Evaluation of $N$-acetylcysteine Amide as a Potential treatment option for Traumatic Brain Injury using tandem LC-MS

**Abstract:** Physical injury from sports and freak accidents are common causes of Traumatic Brain Injury (TBI). Commonly overlooked, is TBI via exposure to explosives with prevalence in military personnel and veterans. Existing diagnostics are costly, time consuming, and sometimes insensitive to milder TBI forms, influencing a need for fast and sensitive techniques for mild TBI detection by investigating potential biomarkers that may be altered due to TBI. A pathophysiological consequence of TBI is oxidative stress from reactive oxygen species proliferation after physical disruption of neurons and glial cells leading to alteration in the levels of endogenous antioxidants and their oxidized products in the brain and peripheral fluids. Antioxidant therapy using $N$-acetylcysteine Amide can be useful mitigators of this oxidative stress characteristic. Additionally, lipid peroxidation by-products and other important small molecule biomarkers can give invaluable information about TBI progression. In our study, rats were exposed to open-field blasts mimicking of a real-life explosion to induce TBI and evaluate antioxidant therapy. Subsequently, various biomatrices were harvested from test animals for analysis. Coupling rigorous sample clean-up with LC-MS/MS analysis, levels of potential biomarkers for TBI in the groups and sample matrices were determined in this study. The LC-MS/MS methods yielded excellent sensitivity, linearity, recovery, and reproducibility for all the investigated analytes.