

ARTIGO DE REVISÃO NARRATIVA/REVIEW ARTICLE

Psychosis Secondary to Traumatic Brain Injury: Critical Literature Review and Illustrative Case Study

Psicose Secundária a Lesão Cerebral Traumática: Revisão Crítica da Literatura e Estudo de Caso Ilustrativo

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Abstract

Psychosis secondary to traumatic brain injury (PSTBI) is rare yet a serious sequela of traumatic brain injury (TBI). We provide a critical literature review on PSTBI, outlining clinical features and approach to the diagnosis and treatment. Finally, we illustrate a case description, to discuss its conceptual framework. Conceptualizing PSTBI as a neurobiological syndrome has clinical relevance, insofar as, it facilitates a rational scheme, by which specific diagnostic dilemmas should be tackled in the workup, to provide a tailored treatment. Additionally, it may shed light on the understanding of psychotic disorders by integrating data on primary and secondary psychosis. TBI can contribute to the emergence of psychotic symptoms in various manners. It may precipitate psychosis in susceptible individuals, occur in a direct relationship to post-traumatic epilepsy, or develop directly due to brain injury. It is this last clinical entity that we focus on in this article. Its neurobiological underpinnings comprise the following mechanisms: damage to frontal and temporal lobes (primary injury); structural and/or functional dysconnectivity in sensory- and other information-processing networks, such as the Default-Mode network, which stem from diffuse axonal injury (DAI) (primary injury); neuroinflammation and neurodegeneration (secondary injury).

The clinical presentation may take two forms: delusional disorder or schizophrenia-like psychosis. Both subtypes are often preceded by a prodromal phase superimposed on other sequelae, namely affective instability, social and occupational functional decline. In comparison to primary schizophrenia, PSTBI has a lower genetic load, fewer negative symptoms, more neurocognitive symptoms, which may be intertwined with frontal-subcortical system dysfunction/ frontal syndromes and are more likely to present findings on neuroimaging and electroencephalographic studies. PSTBI has a bimodal distribution of onset. Latencies of under a year (early-onset) have been associated with DAI and delusional disorder subtype. Schizophrenia-like psychosis subtype usually develops after a latency of 1-5 years (late-onset), and has been more associated with epilepsy, focal brain lesions and a chronic course.

Antipsychotics should be used cautiously considering the increased sensitivity to the sedating, anticholinergic, and seizure threshold-lowering side effects. Late-onset PSTBI might benefit from anticonvulsants, by virtue of its anti-kindling properties. Additionally, further pharmacological approaches may be used to address cognitive, emotional, and behavioural issues.

Resumo

A psicose secundária a lesão cerebral traumática (PSLCT), ainda que rara, constitui uma sequela neuropsiquiátrica grave de lesão cerebral traumática (LCT). Procede-se a uma revisão crítica da literatura sobre PSLCT no que concerne a apresentação clínica, diagnóstico e tratamento, com recurso a um estudo de caso. A conceptualização da PSLCT como uma síndrome neurobiológica tem relevância clínica, na qual pertinentes dilemas diagnósticos devem ser considerados,

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de forma a se estabelecer um tratamento específico. Adicionalmente, permite uma melhor compreensão da fisiopatologia das perturbações psicóticas, através da integração de dados sobre psicose primária e secundária.

A LCT pode precipitar psicose em indivíduos suscetíveis, desenvolver-se secundariamente a epilepsia pós-traumática ou em relação direta com a lesão cerebral. Este artigo debruça-se sobre a última entidade clínica. Os seus fundamentos neurobiológicos compreendem os seguintes mecanismos: lesão focal dos lobos frontal e temporal (lesão primária); desconectividade estrutural e/ou funcional de redes neuronais sensoriais e de processamento de informação, tais como a rede *Default-Mode*, que decorre de lesão axonal difusa (LAD) (lesão primária); neuroinflamação e neurodegeneração (lesão secundária).

