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***Acute and short-term behavioral deficits following mild traumatic brain injury in a mouse model of vitamin C depletion***

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**Introduction:** Children and adolescents are particularly at risk for experiencing mild traumatic brain injuries (mTBI) and long-term cognitive deficits and other behavioral changes frequently follow the initial injury that impact quality of life for sufferers. Increased oxidative stress is also apparent following TBI and exacerbates the neuroinflammatory and excitotoxic response. Vitamin C (ascorbate,) is a critical antioxidant important for maintaining redox balance in the brain and may be an immediate defense mechanism to counteracting oxidative stress following traumatic brain injury. Therefore, dietary deficiency of ascorbate may exacerbate behavioral deficits following traumatic brain injury.

**Methods:** Male and female gulo-/- mice lacking the gulonolactone oxidase, the enzyme necessary for the endogenous synthesis of Ascorbate, were maintained on deficient (0.03g/L, "low") or wildtype-equivalent (1.0g/L, "high") diet. Mice 12-16 weeks of age were exposed to a repeated mild blast injury (3x 38-40PSI) to the frontal cortex, or a sham injury with anesthesia only. Mice underwent the prepulse inhibition task 4 hours following injury treatment (acute) then following two days of recovery from the injury underwent a week of behavioral tasks including the prepulse inhibtion task, rotarod, and tail suspension task to examine learning, memory and emotional function. Mice were euthanized at four hours or nine days following injury and cortex and liver were assessed for ascorbate and oxidative stress measures.

**Results:** Low ascorbate mice had increased oxidative stress levels and disrupted glutamatergic signaling compared to high ascorbate mice 4 hours following mTBI. Additionally, females showed deficits in the prepulse inhibition task that was absent in males in the acute time period following injury. Blast-injured mice exhibited increased anxiety and depressive like behavior, and difficulty with motor learning and memory tasks compared to sham treated animals.

**Discussion:** These studies support a role for mTBI exposure during adolescence leading to persistent changes in behavior. Additionally, insufficient ascorbate in the diet during development may lead to increased oxidative burden following mTBI, thus exacerbating negative behavioral outcomes.

**Keywords:**
Traumatic brain injury (TBI), Vitamin C, Behavior