

Name of Disorder: **Traumatic Brain Injury**

Essay Title : **Brain injury and increased risk of Alzheimer's disease**

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Acquired brain injury (ABI) and traumatic brain injury (TBI) are very common worldwide [1]. In the US, more than 1.7 million individuals experience TBI annually and the economic burden of TBI has been estimated to be more than US\$60 billion in 2000 [2]. In Australia, about 432,700 patients had an ABI and 28,700 of these individuals named ABI as the main cause of limitation in their daily living activities [3]. More than half of these individuals were under age 65, with about half of them aged 15-34 [3]. Prevalence and incidence rates are higher for males at all ages (2) and are exponentially increasing, mostly in developing countries [4]. As TBI is commonly seen in individuals aged less than 60 years old, the brain-injured patients not only lose their ability to productively contribute to society but will inevitably require long-term care and support imposing significant burden to the patient's family and carers.

TBI influences the brain through two different cascades of events, namely primary and secondary cascades. While the primary cascade results from mechanical forces affecting the brain at the time of the injury, the secondary cascade may begin within seconds, weeks, or months after the primary incident due to delayed biochemical responses and metabolic and cellular changes [2]. Unfortunately, the negative effects of TBI are not limited to the time of injury or the recovery period. Even those individuals who recover from TBI and return to previous normal level of functioning are at risk of other complications including neurodegenerative diseases such as dementia, later in life. TBI has been found to be a significant risk factor for Alzheimer's disease (AD), the most common form of dementia [5, 6]. While research is yet to identify the potential mechanisms underlying the TBI and AD relationship, the severity of TBI plays a significant role and this relationship is more pronounced amongst relatives of AD patients. In addition, TBI decreases the age of onset for late onset AD, usually seen in individuals aged 65 years old and over. As a result, a person with a history of TBI is more likely to develop AD [7]. Interestingly, this relationship is heightened in individuals who carry a specific gene, namely apolipoprotein E  $\epsilon$ 4 allele (APOE  $\epsilon$ 4), the main genetic risk factor for late onset AD. In one of the earlier studies, the risk of developing AD in TBI patients with APOE  $\epsilon$ 4 allele was 10 times higher when compared to APOE  $\epsilon$ 4 non-carriers [8]. However, this finding has not been replicated in other studies. In one of these studies, the authors found that the risk of developing AD was higher in APOE  $\epsilon$ 4 non-carriers as compared to carriers [9]. That is, in people without genetic susceptibility to AD, having a history of TBI can dramatically change the course of aging and increase their chances of developing AD. Therefore, the role of APOE  $\epsilon$ 4 in mediating the relationship between TBI and AD remains controversial and should be investigated further.

A potential mechanism linking TBI to future AD is the pathological elevation of amyloid-beta ( $A\beta$ ) protein within a few hours of TBI, and the subsequent accumulation of  $A\beta$  plaques, one of neuropathological hallmarks of AD, in the damaged site [10-12]. As Johnson and colleagues (2010) suggest, formation of  $A\beta$  plaques could be the result of an imbalance between  $A\beta$  production and clearance pathways following TBI, as well as the accumulation of amyloid precursor protein (APP) in damaged axons [10]. These changes are themselves neurotoxic and can result in further damage to the already injured brain tissue.

Clearly, investing in the development of proper and improved treatment modalities for TBI has significant implications for socio-medical costs and, perhaps more importantly, for the quality of life and functional independence of the affected individuals and their families. However, positive effects of TBI research and treatment may very well extend beyond the natural course of TBI itself,

having significant implications for nervous system disorders and diseases that are more likely to be seen in the individuals with a history of TBI.

## References

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