced intrusive memories of the event [22]. Another study carried out in Uganda with 171 subjects who suffered TBI showed that 43.9% presented PTSD [18]. An investigation carried out with 441 subjects reported a prevalence of 14.1% during a maximum period of 7.5 years for the development of PTSD [19].

In a study investigating various anxiety disorders after TBI, it was reported that 19% of individuals developed PTSD [9]. Likewise, another investigation concluded that 8–12% of post-TBI subjects may develop PTSD. In most cases (74%) PTSD persists for more than 6 months and compared to men, women suffer from PTSD symptoms for a longer time [23]. In other research, these figures are controversial, showing that PTSD is not a prevalent post-TBI disorder [21].

In war zones, events that increase the risk of traumatic brain injury, such as combat and explosions, are also associated with extreme psychological stress. Many veterans with a history of TBI also experience PTSD and mood and anxiety disorders, while making timely recovery difficult [24].

Additionally, PTSD can complicate recovery from TBI, as manifestations extend beyond the acute period following trauma exposure leading to significant distress or functional impairment [11]. However, evidence shows that cognitive behavioral therapy can reduce symptoms of acute post-traumatic stress in patients with a history of TBI [24].

5.2. Psychotic syndromes

The association between brain trauma and psychosis is not unequivocal, since the TBI could behave as a triggering factor in subjects with genetic predisposition, or on the contrary, the TBI could be the direct or primary cause in the absence of a family history. In addition, the association between TBI and psychosis could be inverse, the latter being really a risk factor for the former [25].

Several studies have related a higher prevalence in the development of psychotic disorders in patients with a history of TBI, a condition that increases if there are other associated factors such as genetic predisposition, family psychiatric history and older age [26].

Concerning genetic alterations, some studies suggest that previous neurological and psychiatric conditions, especially those with congenital or childhood onset, may be predisposing factors for the development of post-TBI psychotic disorder. This suggests some premorbid predisposition or vulnerability involving a genetic component linked to schizophrenia or other neurological or psychiatric conditions [27].

Regarding the time of onset, some studies suggest that it can occur in the first year, or even after 5 years or 10 years post-TBI. In a study conducted with 64 cases of post-TBI psychosis, 38% of the sample reported psychotic symptoms during the first year and 36% 4 years later [26].

Psychiatric manifestations in patients with psychosis, one study reported that the most common symptoms are persecutory delusions (22%–80%), and auditory hallucinations (47%–84%), while negative symptoms are much less prominent. (15%–22%) [26].

The affected brain areas, Frontal (42%) and temporal (27%) abnormalities correspond to the most common finding in relation to psychotic disorder due to traumatic brain injury compared to enlarged ventricles in people with schizophrenia (22%–35%) [28].

In a study reviewing 24 cases with CT/MRI data, 79% reported positive results. The hemispheric location was distributed as follows: 47% of cases showed lesion in the left hemisphere; 47%, bilateral lesions; and 5%, lesions of the right hemisphere [28].

In most cases, frontal lobe lesions (74%) are described, followed by temporal lobe involvement (47%), subcortical lesions (32%), enlarged ventricles (21%), parietal lobe lesions (16%) and occipital and brainstem lesions (5%) [28].

5.2.1. -Manic syndrome

The incidence of manic disorder is poorly documented, since the diagnosis of causality against TBI is confusing, in addition, it is assumed that the longer the period elapsed for the diagnosis of post-TBI mania, the more questionable its causal relationship may be.

5.2.2. -Schizophrenia

Schizophrenia has been linked to more widespread brain abnormalities than psychotic disorders caused by a TBI, as well as a higher likelihood of negative symptoms and more severe cognitive impairment. Furthermore, both negative symptoms and cognitive functioning for schizophrenia have been proven to be substantially linked with illness severity and long-term prognosis [26].

A study carried out with 64 cases (56 men and 8 women), reported a mean age for suffering a TBI of 23.7, and its association with the appearance of psychosis was 27.3. Among the psychotic disorders that occurred, 35% of the sample manifested psychotic disorder due to traumatic brain injury, 29% schizophrenia, 18% organic mental disorder with psychosis, 12% psychotic disorder NOS, and 6% major depression with psychosis [26].

In the presenting course of psychosis, positive symptoms such as delusions and hallucinations are a common manifestation, in the same study described above. 92% of the patients manifested delusions, with persecutory delusions being the most prevalent (77% of the subjects), 87% of the subjects developed hallucinations, with auditory hallucinations being the most prevalent (93% of the total). In relation to negative symptoms, only 37% of the patients presented them [26].

5.3. Cognitive disorders

Studies in this regard turn out to be few and confusing, so it has not been proven whether people who suffer a TBI in youth have a higher risk of developing dementia [12].

