



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Diagnosics and Biomarkers

Chemokine Ligand 2 Levels in Cerebrospinal Fluid (CSF) as an Early-response Biomarker for Blast- Induced Neurotrauma

The neuroinflammatory response is an early pivotal immune process following brain injury. The inflammatory mediator chemokine ligand 2 (CCL2), also known as monocyte chemoattractant protein-1 (MCP-1), has been implicated in the pathogenesis of brain ischemia, Alzheimer's disease, and other neurodegenerative diseases.¹ Using a rat model of single and repeated blast exposures in a shock tube, researchers at the Walter Reed Army Institute of Research WRAIR investigated the time-course of changes in MCP-1/CCL2 level in the CSF and blood. Significantly increased concentrations of CCL2 in CSF were evident by one hour after blast exposure and persisted over 24 hours with peak levels measured at six hours post-injury. The increased levels of CCL2 in CSF corresponded with both the number and the intensities of Blast Overpressure (BOP) and were also commensurate with the extent of neuro-motor impairment and neuropathological abnormalities resulting from these exposures. CCL2 levels in CSF and in plasma were tightly correlated with the levels of CCL2 messenger ribonucleic acid (mRNA) in the cerebellum, the brain region most consistently neuropathologically disrupted by blast. In view of the roles of CCL2 that have been implicated in multiple neurodegenerative disorders, it is likely that the sustained high levels of CCL2 and the increased expression of its main receptor CCR2 in the brain after blast may similarly contribute to neurodegenerative processes after blast exposure. In addition, the markedly elevated concentration of CCL2 in CSF might be a candidate early-response biomarker for diagnosis and prognosis of blast-induced Traumatic Brain Injury (TBI). Since cytokines such as CCL2 are known to have both beneficial and detrimental effects in the milieu of the injured brain, and contribute to degenerative and regenerative processes, the timing of these responses is critical to their neurobiological importance. By revealing important neurobiological mechanisms that underlie BOP-induced brain injury, these experiments will provide valuable insights into detection and therapeutic countermeasures for affected Service Members.

¹ Wang, Y., Wei, Y., Oguntayo, S., Wilder, D., Tong, L., Su, Y., ... Long, J. B. (2016). Cerebrospinal Fluid Chemokine (C-C Motif) Ligand 2 Is an Early-Response Biomarker for Blast-Overpressure-Wave-Induced Neurotrauma in Rats. *Journal of Neurotrauma*. <https://doi.org/10.1089/neu.2016.4465>