As apresentações clínicas da PSLCT compreendem a perturbação delirante ou a psicose esquizofrenia-like. Ambos os subtipos são frequentemente precedidos por uma fase prodrômica, cujas manifestações se sobrepõem a outras sequelas neuropsiquiátricas, nomeadamente instabilidade emocional e declínio do funcionamento social e ocupacional. Em comparação com a esquizofrenia primária, a PSLCT apresenta menor carga genética, menos sintomas negativos, mais sintomas neurocognitivos, que se podem sobrepor a sintomas de disfunção de circuitos fronto-subcorticais/síndromes do lobo frontal, e maior prevalência de achados neuroimagiológicos e eletroencefalográficos. Destaca-se ainda uma distribuição bimodal de início. Latências inferiores a um ano (início precoce) associam-se a LAD, e subtipo de perturbação delirante. O subtipo psicose esquizofrenia-like emerge habitualmente após uma latência de 1-5 anos (início tardio), e está mais associado a epilepsia, lesões cerebrais focais e uma evolução crónica.

Os antipsicóticos devem ser usados cautelosamente, considerando a sensibilidade aumentada aos efeitos colaterais sedativos, anticolinérgicos e de redução do limiar convulsivo. A PSLCT de início tardio pode beneficiar de tratamento com antiepiléticos, dado as suas propriedades *anti-kindling*. Outras abordagens farmacológicas podem ser proficuas na abordagem de alterações cognitivas, emocionais e comportamentais.

Keywords: Brain Injuries, Traumatic/complications; Psychotic Disorders/diagnosis; Psychotic Disorders/drug therapy; Psychotic Disorders/etiology

Palavras-chave: Lesão Cerebral Traumática/complicações; Perturbações Psicóticas/diagnóstico; Perturbações Psicóticas/etiologia; Perturbações Psicóticas/tratamento farmacológico

INTRODUCTION

Traumatic brain injury (TBI) increases the risk for a wide range of neuropsychiatric disturbances.

Epidemiologic data on psychosis secondary to traumatic brain injury (PSTBI) are highly variable, biased by different methodologies, but most studies report a prevalence ranging from 1% to 9%.¹ A meta-analysis estimated a 60% increase in the risk of schizophrenia after TBI compared with the general population.² Scarce research is available hence little is known as to the neurobiological processes that may contribute to its onset. The *Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition* (DSM-5) guidelines suggest that psychosis due to TBI should be considered in a patient with both a history of TBI and psychosis when there is a temporal association between TBI and psychosis and/or when atypical features of psychosis are present. In practice, the occasionally long latency between TBI and the subsequent development of psychosis makes the required temporal association for the diagnosis of psychosis due to TBI difficult to establish.

OBJECTIVES

We aim to provide a brief up-to-date review on PSTBI, concerning the potential neurobiological mechanisms underlying its pathophysiology, clinical aspects, concerning latency of onset, clinical presentation, and clinical course, as well as diagnostic workup, and therapeutic approach.

We also discuss the conceptual framework and provide literature-based guidance regarding diagnostic workup and treatment for clinicians who are faced with this diagnostic hypothesis, based on a case study.

LITERATURE REVIEW ON PSTBI

a. Clinical Aspects

PSTBI may typically present as two distinct subtypes: delusional disorder and schizophrenia-like psychosis.² Both subtypes are often preceded by a prodrome superimposed on other, usually present, sequelae of TBI, characterized by affective instability, antisocial and inappropriate social behaviour, performance decline at school or work, social withdrawal, and depression.^{3,4} Formal thought disorder, catatonic features, and negative symptoms such as affective flattening and avolition are uncommon.^{4,6} Notwithstanding, negative symptoms may be difficult to distinguish from post-TBI cognitive dysfunction.

Psychopathologic manifestations of delusional disorder subtype of PSTBI often comprise misidentification syndromes, and sometimes somatoparaphrenia.¹ The latter is a type of monothematic delusion where one denies ownership of a limb or the entirety of one's body and has been associated with damage to the temporoparietal junction cortical region.