The chance of developing an organic mental disorder after a mild TBI is four times that of a severe head injury [17]. A study that examined neuropsychological outcomes after TBI discovered that patients could have a higher rate of neurocognitive impairment than the control group (28.4% vs. 6.6%), and concluded that psychomotor speed, attention, visual attention, and working memory obtained the highest rates compared to people without a TBI, with visual attention obtaining the highest rate (16% vs. 2.2%) [18].

Similarly, it is stated that the speed of information processing is considered as a component of care processes and is significantly affected after a TBI [29]. Different studies have found that aspects such as selective attention, sustained attention and focused attention can be altered in people with TBI [5].

On the other hand, memory is also one of the psychological functions most sensitive to brain damage, becoming the most reported subjective complaint by TBI patients and their families. The alteration of declarative memory (episodic and semantic) is the most frequent [5].

5.4. Other associated disorders

5.4.1. -Aggressive behaviors

Aggressive behaviors are a common sequela of TBI. Prevalence rates of 25%–88% have been reported, with rates higher for those with severe TBI. Likewise, problematic behaviors have a high frequency (25–50%), these include: non-compliance with treatment,

anger, agitation, verbal or physical aggressiveness and depression [9].

Changes in social behavior, various studies relate the degree of TBI injury with social behavior and the recognition of emotions or empathy. It is estimated that 39% of people with TBI of moderate to severe intensity had deficiencies in the recognition of emotions and impaired empathy. In contrast, other studies did not estimate a relationship [30].

Different authors have proposed that disinhibition and depression can produce aggressive behavior in some people with brain injuries [9]. Anger and hostility are also associated with depression and anxiety [8]. Similarly, another study found that depression and younger age are predictors of aggressiveness at 6, 24, and 60 months after TBI [9].

5.4.2. -Alterations in sleep pattern

Alterations in sleep pattern have been documented at all levels of severity after TBI [14]. In various studies, lack of sleep is a common symptom associated with TBI [31].

Many of the patients who have suffered a TBI describe fatigue as one of the most prevalent alterations. As an isolated symptom, fatigue can be difficult to find, because on several occasions through the completion of psychological surveys (Beck Depression Inventory) it is associated with other disorders such as depressive symptomatology [14].

It is important to recognize that the pharmacological treatments (sedatives, analgesics, narcotics, and anticonvulsants) that patients undergo after TBI, and the subsequent withdrawal from these drugs, can influence the characteristics of the sleep pattern. Pain also behaves as an important factor that contributes to sleep disturbances after TBI [13].

Concerning TBI and cognitive processes such as memory, it has been found that higher scores on the Glasgow Coma Scale are associated with better performance in immediate memory, but with a higher prevalence of sleep disorders. Thus, those subjects with mild injuries are more aware of the changes in their sleep pattern [14].

5.4.3. -Addictive behaviors

The WHO indicates that 48% of the world population over 15 years of age consumes alcoholic beverages and of the entire global burden of harm attributed to alcohol consumption in developing regions worldwide, the highest has been described in America Latin America and the Caribbean [32].

Addictive behaviors are a serious problem before and after the traumatic event. Between 30 and 60% of people who suffer a TBI present dependency problems, presenting relapses after the injury, which are also associated with depressive symptoms. In addition, consumption after injury negatively affects recovery [9].

Among the most prevalent psychiatric disorders associated with alcohol consumption are mood disorders and anxiety disorders. A study suggests that the concurrence of alcohol use disorders and other mental disorders is prevalent in the Colombian population, finding an association between major depression and alcohol use disorders in men and women. Also, an association between anxiety disorders and alcohol abuse in the male population has been described [32].

In a study that evaluated the relationship between mental disorders and alcohol consumption, these were more prevalent in the addictive group, except for minor depressive disorders, post-traumatic stress disorder, nicotine dependence, and psychotic disorder, defiant negativist. In contrast, in the case of women with alcohol use disorders compared to those without the disorder, a higher prevalence was found for depressive disorders, substance abuse, separation anxiety, oppositional defiant disorder, and behavior disorders [32].

6. Discussion

The main objective of this study was to identify the most prevalent post-TBI psychiatric disorders. Thus, in this review, a total of 32 studies published between the years 2010 and 2021 were addressed.

Head trauma is defined as the presence of brain dysfunction caused by an external force that results in loss or decreased level of consciousness, anterograde or retrograde amnesia, neurological deficit, or any altered mental status at the time of trauma [33].

In particular, it is important to know the injury mechanism of a TBI, since it is directly related to the patient's prognosis. An investigation carried out at "Hospital del niño DIF Hidalgo" that sought to determine the mechanism of the trauma and compare it with the resulting injury to determine a prognosis, found that of the patients who suffered a fall (349 cases in total), 271 subjects (77.6%) presented a cerebral contusion, 39 cases (11.1%) a cerebral concussion with altered state of consciousness or convulsive crisis and injuries related to the mechanism of injury. However, 19 cases suffered linear fracture, 2 sunken fractures, 3 intraparenchymal hemorrhages, 5 subdural hematomas and 10 epidural hematomas, the latter were not related to the mechanism of trauma (fall) and the injury found, therefore it is important to determine if there is another type of injury in imaging studies that worsens the prognosis, increasing the cost and days of hospital stay [34].

