Progress in Neuropsychopharmacology & Biological Psychiatry xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Progress in Neuropsychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

Pain with traumatic brain injury and psychological disorders

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ARTICLE INFO

Keywords:
Post-traumatic headaches
Chronic pain
Traumatic brain injury
Anxiety disorder
Depression

ABSTRACT

Traumatic brain injury (TBI) is the cause for long-term disability in more than 3 million patients in the US alone, with chronic pain being the most frequently reported complain. To date, predisposing mechanisms for chronic pain in TBI patients are largely unknown. Psychological disorders, including post-traumatic stress disorder, depression and anxiety following TBI are commonly reported comorbidities to post-traumatic pain. Long term consequences can be debilitating and affect quality of life even when the injury is mild. In this review, we present the most commonly reported chronic pain conditions across the spectrum of severity of TBI, mainly focusing on mild TBI. We discuss chronic post- traumatic headaches, widespread pain as well as post-traumatic central pain. We discuss pain in the context of injury severity and military versus civilian populations. We are only starting to understand the biological mechanisms behind post-traumatic pain and associated psychological distress following TBI, with genetic, biochemical and imaging studies pointing to the dopaminergic, neurotrophic factors and the role of Apolipoprotein. Physiological and neurological mechanisms are proposed to partially explain this interaction between post-traumatic pain and psychological distress. Nevertheless, the evidence for the role of structural brain damage remains incomplete and to a large extent debatable, as it is still difficult to establish clear causality between brain trauma and chronic pain. Finally, general aspects of management of chronic pain post-TBI are addressed.

1. Introduction

Traumatic brain injury (TBI) is a serious and debilitating condition that affects 1.7 million Americans every year (Gooch et al., 2017). The increased accessibility to motor vehicles in developing countries is leading to more TBIs, making it a worldwide public health issue (Abdelgadir et al., 2017). Sport and recreationally related TBIs are also increasing, accounting for approximately 3.4 million US-emergency department visits between 2001 and 2012 (Coronado et al., 2015). The reported incidence is higher in males and in unfavorable socioeconomic situations (Kisser et al., 2017). With the recent military conflicts and returning veterans, TBIs have also generated attention as a public health concern, as 11–70% of injuries resulting from blasts being classified as TBI (Armistead-Jehle et al., 2017; Lindquist et al., 2017; Mortera et al., 2017).

TBI is defined by a blunt or blast type injury to the brain that results in a sudden acceleration and/or deceleration of brain matter inside the skull leading to an alteration in brain function (Menon et al., 2010). More than 75% of all TBI belong to the category of mild TBI (mTBI), which means that loss of consciousness and/or confusion lasted less than 30 min. Long term follow-up studies have showed that consequences can be debilitating and sometimes fatal, whether the injury is mild with an absence of radiological evidence, or more severe resulting in lacerations and destruction of brain structures (Manley et al., 2017; Ruet et al., 2017). In mild cases, patients are infringed by a myriad of symptoms grouped under the umbrella of post-concussion syndrome (PCS), with the most frequently reported symptom being headache (King et al., 1995; Mullally, 2017). Paradoxically, in moderate-severe TBI, headaches are less common, but fatigue and sleep disturbances are reported by more than 60% of the cases (Beaulieu-Bonneau and Ouellet, 2016; Couch and Bearss, 2001; Sigurdardottir et al., 2009). Much more literature is available in mild TBI and in moderate-to-severe with regards to pain.

As early as 1966, Henry Miller described a mental after-effect of head injury on otherwise healthy individuals. His paper argues that headaches, depression, and other mental states are either driven by financial compensation or a dormant condition triggered by trauma (Miller, 1966).

Until today, it is still unclear if a direct relationship exists between the mental and painful symptoms that follow TBI and the damage to brain tissue itself (Choe, 2016; Dobscha et al., 2009). Many other factors have been demonstrated to contribute to PCS, such as genetics, premorbid conditions, litigation, and environmental factors (Hiploylee et al., 2017; Hou et al., 2012; Lange et al., 2014; Merritt and Arnett,

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http://dx.doi.org/10.1016/j.pnpbp.2017.06.007
Received 26 April 2017; Received in revised form 9 June 2017; Accepted 13 June 2017

2016). Comorbidities post-TBI varies with severity of injury and with population, civilian vs military. For instance, it has been suggested that TBI may be the trigger to other latent physiological problems such as post-traumatic stress disorders and sleep disturbances in military with moderate-to-severe TBI (Seal et al., 2017) and chronic pain in civilians with mild TBI (Ponsford et al., 2000; Scheenen et al., 2017).

In this review, we will focus on post-traumatic pain conditions, psychological distress, as well as on the intimate relationship between them.

2. Pain after TBI

Chronic pain is reported by 58% of mild and 52% of moderate to severe TBI, with headaches being the highest reported, followed by neck, shoulders, back and upper limbs. Systematically in the literature of civilians, the report of chronic pain is inversely correlated with severity of injury (Beetar et al., 1996; Lahz and Bryant, 1996; Nampiaparampil, 2008). On the other hand, in a recent large military study of more than 100,000 veterans, it was shown that the risk of developing chronic pain (more than three month) was higher in moderate-to-severe TBI than in mild TBI. This risk added even more in the presence of PTSD and depression (Seal et al., 2017).

2.1. Acute and chronic post-traumatic headachesB76

Post-traumatic headache (PTHA) is the most common and the most persistent symptom following mTBI with a prevalence ranging from 47 to 95% (Moye and Pradhan, 2017). Acute and chronic headache complaints after TBI are classified under headache attributed to head and/or neck trauma by the International Headache Society Classification II (ICHD, 2004; Nampiaparampil, 2008; Walker, 2004).PTHA prevalence across 23 studies in TBI patients was assessed at 58% in civilians (higher in mild TBI at 75%, and 43% in veterans) (Nampiaparampil, 2008).