Conversely, in schizophrenia-like psychosis subtype of PSTBI the clinical presentation includes delusions and

hallucinations, typically without co-occurring negative symptoms. Delusions are the core clinical manifestation, and the content is mainly persecutory (56%), self-reference (22%), control (22%), and grandiosity (20%).⁴ Auditory hallucinations are also common, with studies reporting 60% to 93% of patients presenting with this symptom.^{4,7} Voices commenting on the patient's behaviour, which are classically associated to schizophrenia, are also frequent.⁵ Visual hallucinations occur in around 8% of patients.^{4,7} Aggressive behaviour is present in around 40% of patients.⁶ Formal thought disturbances, negative symptoms and catatonia are unusual features.⁴ Nevertheless, negative symptoms may be difficult to distinguish from post-TBI cognitive dysfunction. Additionally, in the schizophrenia-like psychosis subtype of PSTBI, the most reported neuroimaging findings are focal lesions or brain atrophy, especially within frontal and temporal lobes.⁸ Other studies had already found a high proportion of frontal and temporal lesions in PSTBI patients.⁴ Around 70% have abnormalities on *electroencephalogram (EEG)*, especially electroencephalographic slowing within temporal lobes, in contrast to frontal topography of electroencephalographic slowing for primary schizophrenia, and almost 30% have seizures.⁸ Indeed, some cases of PSTBI may be an ictal-related process, particularly after severe TBI, where a penetrating / open-head injury occurs, causing a focal damage to the cortex, consequently creating an ictal focus. PSTBI has similar features to interictal psychosis. Nearly 90% of patients with PSTBI have cognitive dysfunction attributable to TBI, typically impairments of attention, language, memory, visuospatial function, and executive function domains.^{7,9}

b. Pathophysiology

Some authors have proposed that the neurobiological mechanisms of PSTBI rely on the dysfunction of the frontal systems, the temporal lobe, and the neurotransmission pathways that are projected in these areas, leading to a relative increase of the temporal limbic activity.¹⁰ Indeed, TBI is the result of mechanical forces applied to the skull and transmitted to the brain. This may lead to focal and/or diffuse brain damage. Focal lesions often result from a direct blow to the head and include brain laceration, contusion, intracerebral haemorrhage, subarachnoid or subdural haemorrhage, and ischemic infarct. Contusion occurs directly beneath or contralateral to the site of impact, commonly referred to as *coup* and *contrecoup* injury. It is most common in the orbitofrontal and anterior portions of the temporal lobes, where acceleration-deceleration forces cause the brain to impact on the bony protuberances of the skull. Focal lesions may give rise to several emotional and neurobehavioural alterations, depending on the topography of the lesion. Contusions to the surface of the anterior temporal lobes can cause sudden and unexpected bursts of anger, memory impairment for recent events, hallucinations, rapid mood swings, and epileptic seizures. Damage to the orbitofrontal region of the frontal lobe results in impairments in behavioural and emotional regulation, impulsivity,

inappropriate or aggressive behaviours, and sudden and unexpected mood swings. In more severe cases of TBI, there can be damage to the dorsolateral and ventromedial regions of the frontal lobe. Damage to the dorsolateral region of the frontal lobe results in impairments of attention, working memory, problem-solving, planning, cognitive flexibility, and judgment. Damage to the ventromedial region of the frontal lobe results in diminished drive, decreased motivation, anhedonia, and apathy.