In the context of the assessment in subjects with TBI, a neurological examination of the patient should be performed. It is recommended to use the Glasgow Coma Scale, which evaluates 3 parameters: palpebral opening, verbal response and motor response, to which a score is given according to the type of response and 3 categories are established: Mild TBI (Glasgow 13–15), Moderate TBI (Glasgow 9–12) and Severe TBI (Glasgow 3–8) which are correlated with severity. In this way, the more severe the TBI, the more days of hospital stay and with it the economic cost [35].

At the beginning of this scope review, questions were raised that were resolved throughout the development of the investigation. In this way, answering the questions "Can head trauma cause psychiatric syndromes?", "Can head trauma cause neurotic, psychotic and cognitive disorders?", "What are the factors that contribute to the appearance of post-TBI psychiatric disorder?", the information was expanded according to the different investigations regarding the molecular bases linked to TBI and psychiatric disorders. This is how

several articles derived from clinical trials carried out especially with animals, highlight the importance in the accumulation of amyloid beta protein (Aβ), alterations in tau protein, TAR DNA-binding protein (TDP-43), alterations in cells endothelial cells, apolipoprotein E, beta secretase, presenilin-1 and caspase-3, in the pathophysiological process associated with TBI, as a product of a cascade of neurovascular stress events that could eventually contribute to the development of psychiatric disorders.

In addition, therapeutic alternatives related to molecular/genetic bases have been proposed in search of improvements in behavior and the regulation of social aspects in clinical trials with animals, such as cell-based regenerative therapy.

Based on the questions previously raised, the classification was made into three psychiatric syndromes that encompass the majority of post-TBI psychiatric disorders found in the literature as follows: neurotic syndromes, psychotic syndromes and cognitive syndromes, with the purpose of studying each one of the alterations based on the simultaneity of symptoms and characteristic signs, where the association between psychiatric disorder and TBI was evidenced.

The main finding in relation to the classification of neurotic syndromes that could answer the question "What are the most prevalent post-TBI psychiatric disorders?" lies in the high rates of subjects who manifest post-TBI depressive disorder. Most of the reviewed literature agrees that this is the most prevalent psychiatric sequela after experiencing a traumatic brain injury.

The findings about the anxiety syndrome turned out to be rather few. Higher rates are reported in relation to generalized anxiety disorder and it is also associated with other mood disorders such as depressive disorder. Also, there were few studies reporting post-TBI OCD, of what is documented, low rates of OCD are reported after TBI.

The findings found in relation to PTSD turned out to be of wide interest. For some studies, the greatest predictive power for developing post-TBI PTSD is based on intrusive memories of the circumstances surrounding the trauma. In this way, answering the question, Is the severity of the traumatic brain injury related to the appearance of a psychiatric disorder? There is a greater risk of developing PTSD in those with a milder TBI. On the other hand, severe brain injury may act as a protective factor for PTSD, since some research suggests that PTSD does not occur in subjects who lost consciousness during TBI, since there is no intrusive memory of the traumatic event.

In the area of psychotic syndromes, low incidence rates were found. The foregoing explains why it is complex to determine that psychosis is a direct consequence of TBI. Alluding to the question "What are the factors that contribute to the appearance of post-TBI psychiatric disorder?", several studies claim that TBI is emerging as a triggering factor for the onset of psychosis in subjects with genetic predisposition, however, other investigations refer that TBI could be the direct or primary cause in the absence of family history. Additionally, a finding of great interest is that CeT can reduce the onset of psychosis in genetically predisposed subjects, a fact that could be due to cell death and neuroendocrine changes resulting from brain trauma. These processes that can mimic or interact with the changes triggered by psychosis.

The most reported psychotic manifestations consisted of positive symptoms such as paranoid, persecutory, grandiose, somatic, mystical delusions, and auditory and visual hallucinations, while negative symptoms were found to be less frequent. On the other hand, in relation to the question "What is the time of establishment of the psychiatric alteration after a cranioencephalic trauma?" The findings found in relation to the time of establishment of psychotic syndromes after a traumatic event, are very variable within investigations. In connection with post-traumatic mania, it is worth mentioning that it is poorly documented.

Among the studies reviewed, the reported cases of post-TBI schizophrenia are scarce since it is difficult to determine if the psychosis is a direct consequence of a TBI or if it contributes to exacerbating the psychotic state. In addition, some investigations report that early manifestations of psychiatric disorders such as agitation or psychosis can increase exposure to TBI.

