Proceedings of ICBioMed 2024 Workshop: Computational Proteomics in Drug Discovery and Development from Medicinal Plants
DOI: 10.54254/2753-8818/65/2024.LA18209

Application of functional magnetic resonance imaging in diagnosing blast-related traumatic brain injuries

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Abstract. This updated review examines the use of functional magnetic resonance imaging (fMRI) for diagnosing blast-related traumatic brain injury (bTBI). In the past ten years, significant advancements have been made in our understanding of the mechanisms underlying bTBI, which is increasingly prevalent among both soldiers and civilians affected by war conflicts. This review summarises key findings from recent bTBI publications, highlighting new evidence regarding the mechanisms, recovery, and diagnostic approaches associated with this condition. It provides a comprehensive overview of the fMRI techniques currently employed to investigate mental processes commonly disrupted by bTBI, such as working memory, selective attention, and emotional processing. Additionally, the review addresses the limitations of fMRI as a diagnostic tool, including issues related to sensitivity and specificity. Finally, it discusses the potential applications of this research in clinical settings, emphasising the need for improved diagnostic methods to better identify and treat individuals suffering from the effects of bTBI.

Keywords: review, functional magnetic resonance imaging, blast-related traumatic brain injuries.

1. Introduction

Traumatic brain injuries (TBI) are induced structural injuries as a result from external forces, causing disruptions in consciousness, memory, and mental state [1]. Blast traumatic brain injury (bTBI) refers to a form of TBI generally resulting from a powerful explosion impacting the head, with primary mechanisms including ballistic head trauma, blunt head trauma, and primary blast-induced head trauma [2]. The bTBI is a disorder that exists on a spectrum, with cases ranging from mild, often presenting symptoms similar to or occurring with post-traumatic stress disorder (PTSD), to severe cases commonly associated with polytrauma [3]. There is a limited amount of research on the long-term effects of bTBI, but we can consider the long-term effects of non-blast-related TBI due to their similarity in nature. Traumatic brain injury may lead to a variety of symptoms, ranging from physical effects like dizziness and nausea, to cognitive difficulties like memory lapses and problems with focusing. It can also trigger behavioural shifts, including emotional instability and, in some cases, loss of consciousness [1]. It is worth mentioning, however, that classifications of TBI symptoms are inconsistent as multiple variables, such as the severity of head trauma or the proximity of medical care, may cause different symptoms [2]. The bTBI has always been frequent in soldiers, and is becoming increasingly prevalent in civilians in war conflicts such as in Ukraine and Iraq [4, 5].

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The fMRI is a technique that measures changes in blood flow and oxygenation resulting from increased neural activity [6]. Common imaging techniques like CT and MRI may not always be able to diagnose mild bTBI, so investigating using fMRI to diagnose bTBI will act as a useful alternative. The goal of the current review is to update the previous review [7] with more recent findings and considerations for using fMRI in bTBI diagnosis.

2. Summary of Recent bTBI Publications

2.1. The understanding of bTBI

Blast traumatic brain injury (TBI) shares similarities with closed head injuries. It includes primary blast injuries from pressure changes, secondary injuries from flying debris, tertiary injuries from body acceleration by blast winds, and quaternary injuries encompassing burns and lung damage from toxic gases. Each of these types of bTBI arise from different blast effects [8-10].

The exact processes through which primary blast exposure leads to tissue damage remain unclear, but several critical factors have been identified, which includes spallation, implosion, cavitation, and inertial forces [11, 12]. Spallation takes place when a shock wave moves from a more dense medium to a less dense one, causing pieces of the denser material to break away and become embedded in the less dense material [12]. Cavitation and implosion are interconnected phenomena that occur when negative pressure causes dissolved gases in fluids to form bubbles. Under negative pressure, these bubbles can be compressed and then quickly expand when the pressure shifts. The phenomena of cavitation and implosion have both been associated with lung injuries caused by primary blast exposure [13-15]. Inertial effects occur at the boundaries between tissues with different densities when blast pressure causes these materials to accelerate at varying rates. This differential acceleration creates shearing forces that can lead to injury [12].