On the other hand, diffuse brain injury also results from the differential motion of the brain within the skull, causing a shearing and stretching of the axons. This can produce a wide spectrum of injuries, ranging from brief physiological disruption to widespread axonal tearing, called diffuse axonal injury (DAI). In addition to brain damage resulting from mechanical injury occurring at the time of the insult (primary injury), most of the neuropsychiatric manifestations stem from the secondary injury caused by the physiologic response to the initial injury, comprising loss of cerebral autoregulation, excitotoxicity, mitochondrial dysfunction, oxidative stress, neuroinflammation and neurodegeneration, which may evolve over several years.^{11,12} At the microscopic scale, diffuse axonal injury (DAI) can interrupt axonal transport, produce axonal bulbs, and trigger neuroinflammation through microglial activation in the early phase post-traumatic brain injury (TBI). Eventually, in the chronic phase post-TBI, diffusion of misfolding proteins may ensue, triggering neurodegenerative processes. These abnormalities can eventually lead to neurodegeneration which over time can bring about brain atrophy in brain regions that are far removed from the focal injuries as it tracks the Wallerian degeneration of damaged axons. Therefore, at the whole brain scale, damage to tracts interrupts long-distance communication between brain regions within large-scale intrinsic connectivity networks. Following TBI, regionally selective atrophy is common in parts of the Default Mode Network (DMN).¹¹ The DMN can be separated into hubs (core nodes) and subsections. The core nodes include the ventromedial prefrontal cortex, the posterior cingulate cortex, and the angular gyrus.^{11,13} Some subsections encompass the temporoparietal junction, involved in theory of mind, and the lateral temporal cortex, involved in the retrieval of social semantic and conceptual knowledge.¹³

Some authors have emphasized the involvement of the right hemisphere in the delusional phenomena of PSTBI.¹ A recent study proposes an aetiological mechanism whereby right hippocampal head atrophy, that occurs in the chronic stages of moderate-to-severe TBI, may play a role in the delayed onset of psychotic symptoms after TBI, leading to the dysregulation of dopaminergic networks following TBI, possibly accounting for the observed clinical features of the PSTBI, namely the predominance of positive symptoms.¹⁴ This is explained by the presence of inhibitory GABAergic neurons in the hippocampus, largely localized to the hippocampal head, which exert regulatory control over dopaminergic neurons of the mesolimbic system. Notably, similar neurobiological processes underlie primary schizophrenia, with hippocampal head atrophy in early

psychosis, and further spreading of the degeneration along the hippocampal axis, during the longitudinal course of the illness.¹⁵ Findings from other studies suggest that TBI may directly induce structural and/or functional brain changes in sensory- and other information-processing networks that manifest with hallucinations and delusions, respectively.⁹

c. Risk Factors

All the individuals may be virtually susceptible, but those having a genetic predisposition would have a lower threshold for the emergence of symptoms when they are exposed to TBI.⁶ Risk factors for PSTBI may be divided into pre-injury, injury and post-injury risk factors. Male gender, pre-injury neurodevelopmental and neuropsychiatric problems, and family history of schizophrenia are among the strongest pre-injury risk factors for post-traumatic psychosis.¹⁶ Regarding injury related risk factors, the topographic localization of brain lesions in the frontal and temporal lobes is the most consistent factor.^{7,16} Conversely, the correlation between psychosis and the severity of TBI is not consistent.^{2,16} Among the many post-injury factors potentially relevant to the development of post-traumatic psychosis, EEG abnormalities, post-traumatic epilepsy, and cognitive impairments appear to be most strongly associated with this condition.¹⁶

d. Clinical Onset and Course

The onset of PSTBI is often gradual, with a subacute or chronic course.¹ Despite the wide range of latencies between TBI and the onset of psychosis, ranging from a few days to over two decades, most studies suggest that the first psychotic symptoms emerge within the first year in around 40% of the patients, with an increase of this prevalence to roughly 70% in the fifth year after TBI.^{8,10,16} There is some evidence that the duration of the latency between TBI and the onset of PSTBI might have clinical significance. The delusional disorder subtype of PSTBI tends to develop during the first year after TBI.³ Latencies of under a year before the onset of psychotic symptoms have been associated with DAI, paranoid symptoms, and visual hallucinations.^{7,17} By contrast, schizophrenia-like psychosis subtype of PSTBI is generally of delayed onset, with a latency of 1-5 years.³ Longer latencies were found to have more localized damage to the temporal lobe, presence of epilepsy and higher proportion of auditory hallucinations.^{7,17}