When comparing schizophrenia with psychotic disorder due to a TBI, more global brain abnormalities are found in the former, in addition, more negative symptoms and greater dysfunction in executive functions (EF) are reported.

In the cognitive dimension, it was found that people with CeT presented alterations in these functions. Inefficient information processing, disturbances in attention (visual, selective, sustained, and focused attention may be impaired after injury) have been reported; memory loss, being one of the most reported subjective complaints by TBI patients. In addition, EF alterations have been described together with a decrease in cognitive reserve.

The results show that there is a higher rate of neurocognitive impairment compared to subjects without a history of TBI, which increases the risk of suffering from an organic mental disorder. However, to date, the studies carried out turn out to be rather few.

The findings also suggest the appearance of psychiatric manifestations that fall within the category of disruptive, impulse control, and conduct disorders. Problem behaviors are significantly related to TBI, such as aggressive behaviors, changes in social behavior (breakdown of family relationships, decreased levels of empathy, poor occupational performance), anger, and oppositional defiant disorder.

Additionally, research documents the association between anger and hostility with major depression and anxiety, respectively, which was also associated with poor social functioning. Studies suggest that people who show aggressiveness early in post-TBI recovery are at greater risk of becoming depressed. On the contrary, other authors suggest that depression can produce aggressive behavior.

Within this review, sleep disturbances such as insomnia, hypersomnia, and excessive daytime sleepiness were also documented. In the studies consulted, many patients describe tiredness (psychological and physical tiredness) as one of the most prevalent alterations, which can be associated with other mood disorders. In addition, it should be kept in mind that the pharmacological treatment to which patients are subjected after a TBI can alter the sleep-wake cycle.

Addictive behaviors are also described, which constitute a serious problem before and after the traumatic event. Regarding a possible answer to the question "Can previous psychiatric disorders increase exposure to traumatic brain injury?", studies document an association between mood disorders (major depression and anxiety disorders) and behavioral disorders with post-TBI alcohol use disorders.

Certainly, some limitations must be considered in the search for information that may affect the systematic nature of said process. In the first place, the reviewed articles assume different diagnostic criteria for each of the psychiatric disorders and different instruments for their classification, therefore, since it is a process that starts from a bibliographic review, it is based on reliability evaluations diagnosis and possible biases underlying each of the articles.

Second, the follow-up times are different for each study, so the prevalence rates of disorders may vary depending not only on time, but also on the population that constitutes the sample.

Thirdly, it must be considered that the etiology of all psychiatric disorders has a multifactorial origin, with different triggers or attributable causes, therefore, each patient must be individualized according to their personal, family and environmental context.

Finally, it is important to highlight the degree of reliability and the strong point of this review because most of the literature reviewed from the different databases was taken from categorized journals (located between quartiles 1 and 2), which is an indicator of a higher level of quality and scientific positioning of the reviewed articles.

7. Conclusions

The literature reviewed in this paper responds to the hypothesis initially raised, which assumes that TBI behaves as an important etiological factor in the appearance of some psychiatric disorders. This premise highlights the value for the clinician of being able to assess the traumatic history as a fundamental part of taking a complete clinical history, which will represent the most important pillar in the evaluation, diagnosis and comprehensive management of the patient in a context of psychiatric care.

The review carried out fulfilled the initial purpose, which sought to identify the most prevalent post-TBI psychiatric disorders, which were grouped according to syndromes based on the clinical characteristics of each of them. Neurotic syndromes (depressive disorder, anxiety disorder, OCD, PTSD) were described, followed by psychotic syndromes (manic syndrome, schizophrenia), cognitive disorders, other associated disorders (aggressive behaviors, alterations in sleep patterns, addictive behaviors).

It is important to highlight a finding different from the one proposed, since it was found that paradoxically the previous psychiatric alteration can behave as a causal agent of TBI. This finding was incidental and represents an inverse behavior to that initially proposed, which assumes the TBI as the cause of the psychiatric alteration and not the other way around.

This work was guided by professionals in the research area, the scientific nature of the articles included in the Scimago Journal & Country Rank portal was verified, most of them categorized as Q1-Q2. However, the present study had several limitations. In the first place, articles that did not have open access were excluded, because there was no funding to access other types of scientific articles.

Second, this study considered only clinical criteria instead of imaging criteria to determine the degree of severity of TBI. It is proposed for future research to compare the psychiatric clinical characteristics linked to structural or functional damage secondary to traumatic brain injury according to the findings obtained in diagnostic images.

Third, the clinical criteria published in each reviewed article for each of the psychiatric disorders turn out to be highly variable, so they cannot be defined exactly. Lastly, it cannot be exactly established that the appearance of psychiatric alteration is secondary to TBI, due to its multifactorial origin.

Traumatic brain injury represents a public health problem worldwide, because according to the findings found in the literature, TBI behaves as a predisposing factor for the appearance of psychiatric disorders, which compromises the functionality of the individual causing clinical discomfort significant and social deterioration. Understanding all the implications of TBI helps to identify prevention strategies to avoid psychiatric disorders in the short, medium and long term.