In the acute post-TBI period, a study showed that 40% of patients with mTBI reported headache in the first 10 days that impacted their mood and sleep quality (Chaput et al., 2009). Among all post-concussion symptoms assessed by the Rivermead post-concussion symptoms questionnaire, eight symptoms are identified as being specific to mTBI at 3 months when compared to other injuries without head injury, namely headaches, dizziness, intolerance to stress, forgetfulness, poor concentration, taking longer to think, blurred vision, and personality change (Kraus et al., 2005; Laborey et al., 2014). The authors emphasize that a greater incidence of headache exists, even more than the other symptoms, specifically following mTBI in comparison with other injuries. In another study, it was shown that while 54% of mTBI patients reported headaches immediately after injury, the prevalence peaks at six months to reach 70%. More than one third reported persistent headaches across all measured time points, with age being an important risk factor (Lucas et al., 2014).

On the other hand, in combat veterans, the intensity of PTHA was rated moderate to severe in 60% of patients (Bosco et al., 2013). In this population, one has to be careful attributing PTHA to TBI as it can also be a result of post-traumatic stress disorder (PTSD). In fact, it was shown that pain was higher in the presence of PTSD and mTBI than with mTBI alone (Stojanovic et al., 2016).

In moderate to severe TBI, PTHA is reported by 33–38% of patients on a daily basis and tends to decrease with time. Interestingly, PTHA improvement is associated with less anxiety and depression. Those that reported PTHA at 6 months also did at one year with six months suggested to be a turning point to the chronicity of symptoms (Uomoto and Esselman, 1993; Walker et al., 2005).

In rare cases, other types of headaches have been described in case reports following TBI. There is a description of post-traumatic short-lasting unilateral neuralgiform pain with conjunctival injection and tearing (SUNCT) belonging to the family of trigeminal neuralgia. This type of headache is described as sharp, stabbing in the frontal and orbital areas radiating to the temporal area (Jacob et al., 2008; Putzki et al., 2005). Although only a few case reports have been described, TBI was the common denominator that directly triggered SUNCT.

2.2. Chronicity of other pain complaints

The transition of acute TBI pain to chronic pain involves a complex interaction of neurobiological and psychosocial factors. The risk of developing chronic pain after TBI approached 6 times higher with high initial pain intensity in mTBI. History of depression, PTSD and presence of sleep disturbances are also crucial factors for the development of chronic pain (J. L. Ponsford et al., 2000; Radresa et al., 2014). On the other hand, amnesia, whether retrograde or anterograde is not associated with chronicity of post-concussion symptoms, in favor of the idea that severity of TBI is inversely associated with chronic pain (Luoto et al., 2015). However, one has to keep in mind that in more severe injuries, opioids and other pain medication consumption might interfere with reported pain (Hudson et al., 2017).

Another important factor that one should consider when assessing symptoms following TBI is the presence of other diagnosis, for instance, the presence of spinal cord injuries and orthopedic injuries. In fact, TBI is accompanied by another diagnosis in more than 40% of cases (Jodoin et al., 2016). Most of the literature available centers in the description of post-traumatic headaches; however, one should keep in mind other musculoskeletal conditions especially in the presence of other injuries. In moderate-to-severe TBI, musculoskeletal complaints (stiffness and aching in joints) were present in 79% of patients, more than 15 years after trauma (Brown et al., 2011).

There is an interesting construct of pain between genders. Some studies have reported no gender difference in pain intensity after mTBI (Mollayeva et al., 2017; Pugh et al., 2016). However, in males, depression and anxiety explain the highest variance, whereas in females, this was mainly explained by the level of education and sleep disturbances (Mollayeva et al., 2017). In another study, a stratified gender effect was analyzed in a veteran population of mTBI where it was concluded that women were more likely to have headaches and depression, whereas men were more likely to report low back pain and report substance abuse problems. However, both genders combined had a higher chance of reporting the polytrauma triad (pain, mental health and TBI) (Pugh et al., 2016). On the other hand, other studies show that females tend to sustain more PTHA over time (Hoffman et al., 2011; Jensen and Nielsen, 1990). In conclusion, the gender difference in post-traumatic pain is complex and implies different comorbidities.

A less commonly reported severely painful condition occurs after neurogenic heterotopic ossification, which is defined as the formation of mature, lamellar bone inside soft-tissue. Its prevalence ranges between 4% and 20% following TBI (Cipriano et al., 2009; J. E. Reznik et al., 2017; J.E. Reznik et al., 2014; Van Kampen et al., 2011). Neurogenic heterotopic ossification can be classified as a musculoskeletal pain condition following TBI, however, the mechanism by which it is triggered remains unknown (Morgan and Morgan, 2014).

Pain assessment in the emergency department is an area where much more improvement should be done. In a study by Bazarian et al. it was shown that assessment of pain in the ER was only done in 44% of mTBI patients, with less than half given analgesics in presence of pain. Moreover, recommendations for pain follow-up were lacking as it will be described in the next section (Bazarian et al., 2005).

In complaints of PTHA or pain in general, dysfunctional pain modulation mechanisms are thought to play an important role (Defrin, 2014; Defrin et al., 2010; Defrin et al., 2014). Pain onset and persistence in TBI patients can also be due to the single or combined effect of several mechanisms: 1) central pain buildup due to brain insult; 2) dysfunctional pain input modulation to reduce ascending sensory information to the central nervous system, or reduced activation or descending pain inhibition; 3) alterations in the midbrain periaqueductal