There is much variability in illness course and treatment responsiveness, with some patients demonstrating relatively short courses and others being more chronic. In addition to the schizophrenia-like psychosis subtype of PSTBI, a premorbid schizoid personality is associated with a chronic course.¹⁸

e. Clinical Evaluation

Regarding the approach to the evaluation of psychotic patients with a previous TBI, anamnesis should focus on characterizing the severity of brain injury, identifying pre-injury risk factors for PSTBI, and on a thorough probing of the weeks and months prior to TBI, which can reveal prodromal psychotic symptoms that may have gone

unrecognized. Atypical age of onset and a temporal relationship of psychosis to TBI can be helpful in establishing the diagnosis. Obtaining collateral information from knowledgeable informants and from the medical records is essential, as posttraumatic cognitive dysfunction, impaired self-awareness, and psychotic symptoms may hamper a patient's ability to serve as a reliable source of information. Mental state examination should evaluate for the presence of delusions, hallucinations (auditory and otherwise), and although rare, negative symptoms should be explored, being mindful that it may be difficult to parse from post-TBI cognitive dysfunction. Neurological examination should be performed.

Diagnostic workup should comprise the following ancillary studies: routine serum laboratory testing, to rule out metabolic derangements known to produce delirium or psychotic-like symptoms; structural neuroimaging studies, preferably magnetic resonance imaging (MRI), wherein focal microglial scars, and sometimes also signs of diffuse lesions / DAI, appear as hyperintense in T2 and fluid-attenuated inversion recovery (FLAIR) sequences; EEG, especially when the history suggests paroxysmal events, with consideration of prolonged and/or video-EEG monitoring if the suspicion for posttraumatic epilepsy is high; neuropsychological testing, which commonly clarifies the nature and extent of cognitive impairments, and may help to identify patterns of impairment typical for TBI versus primary schizophrenia.¹⁸

f. Differential Diagnosis

The main considerations in the differential diagnosis of PSTBI should include acute confusional state / delirium, psychosis secondary to adverse effects of medication, posttraumatic epilepsy with an ensuing epileptic psychosis, confabulation in association with severe posttraumatic cognitive impairment and primary schizophrenia spectrum disorders.¹⁵

Psychosis occurring within days or weeks of injury must be distinguished from the posttraumatic confusional state, a period of fluctuating disorientation, cognitive impairment, psychomotor restlessness, and sleep-wake disturbance that appears early in the TBI recovery course and can involve transient psychotic symptoms. Delirium due to substance intoxication or withdrawal, such as benzodiazepines, anticholinergic and antihistaminergic medications, must also be ruled out. Medication-induced psychotic symptoms may be caused by some drugs prescribed for cognitive enhancement following severe TBI, namely amantadine, which may produce hallucinations and delusions in some patients, as well as by some anticonvulsants, namely levetiracetam, topiramate, zonisamide, ethosuximide, vigabatrin and tiagabine.

When psychosis occurs in association with posttraumatic epilepsy, a diagnosis of posttraumatic psychosis should be deferred until it is clear that psychotic symptoms persist despite effective seizure control. Posttraumatic epilepsy can present as ictal, post-ictal, or interictal psychosis. Schizophrenia should be considered when negative symptoms or formal thought disorder are prominent and when

the severity of TBI is mild enough (e.g., single, uncomplicated, very remote concussion) so that psychosis is implausibly attributable to it.