The bibliographic review of psychiatric disorders made it possible to know the multifactorial origin of this clinical phenomenon, contributing to the understanding that TBI is not the only factor that explains the psychiatric manifestation. Indeed, all the patient's background should be evaluated as genetic, family, pathological, and social variables, among others.

It is worth mentioning that the high rates of morbidity and mortality due to TBI justify the need for multidisciplinary care that includes psychotherapeutic and psychoeducational rehabilitation programs to reduce the sequelae generated and favor the process of social reintegration.

Comprehensive management allows early identification of which patients may have a favorable neurological prognosis and reduces the likely psychiatric consequences in the future.

It is convenient to highlight the concept of mental health within this review because it is common that after a traumatic event, the emotional, psychological and social well-being of the individual is altered, affecting the establishment of relationships that promote an adequate development of the community.

Finally, this review provides evidence that a significantly higher range of psychiatric disorders occur after the individual suffers a traumatic brain injury. For this reason, it is important to generate preventive measures such as the implementation of road safety practices to avoid traffic accidents. In addition, the problems at the level of security and violent acts that each country faces must be considered, so it is necessary to implement measures that reduce these events.

Finally, it is essential to optimize health services and develop interventions that lead to confronting the magnitude and complexity of this problem.

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The authors declare no competing interests.

Annexes.

Information of interest for future research

Pathological/brain imaging interpretation

The most common findings found in computed tomography (CT) and magnetic resonance imaging (MRI) in patients with post-TBI psychotic disorder are focal lesions, at the level of the frontal (74%) and temporal (47%) lobes. In contrast, enlargement of the ventricles is the most common finding in subjects with schizophrenia [26].

In addition, the electroencephalographic (EEG) recording shows slowing of electrical activity at the level of the temporal lobe, compared to patients with schizophrenia without a history of TBI, in whom slowing of the frontal lobe region is observed more frequently [26].

From a pathological standpoint, chronic traumatic encephalopathy (CTE) is described because of CeT exposure associated with the risk of late neurodegeneration [36], which is present in subjects who have suffered multiple TBIs, as is the case with boxers and hockey players throughout their sports careers [37]. This diagnosis proposes two syndromes: a psychiatric illness that is largely behavioral and emotional, frequently accompanied by paranoia, and a cognitive impairment that is diagnosed as Alzheimer's disease [28]. Among the brain abnormalities identified, cerebral atrophy, particularly in the frontal and temporal regions, is a prevalent feature in CeT [38].

Regarding molecular alterations, several articles describe the accumulation of amyloid beta protein (Aβ) in the pathophysiological process of TBI, as a result of processes such as hypoperfusion, vascular dysfunction, ischemia, and endothelial damage. This cascade of neurovascular stress events could contribute to the development of pathology similar to Alzheimer's Disease and dementia later in the life cycle [37].

Also, tau pathology is described as a product of blood flow alteration, vascular damage and inflammatory response after a TBI, which, like the accumulation of Aβ, generates neuronal dysfunction and self-propagation of neurodegeneration [37].

In some research, chronic traumatic encephalopathy (CTE) is referred to as a "tauopathy" based on the fact that the main pathology of CTE is based on alterations in the tau protein. Other alterations documented from autopsy studies refer to the concept of "poly-pathology", which includes abnormalities of tau and Aβ, as well as neuroinflammation, white matter degeneration, neuronal loss, diffuse axonal injury and abnormalities of the substantia nigra, which, on pathologic examination of TBI patients, is described as "pale" [38].

Along the same lines, another study describes the accumulation of tau pathology, amyloid β and TDP-43 deposition, neuro-inflammation, axonal degeneration, white matter degradation, neuronal loss and alteration of the blood-brain barrier [36]. Other research associates amyloid beta protein and tau protein, present in neurodegenerative diseases such as Alzheimer's disease, with head trauma due to the activation of molecular pathways and the presence of degeneration of frontotemporal regions of the brain [39].

Cerebral ischemia associated with TBI reports altered expression of the tau gene, accumulation of amyloid beta (Aβ)/tau protein, impaired cerebral clearance, neuronal dysfunction, and self-propagating neurodegeneration. This has also been found in Alzheimer's disease, boxers with TBIs, hockey players, and military personnel with multiple TBIs [37].

Likewise, in another investigation, the presence of neurofibrillary tangles (NFT), Aβ and TAR DNA binding protein (TDP-43) has been reported as a product of axonal pathology caused by a TBI, especially in those subjects with repetitive TBI such as boxers, retired football or ice hockey players [38].

Another study affirms that genetic variations play an important role in the susceptibility of people to present effects regarding TBI during old age. For example, apolipoprotein E has been associated with the risk of Alzheimer's disease and has shown a variable interaction with mild TBI [36].

