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

Amanda L. Marino, Ellen C. Cox, Krista C. Paffenroth, Adriana A. Tienda, Tonia S. Rex, Fiona E. Harrison

VANDERBILT KENNEDY CENTER

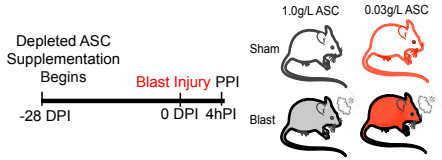
VANDERBILT UNIVERSITY MEDICAL CENTER

BACKGROUND

- Children and adolescents are at increased risk of a mild traumatic brain injury (mTBI)
- Long lasting cognitive and behavioral deficits are common following TBI
- Vitamin C (Ascorbate, ASC) is a critical antioxidant in the brain and is an essential cofactor for the enzyme tyrosine hydroxylase in converting L-Tyrosine to L-Dopa
- **Hypothesis: Dietary depletion of ASC may exacerbate behavioral deficits following traumatic brain injury**

METHODS

- Gulo -/-mice on sufficient (1.0g/L) or depleted (0.03g/L) ASC supplementation received 3 repeated blasts (38-40PSI) or a sham injury
- 4 hours following injury, mice underwent behavioral testing to assess sensorimotor gating deficits via prepulse inhibition of the startle response (PPI)



EXPERIMENTAL RESULTS

Fig. 1. Blast injury and ASC level disrupts PPI

Female mice receiving sufficient ASC show impaired PPI following blast injury compared to sham injured mice that is not observed in depleted ASC mice. Male mice only have a main effect of ASC. (* # p< 0.05, **, ## p< 0.01, effects of ASC or blast, respectively)

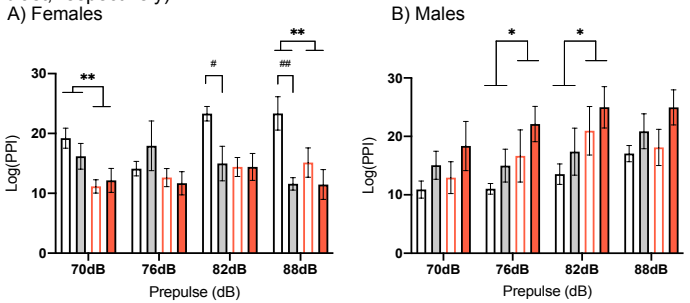


Fig. 2. Decrease in ASC following blast injury and increase in lipid peroxidation in mice with depleted ASC levels

Blast injury caused an acute decrease in brain ASC compared to sham injured animals, but only in sufficient ASC animals. No immediate changes were observed in lipid peroxidation (malondialdehyde) which was already elevated in depleted ASC mice. (* **, p< 0.05, < 0.01, differences as marked)

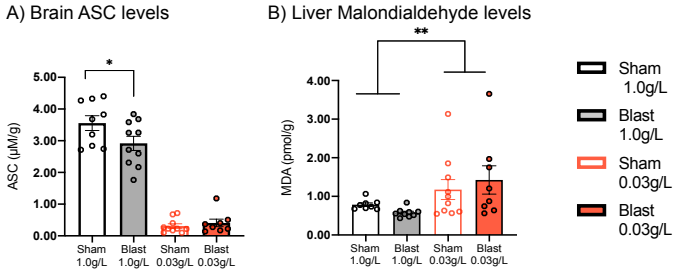
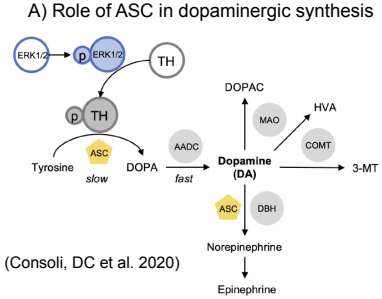
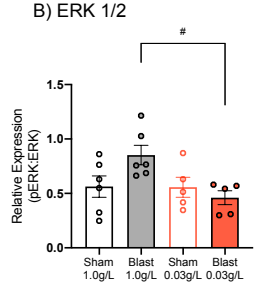


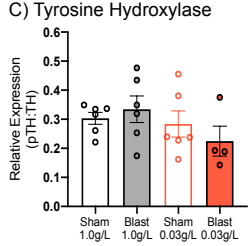
Fig. 3. Altered dopaminergic signaling 4 hours following mTBI

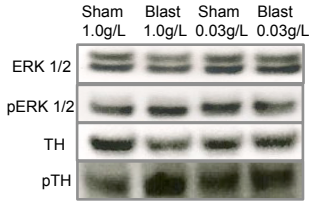
Low ASC mice show significantly decreased phosphorylated ERK and trending towards decreased phosphorylated tyrosine hydroxylase (* p<0.05)



(Consoli, DC et al. 2020)







CONCLUSIONS

- Behavior and neurotransmission changes due to blast were observed at sufficient ASC levels. There was no further effect in mice with ASC depletion which were already impaired
- The opposite effect of blast on PPI was seen in male and female mice
- Acute changes in dopaminergic function were seen 4 h following mTBI