Isolated hallucinations after TBI are rare and their presence should prompt consideration of other aetiologies such as peduncular hallucinosis due to brainstem injury or release phenomena due to vision or hearing loss.

g. Treatment

The mainstay of treatment are antipsychotics. Secondary brain damage, that ensues in the following few years after TBI as a result of chronic neuroinflammatory and neurodegenerative processes, occur in parallel with neural repair and plasticity processes.¹⁹ According to studies using in vitro human models and in vivo animal models, these neural recovering processes might be undermined by haloperidol and worsen the patients' prognosis in the years following TBI.^{20,21} Chlorpromazine was reported to worsen the condition and produce psychosis after TBI in one case, possibly due to its prominent anticholinergic properties.²² Therefore, atypical antipsychotics are the preferred pharmacologic treatment. Nevertheless, even atypical antipsychotics should be used with caution, considering the increased sensitivity of the injured brain to the sedating, anticholinergic, and seizure threshold-lowering side effects.⁴ The initial dosage should be one-third to one-half of the usual starting dose, and increased gradually and carefully. Although unsupported, some pharmacological strategies include the use of anti-kindling drugs (anticonvulsants) for late-onset psychosis.⁶ When an epileptic psychosis secondary to TBI is diagnosed, anticonvulsants for seizure control are the mainstay of treatment. Additionally, further pharmacological approaches may be used to treat concomitant problems, such as cognitive dysfunction and emotional and behavioural symptoms. In this regard, methylphenidate has beneficial effects on depressive symptoms, improving emotional dysregulation and impulsivity, as well as on cognitive symptoms, improving attention, working memory, and speed of processing, additionally reducing daytime sleepiness.^{23,24} Donepezil improves short-term memory and sustained attention of post-TBI patients, being useful in moderate-to-severe TBI cases.^{25,26} Selective serotonin reuptake inhibitors (SSRI) antidepressants are useful as a therapeutic approach for depression, and emotional and behavioural symptoms of post-TBI patients.²⁷ The theoretical rationale for the use of SSRI antidepressants is grounded on the neurobiological underpinnings of the chronic phase post-TBI in which a downregulation of serotonin receptors occurs.

CASE STUDY

A male patient with no family history of psychosis and irrelevant past medical history, had his first psychotic episode around 3 years after a severe TBI. He had suffered a car accident at the age of 18, with loss of consciousness, had been in coma for 2 weeks, and had presented post-traumatic amnesia. The first psychotic episode emerged at the age of 21, characterized by persecutory delusions

and auditory hallucinations. He had two further psychotic episodes in his thirties, with the same clinical features. Negative symptoms were always absent both during acute psychotic episodes and in the inter-episodic periods. Information collected from his relatives confirmed that he had developed personality and behavioural alterations, namely emotional dysregulation, impulsivity, and impairment of social pragmatic skills. Regarding his personal and social history, he had concluded high school, had gotten married, however had a poor social and occupational adjustment. When 41 years-old he was hospitalized in our ward, for a psychotic episode, in which he had bought a gun and delivered it to the judiciary police, with a delusional conviction that he would become a police officer. At mental state examination, he presented perplexity, disorganized behaviour, prolixity, tangentiality, asyndetic thought, non-systematized grandiose and pseudo-philosophical delusions, rapid mood swings with irritability and emotional lability, and lack of insight. Laboratory testing was unremarkable: haematological and biochemical screening, thyroid function, folic acid, and cyanocobalamin were normal; serologies for Venereal Disease Research Laboratory (VDRL), human immunodeficiency virus (HIV), hepatitis B and C were negative. The magnetic resonance imaging (MRI) revealed subcortical focal lesions, suggestive of gliosis, in right frontal and left parietal topography, alongside atrophy of the right posterior temporal cortex. The EEG displayed a background with slight generalized slowing, yet no focal abnormalities, neither focal slowing nor paroxysmal activity, allowing to rule out the diagnostic hypothesis of epileptic psychosis. The neuropsychologic assessment revealed mild impairments in sustained attention, verbal and visual memory, abstract conceptualization, and abstract-logical reasoning domains. The patient improved with a therapeutic regimen comprising antipsychotics (haloperidol decanoate 200 mg/month) and valproic acid 1000 mg/day.