Computer simulations suggest additional potential injury mechanisms, such as high strain in coup and contrecoup regions [16], and shear stresses in white matter linked to diffuse axonal injury [17]. A thoracic mechanism proposes that primary blast waves indirectly impact the brain by compressing the abdomen and chest, which in turn generates harmful pressure waves that reach the brain [17].

2.2. Assessment and diagnostic of bTBI

Research on blast-induced traumatic brain injury (bTBI) focuses on identifying reliable biomarkers that can aid in the diagnosis and treatment of injuries. Computed tomography (CT) is the standard imaging method for suspected TBI, primarily used to rule out severe injuries. Other imaging techniques such as MRI and fMRI are used less often in military settings [2]. Despite efforts to establish definitive biomarkers, challenges remain due to the heterogeneous nature of bTBI, the complexity of blast scenarios, and the lack of quality longitudinal data. Ongoing research is needed to develop reliable biomarkers that can provide critical insights into bTBI [3].

In the past 10 years, there have been notable advancements in the diagnostic and assessment techniques for bTBI. In 2018, the U.S. The Food and Drug Administration approved the first blood test for assessing mild traumatic brain injury (mTBI) [18]. In addition, research has referenced the use of positron emission tomography (PET) and diffusion tensor imaging (DTI) [19]. Functional imaging techniques like PET are used to assess traumatic brain injury (TBI), but they are not standard during the evaluation of mild TBI in clinical or military settings. PET is thought to be more effective in detecting mild trauma compared to standard imaging methods like CT or MRI, as it can reveal abnormalities in mild TBI that are associated with prognosis and neuropsychological decitis, even when traditional structural imaging appears normal [20-22]. DTI is a technique that measures the integrity of white matter fibres using metrics like fractional anisotropy and mean diffusivity. DTI is sensitive to subtle damage and diffuse axonal injury, making it a valuable tool for assessing blast-related mild TBI [23].

3. Current fMRI Techniques for Investigating bTBI

Clinical evaluations using standard CT and MRI often show limited results for mild traumatic brain injury (mTBI). Advanced neuroimaging methods, like fMRI, can effectively monitor the functional state of grey matter during tasks or at rest, correlating with outcomes such as post-concussive syndrome (PCS), PTSD, and depression [24]. A review by Mu et al. summarises the results of 9 fMRI studies, involving 242 veterans suffering from mild traumatic brain injury (mTBI) caused by blast exposure. Six of these studies employed task-based fMRI, with two focusing on emotional processing and four on executive functions, while three utilised resting-state fMRI [24]. Results from task-based studies showed notable brain activation in areas linked to emotional processing and executive function, particularly among mTBI patients with conditions like PTSD and major depressive disorder (MDD). Additionally, military mTBI patients exhibited greater activation in certain brain regions compared to their civilian counterparts [24]. These findings are consistent with established theories regarding dysfunction in mTBI. However, the variability in study designs and analytical methods complicates the ability to synthesise the results effectively [24]. In the case of bTBI, resting-state fMRI is more likely to be used as it can be done to patients who are unable to follow task instructions [25]. Overall, more evidence is needed to better understand whether fMRI can be used for mTBI.

4. Limitations of using fMRI for diagnosis of bTBI

There are several limitations of fMRI. Firstly, the temporal resolution is affected by the delay in the hemodynamic response, which hampers the assessment of rapid neural events. Additionally, the complexity of the data necessitates sophisticated analysis and preprocessing, given the large datasets involved. The BOLD signal is also sensitive to vascular conditions, which can influence its changes and impact the accuracy of results. Finally, interpreting resting-state fMRI data is complex and demands knowledge of both anatomy and neuroscience in order to draw meaningful conclusions [25].

5. Conclusion

This review has highlighted the progress in utilising functional magnetic resonance imaging (fMRI) for the diagnosis of blast-related traumatic brain injury (bTBI). Key points include in-depth understanding of bTBI mechanisms, reliable diagnostic techniques, and the effectiveness of fMRI in examining disrupted mental processes, like working memory and emotional processing. fMRI is regarded as a useful tool for investigating the neurophysiological mechanisms and functional deficits associated with bTBI, offering insights that traditional imaging methods may miss, particularly in cases of mild injury. Continued research is crucial to enhance our understanding of bTBI and to refine diagnostic approaches further. As the field evolves, it is essential to address the existing limitations of fMRI, such as temporal resolution and data complexity, to optimise its application in clinical settings. Ongoing advancements in neuroimaging techniques will pave the way for improved diagnostics and interventions for individuals affected by bTBI.