Diverse studies and clinical trials with animal models seek to understand the molecular mechanisms involved in the genesis of post-TBI psychiatric disorders, with the aim of establishing future therapeutic measures. Therefore, it is important to mention a clinical trial conducted with rats which focused on the effects of cell-based regenerative therapy in animals with TBI to treat neuropsychiatric deficits after juvenile TBI. This procedure employed stem cells/progenitors including neural stem cells (NSCs) and induced pluripotent/embryonic stem cell-derived neural progenitor cells (iPSC-NPCs and ESC-NPCs) [40].

Postnatal day 14 (P14) Wistar rats were subjected to TBI induced by a controlled cortical impact (CCI). The impact caused visible damage in cortical regions, particularly the sensorimotor cortex. Three days after TBI, rats were given intracranial transplants of mouse iPSC-derived neural progenitor cells cultured normally (N-iPSC-NPCs) or mouse iPSC-derived neural progenitor cells pretreated with

hypoxic preconditioning (HP-iPSC-NPCs) [40].

The ability of iPSC-NPC pretreated with regular or hypoxic culture conditions to attenuate post-TBI neuropsychiatric deficits was studied in the rat assay. Seventeen days post-TBI the animals were examined and subjected to various tests (functional sensorimotor tests, social behavior tests and a social transmission of food preference test (STFP)) [40].

The most relevant results of the study are listed below:

1 Seven days after the TBI, the animals subjected to the test presented significant sensorimotor deficits. However, 17 days after TBI, most functional deficits were undetectable due to intracranial neural stem cell transplantation [40].
2 The transplantation of iPSCs-NPCs showed significant benefits in social behavior; however, the transplantation of HP-iPSCs-NPCs reported greater benefits [40].
3 The transplantation of HP-iPSCs-NPCs increased the levels of oxytocin and its receptors, which provides an important molecular mechanism for improvements in social behavior and regulation of social behaviors, which could be a starting point for future studies [40].

From this clinical trial, it can be concluded that stem cell transplantation results in notable improvements in the social sphere after TBI, which is recognized as a key aspect to guide future research regarding the therapeutic management of post-TBI patients. In addition, it highlights the importance of how animal studies can influence the course of therapeutic interventions that will be carried out with humans, being a clear example of how biomedical research based on animal models can lead to research applied to humans [40].

How aging may affect the pathological and psychological changes and mechanisms

The age of presentation of the trauma is a key factor in the development of a post-TBI psychiatric disorder. Various investigations aim to study TBI in the pediatric age, since there are many anatomical and physiological factors that differ from those of an adult (for example, children have a disproportionately larger brain in relation to the body, they have less cervical muscle tone and lack of myelination of brain regions) [41].

"Neuronal neuroplasticity" is recognized as a protective factor in the sequelae of a TBI in the pediatric age since it is assumed that there is less susceptibility to brain damage during childhood, however, other authors suggest that it should also be considered the concept of "early vulnerability", which assumes that the immature or developing brain is especially sensitive to brain damage [41].

Starting from the previous premise, a study published in 2020, which was carried out in the Spanish population between 2000 and 2015, with a sample of 71 subjects aged between 6 and 16 years in the neurology service of the Sant Joan de Déu Hospital in Barcelona, it was proposed to determine the neuropsychological deficits in children with TBI and the impact of factors such as age at the time of the injury and its severity, as well as socioeconomic, cultural and relational aspects of the family [41].

The study evaluated measures of intelligence (intellectual quotient), executive functions and behavioral aspects, concluding that there is a trend in terms of "early vulnerability", because children with post-TBI at earlier ages (between 0 and six years), showed a higher risk of suffering deficits in intellectual capacity and executive functions, because the skills are in the process of development compared to older children, who are more exempt from presenting sequelae. In addition, the impact of socioeconomic and cultural level as determining predictors for the development of cognitive and behavioral skills after suffering a TBI was evidenced [41].

Similarly, other recent research from 2017 suggests that, in the pediatric age, a TBI interferes with the process of neuronal development, which can have lasting consequences on brain function, as occurs in cognitive dysfunctions [42].

In the USA, the Traumatic Brain Injury Model Systems (TBIMS) program is responsible for carrying out a 1-year, 2-year and 5-year longitudinal follow-up of people in hospital rehabilitation associated with a diagnosis of TBI. The result of research has reported that older age at the time of injury is associated with worse outcomes and a more rapid rate of decline in post-TBI individual functionality [36].

However, they emphasize that age is not the only risk factor; lifestyles prior to the injury, alcohol and drug abuse, and the presence of prior neurological diseases should be considered [36].

In this sense, another study related to mortality after a TBI reported a higher death rate in the older population, with a 4% increase in the risk of death for each additional year of age at the time of surgery. injury, and a 33% increase for those who used drugs before the injury compared to those who did not. In addition, the older adult population was at higher risk of suffering TBI as a result of falls from their own height with prolonged hospital stay, however, less serious injuries were reported according to the Glasgow Coma Scale [43].