DISCUSSION

Our patient presented a clinical picture of PSTBI, of schizophrenia-like psychosis subtype. The differential diagnosis with primary psychosis was made considering the absence of family history of psychiatric illness, the accurate temporal relationship between TBI and the first psychotic episode, the absence of negative symptoms in both acute psychotic episodes and inter-episodic periods, as well as neurocognitive impairment in association to brain damage documented by positive findings on neuroimaging studies. Moreover, he presented emotional and behavioural alterations since the early post-TBI stage, which may be interpreted as a prodromal state of PSTBI.

The neurocognitive symptoms, which may mimic thought and behavioural disturbances, alongside the emotional and behavioural alterations, might rather be ascribed to frontal-subcortical circuitry dysfunction and related frontal syndromes (dorsolateral syndrome and orbitofrontal syndrome), caused by the right subcortical frontal lesion, than solely the process of psychosis.

The absence of epileptiform activity on the patient's EEG ruled out the hypothesis of an epileptic psychosis secondary to TBI. We hypothesize that the focal brain lesion, localized in the subcortical right frontal region, might have had a significant role in the emergence of the psychotic syndrome. Likewise, the same topography of brain focal lesions, namely the involvement of the right inferior frontal gyrus and underlying white matter, including the superior longitudinal fasciculus and anterior corona radiata, are reported as relevant pathophysiologic factors in some cases of post-stroke psychosis.²⁸ Additionally, according to literature, the early onset of the PSTBI, suggests an underlying DAI. Thus, structural dysconnectivity might have also contributed to the pathophysiology of the PSTBI of our patient.¹⁶ Besides the right subcortical frontal lesion, the MRI displayed right posterior temporal cortical atrophy. We also hypothesize that the cortical atrophy localized in the right posterior temporal lobe might have resulted from the long-term neurodegenerative processes, with axonal degeneration that occurs within large-scale intrinsic connectivity networks, with ensuing brain atrophy in distant regions from the initial focal brain lesions.¹⁰ Notably, the posterior temporal cortex is a component of the DMN, a neural network commonly involved in degenerative processes following TBI.¹⁰ This region is particularly relevant in social cognition related functions. In agreement with the lateralization trend described in the literature, both focal frontal brain lesion and temporal lobe atrophy were localized in the right hemisphere.

a. Limitations

The current literature on PSTBI is scant by reason of the paucity of research on this issue. Its neurobiological model is hitherto not completely understood. Further research should focus on elucidating how neurochemical circuits and neuroanatomy interact through more sophisticated neuroimaging studies (such as neurochemical imaging with

positron emission tomography, diffusion tensor MRI, fibre tractography); examining the impact of TBI on developing psychosis through prospective studies, as well as TBI as a risk factor in psychosis and in other populations at risk for psychosis through retrospective studies; experimenting strategies to prevent psychosis in TBI sufferers.

CONCLUSION

Summarizing, TBI can constitute the primary cause of psychosis or contribute to its development through the following mechanisms: 1) causing damage to frontal/temporal structures or to the dopamine system that triggers psychosis; structural and/or functional brain changes in sensory and other information-processing networks resulting in hallucinations and delusions; 2) inducing physiological and psychological changes that render the individual more vulnerable to stress, especially in those who are biologically predisposed to psychosis; 3) inducing a secondary epilepsy with an ensuing epileptic psychosis.

The neurobiological mechanisms of PSTBI in our patient might have stemmed from the right subcortical frontal lesion, alongside DAI, and hence structural dysconnectivity, as well as neurodegenerative processes with consequent selective atrophy of the posterior portion of temporal cortex, which is a component of the DMN.

According to the evidence-based literature, and in line with this illustrative case, in comparison to primary schizophrenic psychosis, PSTBI has a lower genetic load, fewer negative symptoms, presents more neurocognitive symptoms, which may be intertwined with frontal-subcortical circuitry dysfunction/ frontal lobe syndromes, and is more likely to present positive findings on neuroimaging studies and EEG. Therefore, addressing PSTBI patients from a standpoint of a complex psychotic and neurobehavioral syndrome may be more rational.

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