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Traumatic Brain Injury Induced Lipid Profiling of Lipids in Mice Serum Using UHPLC-Q-TOF-MS

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Abstract : Introduction: Traumatic brain injury (TBI) is defined as the temporary or permanent alteration in brain function and pathology caused by an external mechanical force. It represents the leading cause of mortality and morbidity among children and youth individuals. Various models of TBI in rodents have been developed in the laboratory to mimic the scenario of injury. Blast overpressure injury is common among civilians and military personnel, followed by accidents or explosive devices. In addition to this, the lateral Controlled cortical impact (CCI) model mimics the blunt, penetrating injury. Method: In the present study, we have developed two different mild TBI models using blast and CCI injury. In the blast model, helium gas was used to create an overpressure of 130 kPa (±5) via a shock tube, and CCI injury was induced with an impact depth of 1.5mm to create diffusive and focal injury, respectively. C57BL/6J male mice (10-12 weeks) were divided into three groups: (1) control, (2) Blast treated, (3) CCI treated, and were exposed to different injury models. Serum was collected on Day1 and day7, followed by biphasic extraction using MTBE/Methanol/Water. Prepared samples were separated on Charged Surface Hybrid (CSH) C18 column and acquired on UHPLC-Q-TOF-MS using ESI probe with inhouse optimized parameters and method. MS peak list was generated using Markerview TM. Data were normalized, Pareto-scaled, and log-transformed, followed by multivariate and univariate analysis in metaboanalyst. Result and discussion: Untargeted profiling of lipids generated extensive data features, which were annotated through LIPID MAPS® based on their m/z and were further confirmed based on their fragment pattern by LipidBlast. There is the final annotation of 269 features in the positive and 182 features in the negative mode of ionization. PCA and PLS-DA score plots showed clear segregation of injury groups to controls. Among various lipids in mild blast and CCI, five lipids (Glycerophospholipids {PC 30:2, PE O-33:3, PG 28:3;O3 and PS 36:1 } and fatty acyl { FA 21:3;O2}) were significantly altered in both injury groups at Day 1 and Day 7, and also had VIP score >1. Pathway analysis by Biopan has also shown hampered synthesis of Glycerolipids and Glycerophospholipiods, which coincides with earlier reports. It could be a direct result of alteration in the Acetylcholine signaling pathway in response to TBI. Understanding the role of a specific class of lipid metabolism, regulation and transport could be beneficial to TBI research since it could provide new targets and determine the best therapeutic intervention. This study demonstrates the potential lipid biomarkers which can be used for injury severity diagnosis and identification irrespective of injury type (diffusive or focal).

Keywords : LipidBlast, lipidomic biomarker, LIPID MAPS®, TBI
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