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

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CONCLUSIONS

- 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

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)

A) Females

B) Males

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<0.01, differences as marked)

A) Brain ASC levels

B) Liver Malondialdehyde levels

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)

A) Role of ASC in dopaminergic synthesis

B) ERK 1/2

C) Tyrosine Hydroxylase

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)

BACKGROUND

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

- Depleted ASC
- Supplementation
- Begins
- Blast Injury

- Sham
- 1.0g/L ASC
- 0.03g/L ASC

- Blast
- 1.0g/L ASC
- 0.03g/L ASC

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