# Neurocognitive and Psychological Health Treatment Strategies

## Serotonin Effects of Blast Traumatic Brain Injury (TBI) and Neurocognitive Behavior

Patients who have experienced blast-induced mild TBI (mTBI) are also at an increased risk for developing depression and posttraumatic stress disorder (PTSD) compared to the general population through unknown mechanisms. Serotonin is a monoaminergic neurotransmitter synthesized by serotonergic neurons, known to protect the brain due to its antioxidant properties.[1] People with low brain serotonin have reported increased incidence of PTSD.[2,3] In addition to the brain, other sources of endogenous serotonin are platelets and the small intestine. Characterization of serotonin levels in blood, brain, and intestine in relation to the neurocognitive deficits often experienced in response to blast-induced TBI has not been examined before. This Defense Advanced Research Projects Agency (DARPA)-sponsored research project conducted by researchers at the Uniformed Services University of the Health Science (USUHS) is designed to determine the concentration of serotonin in serum, cererbospinal fluid (CSF), and small intestine following blast-induced TBI and investigate any associated depression like effects following repeat blast exposures in rats. Male Sprague Dawley rats were exposed to repeat blast TBI followed by evaluations of cognitive deficits. Animals were followed for either seven days or 28 days, at which time tissue samples were collected for serotonin analysis. Researchers found that serum serotonin levels of blast-induced TBI animals were significantly lower than those of naïve animals throughout the 28 day follow-up period. In contrast, serotonin levels in the CSF and small intestine of the blast-induced TBI animals were significantly elevated at day seven, but returned to baseline by day 28. In addition, animals with blast-induced TBI demonstrated depression like behaviors exhibited by less vertical activity in the open field activity measurements at day three and six post blast but subsided by day 28. This suggests an adaptive mechanism of increased serotonin response by the brain and intestine during the initial stages of blast-induced TBI. Therefore, opportunities may exist for serotonin targeted pharmacological interventions that might benefit at least some components of the cognitive and behavioral symptoms that develop after blast-induced TBI.

---

1 Munoz-Castaneda, J. R., Montilla, P., Padillo, F. J., Bujalance, I., Munoz, M. C., Muntane, J., & Tunez, I. (2006). Role of serotonin in cerebral oxidative stress in rats. Acta Neurobiologiae Experimentalis, 66(1), 1–6.

2 Davis, L. L., Suris, A., Lambert, M. T., Heimberg, C., & Petty, F. (1997). Post-traumatic stress disorder and serotonin: new directions for research and treatment. Journal of Psychiatry & Neuroscience : JPN, 22(5), 318–326.

3 Gardner, A., & Boles, R. G. (2011). Beyond the serotonin hypothesis: mitochondria, inflammation and neurodegeneration in major depression and affective spectrum disorders. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 35(3), 730–743. https://doi.org/10.1016/j.pnpbp.2010.07.030