Some studies link a history of TBI with the appearance of dementia in later years among the neurological alterations following a TBI [36]. A study explains the main mechanistic theories linking TBI and dementia, which include "1) the activation of a progressive neurodegenerative cascade, 2) the acceleration of an established neurodegenerative cascade, and 3) a static brain injury that reduces cognitive reserve." They do, however, mention the numerous risk and protective factors, which range from genetics and medical comorbidities to environmental exposures and the specific features of TBI [44].

Potential treatments

The initial management of the patient with traumatic brain injury should be guided in the same way as any polytraumatized individual. Prehospital strategies include airway management and cervical spine monitoring, ventilation, circulation, followed by rapid examination for neurologic deficit, patient exposure, and body temperature monitoring. The goal should be euvolemia and avoid hypotension. In addition, within the primary evaluation, patients in need of referral to specialized plot centers should be quickly identified [45].

In the hospital setting, a comprehensive evaluation should be performed that includes medical history, comprehensive neurological evaluation (Glasgow coma scale score), and psychiatric evaluation, including cognitive evaluation, laboratory tests, and neuroimaging. Based on the clinical, paraclinical and imaging findings, the need for medical or surgical intervention should be considered. Treatment modalities vary widely depending on the severity of the injury and range from daily sessions of cognitive therapy to radical surgery [46].

Treatment of psychiatric disturbances after brain injury should be individualized, based on personal factors and the nature and severity of symptom presentation, and may include physiotherapeutic, psychotherapeutic, and pharmacological treatment modalities.

Therapeutic strategies include

- Physical rehabilitation such as physiotherapy, occupational therapy, speech therapy.
- Psychotherapy such as initial personal education, support groups, family education.
- Medications: antidepressants, anxiolytics, antipsychotics, affect modulators.
- Management of sleep dysfunction.

It is worth mentioning that management of the patient with traumatic brain injury is multidisciplinary because many organ systems can be affected by a brain injury [2].

Pharmacotherapy

- **Mood stabilizers:** the most used are: lithium, valproic acid and carbamazepine.
- **Antipsychotics:** Two large groups of antipsychotics are described: typical antipsychotics and atypical antipsychotics.
- *Typical antipsychotics:* The most used medications are: haloperidol, levomepromazine and pipotiazine.
- *Atypical antipsychotics:* Within this group are: risperidone, paliperidone, clozapine, quetiapine, aripiprazole, olanzapine, ziprasidone, amisulpride.
- Antidepressants:
- *Tricyclic antidepressants (TCAs):* amitriptyline, imipramine, desipramine, nortriptyline.
- *Selective serotonin reuptake inhibitors (SSRIs):* fluoxetine, sertraline, escitalopram, paroxetine.
- *Dual antidepressants:* duloxetine, desvenlafaxine, venlafaxine.
- *Other antidepressants:* bupropion, trazodone, mirtazapine.

Benzodiazepines: Due to their fast-acting anxiolytic effects, they are commonly used. However, it is not recommended as a chronic treatment because it generates dependency.

Note: The drugs described were taken from the clinical practice guidelines and the synopsis of psychiatry by Kaplan and Sadock [6].

The therapeutic approach for this group of disorders must be comprehensive, many clinical practice guidelines consider that it is not enough to treat exclusively with medication. In many cases, non-pharmacological measures such as preventive and treatment psychotherapy should be included. Likewise, other important variables must be considered for the choice of pharmacological treatment, which will depend on the patient's comorbidity, the side effect profile of the drug, the individual's condition and the route of administration chosen [47].

Management of Pediatric Severe Traumatic Brain Injury: 2019 Consensus and Guidelines-Based Algorithm for First and Second Tier Therapies

A review of the article called: "Management of Pediatric Severe Traumatic Brain Injury: 2019 Consensus and Guidelines-Based Algorithm for First and Second Tier Therapies" where Approaches and Decisions in Acute Pediatric TBI (ADAPT) are exposed to provide guidance on management respective.

The document is about the clinical management of acute pediatric TBI, however, it is important to clarify that the article mentioned moves away from the initial focus of the scoping review, since it does not include a relationship TBI/psychiatric disorders. The therapeutic approaches proposed in said article are summarized below [48]:

APPROACH TO THERAPIES

Herniation Pathway

The key issue is recognizing when acute herniation of brain tissue is about to occur or is already occurring. Clinical symptoms include traction on neural and vascular structures as well as brainstem compression.

