Proposal: Diagnostics for Early Detection of Blood-Brain Barrier Disruption in Mild Traumatic Brain Injury Using Multi-Modal Approaches

Yan Lu, Ph.D. Assistant Professor[a] and Ross Gore, Ph.D. Research Associate Professor[b]

[a]School of Engineering and Computing, Christopher Newport University, Newport News, VA
[b]Office of Enterprise Research and Innovation (OERI), Old Dominion University, Norfolk, VA

Mild traumatic brain injury (mTBI) presents a significant health challenge, particularly in military settings where blast exposures and concussions are common. Despite its high prevalence, early detection remains difficult due to symptom variability, co-occurring conditions, and the reality that many cases go untreated or are managed outside of hospital environments. The blood-brain barrier (BBB)—a selective, protective interface that regulates molecular movement between the blood and the brain—plays a critical role in mTBI pathophysiology. When compromised following trauma, BBB disruption permits harmful substances to enter the brain, potentially worsening neural injury and contributing to long-term neurological consequences.

Recent studies have shown that meningeal enhancement and cerebrospinal fluid enhancement in the subarachnoid space serve as imaging biomarkers of BBB disruption in mTBI patients, even when conventional CT scans appear normal. Notably, such BBB compromise often occurs near the falx and dural sinuses, suggesting a possible connection to the brain's lymphatic system and immune surveillance pathways.

Current diagnostic methods frequently fail to detect subtle BBB disruptions that precede long-term damage. In collaboration with the Virginia Modeling, Analysis and Simulation Center (VMASC), Fort Eustis, and Naval Medical Center Portsmouth, we propose an integrated research methodology that combines blood biomarker analysis with advanced imaging techniques for BBB assessment. This prospective study will follow individuals with suspected mTBI who will undergo neuropsychological testing, alongside comprehensive, longitudinal neuroimaging. Imaging will include specialized diffusion tensor imaging (DTI) sequences to evaluate BBB integrity and white matter tract damage in key regions such as the Corpus Callosum, Cingulum, Fornix, and Internal/External Capsule.

To our knowledge, no existing study has integrated imaging and neuropsychological evaluation at this scale in a controlled, longitudinal framework. The significance of this research lies in its focus on BBB dysfunction—a central mechanism in mTBI pathology—and its development of a multi-modal analytical framework that integrates diverse data sources. This includes imaging data, blood biomarkers, and neurophysiological evaluations, all processed through advanced AI models. Our approach directly addresses the limitations of current single-modal diagnostic models by capturing the complexity and multifaceted nature of BBB disruption.

Through this collaborative effort led by VMASC, Christopher Newport University (CNU) will play a key partner role in the research and engage with regional partners in government and healthcare. The project will employ data science, artificial intelligence (DS/AI), and multi-modal learning techniques to achieve its outcomes. Ultimately, this initiative aims to establish long-term, high-impact research collaborations between CNU researchers and the broader community. The anticipated results of this study will serve as a foundation for research papers, and a major funding proposal to agencies such as the Department of Defense (DOD) USAMRDC under the Extramural Medical Research program.

Further author information:
Yan Lu: E-mail: yan.lu@cnu.edu, Telephone: 757-594-7626
Ross Gore.: E-mail: rgore@odu.edu, Telephone: 757-638-7002