References

[1] Blennow, K., Brody, D.L., Kochanek, P.M., Levin, H., McKee, A., Ribbers, G.M., Yaffe, K. and Zetterberg, H. (2016). Traumatic brain injuries. *Nature Reviews Disease Primers*, *2*(1). doi: https://doi.org/10.1038/nrdp.2016.84.

[2] Bryden, D.W., Tilghman, J.I. and Hinds, S.R. (2019). Blast-Related Traumatic Brain Injury: Current Concepts and Research Considerations. *Journal of Experimental Neuroscience*, *13*, p. 117906951987221. doi:https://doi.org/10.1177/1179069519872213.

[3] Agoston DV;Kamnaksh A (2015). Modeling the Neurobehavioral Consequences of Blast-Induced Traumatic Brain Injury Spectrum Disorder and Identifying Related Biomarkers. Available at: https://pubmed.ncbi.nlm.nih.gov/26269904/.

[4] Zhang, J.K., Botterbush, K.S., Bagdady, K., Lei, C.H., Mercier, P. and Mattei, T.A. (2022). Blast-related Traumatic Brain Injuries Secondary to Thermobaric Explosives: Implications for the War in Ukraine. *World Neurosurgery*. doi:https://doi.org/10.1016/j.wneu.2022.08.073.

DOI: 10.54254/2753-8818/65/2024.LA18209

[5] Hoz, S.S., Al-Sharshahi, Z.F., Dolachee, A.A., Al- Smaysim, A.M., Matti, W.E., Bydon, A. and Kadhum, H.J. (2021). Blast-Induced Traumatic Brain Injuries: Experience from the Deadliest Double Suicide Bombing Attack in Iraq. *World Neurosurgery*, 145, pp.e192–e201. doi:https://doi.org/10.1016/j.wneu.2020.09.167.

[6] Logothetis, N.K. (2008). What we can do and what we cannot do with fMRI. *Nature*, 453(7197), pp.869–878. doi:https://doi.org/10.1038/nature06976.

[7] Graner, J., Oakes, T.R., French, L.M. and Riedy, G. (2013). Functional MRI in the Investigation of Blast-Related Traumatic Brain Injury. *Frontiers in Neurology*, 4. doi:https://doi.org/10.3389/fneur.2013.00016.

[8] Aswati Aravind, Arun Reddy Ravula, Chandra, N. and Pfister, B.J. (2020). Behavioral Deficits in Animal Models of Blast Traumatic Brain Injury. *Frontiers in Neurology*, *11*. doi:https://doi.org/10.3389/fneur.2020.00990.

[9] Yamamoto, S., DeWitt, D. and Prough, D. (2018). Impact & Blast Traumatic Brain Injury: Implications for Therapy. *Molecules*, 23(2), p.245. doi:https://doi.org/10.3390/molecules23020245.

[10] Mayorga, M.A. (1997). The pathology of primary blast overpressure injury. *Toxicology*, 121(1), pp.17–28. doi:https://doi.org/10.1016/s0300-483x(97)03652-4.

[11] Stuhmiller, J., Phillips, Y. and Richmond, D. (2024). Chapter 7 - The Physics and Mechanisms of Primary Blast Injury. Google.com. Available at: https://scholar.google.com/scholar_lookup?title=The+Physics+and+Mechanisms+of+Primary+Blast+Injury:+Conventional+Warfare:+Ballistic.

[12] Wolf, S.J., Bebarta, V.S., Bonnett, C.J., Pons, P.T. and Cantrill, S.V. (2009). Blast injuries. *The Lancet*, 374(9687), pp.405–415. doi:https://doi.org/10.1016/s0140-6736(09)60257-9.