Baseline care

Initial care should include the following protocols:

- ***Maintenance of an Appropriate Level of Analgesia and Sedation:*** For initial sedative/analgesic therapy, the guidelines committee recommends a benzodiazepine-opiate combination.
- **Controlled Mechanical Ventilation:** The guidelines committee advises a target partial pressure of oxygen (PaO_2) of 90–100 mmHg and the partial pressure of carbon dioxide ($PaCO_2$) between 35 and 40 mmHg.
- ***Maintaining Normothermic Core Temperature and Preventing and Treating Fever:*** Protocols have specified initial temperature targets of greater than 35 °C and less than 38 °C.
- ***Ensuring an Appropriate Intravascular Volume Status:*** More recent protocols have described a target central venous pressure (CVP) threshold of 4–10 mmHg or 8–12 mmHg. According to the committee, achieving normal blood volume necessitates at least 75% maintenance fluids and a neutral fluid balance with a urine flow rate greater than 1 mL/kg/hr. In terms of glucose target, protocols have described aiming for normoglycemia or concentrations of up to 180 mg/dL. If the glucose level is higher than 198 mg/dL on two consecutive measurements, insulin should be used. To avoid hypoglycemia, strict glucose monitoring should be implemented. Many protocols use ranges with a lower limit greater than 135 mEq/L and an upper limit less than 150 mEq/L for the baseline [Na+] target. Nutritional support should be initiated as soon as possible, ideally within 72 h.
- ***Maintaining Minimum Blood [Hemoglobin]:*** In the case of a pediatric patient with severe TBI, the committee recommends a minimum target of greater than 7.0 g/dL.
- ***Treatment of Coagulopathy:*** Recent research suggests that overresuscitation with plasma to normalize INR after TBI in children may worsen coagulopathy, resulting in fibrinolysis shutdown, and that coagulopathy treatment should address active bleeding and/or be titrated to thromboelastography.
- **Neutral Head Positioning with Head-of-Bed Elevation:** The committee favors neutral head positioning with an initial head-of-bed elevation of 30°.
  - **Antiepileptic Drug Therapy and Use of Continuous Electroencephalography:** The committee could not agree on antiepileptic drug (AED) indications or the type of medication and dosing that should be used. The use of continuous electroencephalography (cEEG) throughout the management course is supported by evidence, particularly when neuromuscular blockade is used.

FIRST TIER THERAPIES

Linear sequences were provided to the algorithm for first-level management of intracranial pressure (ICP), cerebral perfusion pressure (CPP), and brain tissue partial pressure of oxygen ($PbrO_2$) in pediatric patients with severe TBI.

- ***ICP Pathway:***

The guidelines committee supports using less than 20 mmHg as an initial ICP target in all age groups, as well as the need for intervention when ICP rises above 20 mmHg for at least 5 min.

- ***CPP Pathway:***

It advocates for the implementation of age-specific thresholds ranging from 40 to 50 mmHg, with infants at the lower end and adolescents at the upper end of this range. Because ICP and CPP are linked, interventions aimed at raising ICP frequently, but not always, improve CPP.

- ***Pbro2 Pathway***

A minimal target level of 10 mmHg is supported by evidence. Because ICP, CPP, and PbrO2 are all linked, therapies that target ICP and CPP will enhance PbrO2 readings.

SECOND TIER THERAPIES

Second-tier therapy should be considered for cerebral hypertension or inadequate CPP or PbrO2 that is resistant to first-tier interventions. A CT scan should be performed to identify any lesions that could be surgically repaired. Neurosurgery and/or four medical treatments are being evaluated as second-level therapy.

- Neurosurgery:

There are various surgical approaches available for decompressive craniectomy. In the methods documented in the literature, the time and indications for decompressive craniectomy for cerebral hypertension vary.

- Barbiturate Infusion:

Pentobarbital is the most often mentioned medicine. It is considered when osmotherapy and hyperventilation have failed to keep ICP below 25 mmHg. Decompressive craniectomy or one of the other second-tier therapies should be explored if barbiturate infusion

fails to control ICP, as defined by persistent ICP more than 25 mmHg. In patients with ICP less than 20 mmHg for 24 h while receiving a steady pentobarbital infusion dose, the infusion can be reduced and eventually removed over a 24-96-h period.

- Late Application of Moderate Hypothermia

Early mild hypothermia is not advised. The recommendations committee, on the other hand, believes that late application of moderate hypothermia to manage refractory intracranial hypertension is acceptable. Recent publications specified a target temperature of 32–33 °C or 34–35 °C.

- Induced Hyperventilation and Hyperosmolar Therapies

The "Hypertonic Saline Sliding Scale" regimen aims for hyperventilation with a PaCO2 between 28 and 34 mmHg, serum [Na+] between 155 and 160 mEq/L, and osmolarity between 320 and 340 mOsm/L, as well as a pentobarbital infusion at a rate of 2–4 mg/kg/hr.

Finally, the treating physician must acknowledge that management strategies must be tailored to the needs of the patient and may not be as straightforward as following a linear therapy plan. Furthermore, novel therapy choices may arise in real time.

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