[13] Goeller, J., Wardlaw, A., Treichler, D., O'Bruba, J. and Weiss, G. (2012). Investigation of Cavitation as a Possible Damage Mechanism in Blast-Induced Traumatic Brain Injury. *Journal of Neurotrauma*, 29(10), pp.1970–1981. doi:https://doi.org/10.1089/neu.2011.2224.

[14] Ho, A.M.-H. (2002). A simple conceptual model of primary pulmonary blast injury. *Medical Hypotheses*, 59(5), pp.611–613. doi:https://doi.org/10.1016/s0306-9877(02)00153-6.

[15] Nakagawa, A., Manley, G.T., Gean, A.D., Keita Ohtani, Armonda, R.A., Tsukamoto, A., Yamamoto, H., Takayama, K. and Tominaga, T. (2011). Mechanisms of Primary Blast-Induced Traumatic Brain Injury: Insights from Shock-Wave Research. *Journal of Neurotrauma*, 28(6), pp.1101–1119. doi:https://doi.org/10.1089/neu.2010.1442.

[16] Zhang (2014). A finite element study of blast traumatic brain injury - biomed 2009. *Biomedical sciences instrumentation*, 45. Available at: https://pubmed.ncbi.nlm.nih.gov/19369750/ [Accessed 1 Sep. 2024].

[17] Courtney, A.C. and Courtney, M.W. (2009). A thoracic mechanism of mild traumatic brain injury due to blast pressure waves. *Medical Hypotheses*, 72(1), pp.76–83. doi:https://doi.org/10.1016/j.mehy.2008.08.015.

[18] Commissioner, O. of the (2020). FDA authorizes marketing of first blood test to aid in the evaluation of concussion in adults. *FDA*. Available at: https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-first-blood-test-aid-evaluation-concussion-adults.

[19] Elder, G.A., Mitsis, E.M., Ahlers, S.T. and Cristian, A. (2010). Blast-induced Mild Traumatic Brain Injury. *Psychiatric Clinics of North America*, 33(4), pp.757–781. doi:https://doi.org/10.1016/j.psc.2010.08.001.

[20] Newberg, A.B. and Alavi, A. (2003). Neuroimaging in patients with head injury. *Seminars in Nuclear Medicine*, 33(2), pp.136–147. doi:https://doi.org/10.1053/snuc.2003.127299.

[21] Van Heertum, R.L., Greenstein, E.A. and Tikofsky, R.S. (2004). 2-deoxy-fluorglucose–positron emission tomography imaging of the brain: Current clinical applications with emphasis on the dementias. *Seminars in Nuclear Medicine*, 34(4), pp.300–312. doi:https://doi.org/10.1053/j.semnuclmed.2004.03.003.

[22] Ward, J., Ly, M. and Raji, C.A. (2023). Brain PET Imaging. *PET Clinics*, 18(1), pp.123–133. doi: https://doi.org/10.1016/j.cpet.2022.09.010.

[23] Wilde, E.A., McCauley, S.R., Hunter, J.V., Bigler, E.D., Chu, Z., Wang, Z.J., Hanten, G.R., Troyanskaya, M., Yallampalli, R., Li, X., Chia, J. and Levin, H.S. (2008). Diffusion tensor imaging of acute mild traumatic brain injury in adolescents. *Neurology*, 70(12), pp.948–955. doi:https://doi.org/10.1212/01.wnl.0000305961.68029.54.

[24] Mu, W., Catenaccio, E. and Lipton, M.L. (2017). Neuroimaging in Blast-Related Mild Traumatic Brain Injury. *Journal of Head Trauma Rehabilitation*, 32(1), pp.55–69. doi:https://doi.org/10.1097/htr.0000000000000213.

[25] Lv, H., Wang, Z., Tong, E., Williams, L.M., Zaharchuk, G., Zeineh, M., Goldstein-Piekarski, A. N., Ball, T.M., Liao, C. and Wintermark, M. (2018). Resting-State Functional MRI: Everything That Nonexperts Have Always Wanted to Know. American Journal of *Neuroradiology*, 39(8). doi:https://doi.org/10.3174/ajnr.a5527.