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Nanoparticle Treatment to Counter Reactive Oxygen Species after Traumatic Brain Injury

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Background

Traumatic Brain Injury (TBI) is defined as damage to the brain, resulting from an external mechanical force.[1] TBI is currently the leading cause of death and disability in children and young adults, with 1.7 million reported cases annually in the United States alone.[2] The initial trauma is followed by secondary corrosive damage to the brain. There are currently no treatments to protect the brain from this deterioration. The aim for this project was to study the effects of nanoparticle (NP) treatments on reducing this secondary damage using a mouse model of TBI.

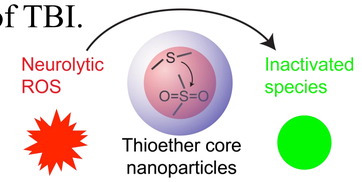

Figure 1:
Thioether core NPs utilized in these experiments.

Nanoparticle Therapy

Secondary damage is caused by an increase in oxidative stress, which forces a biochemical imbalance in the brain. The spread of reactive oxygen species (ROS) is one of the main components for the long-term development in TBI. We used the NPs of Yoo et al. 2017, shown in Figure 1, in efforts to bind and inactivate ROS, reducing the spread of damage.[3]

Controlled Cortical Impact

Controlled Cortical Impact (CCI) is a commonly utilized method for modeling a TBI. The impactor is placed over the left frontoparietal cortex of the mouse's brain. Impact parameters include 4 m/s velocity to a depth of 2.5 mm with a 80 ms dwell time followed by NP tail vein injections.

Superoxide Dismutase Activity Assay

Superoxide Dismutase (SOD) is an antioxidant enzyme involved in the body's oxidative equilibrium system, which converts ROS into oxygen and hydrogen peroxide, as shown in Figure 2.[4] Xanthine Oxidase (XO) is an enzyme that catalyzes the reaction of hypoxanthine into uric acid and ROS.[5] Hypoxanthine is a purine derivative catabolized from nucleic acids or ATP. In this assay, Tetrazolium Salt WST-1 is reduced into a water soluble dye upon the reaction with ROS. SOD will reduce levels of ROS, which are generated by XO, by converting them into oxygen and hydrogen peroxide. The higher the levels of SOD activity, the less dye will be produced. In order to counter oxidative stress, brain tissue will increase the expression of SOD. Our hypothesis states that NP treatments will reduce oxidative stress in the brain, reducing SOD expression.

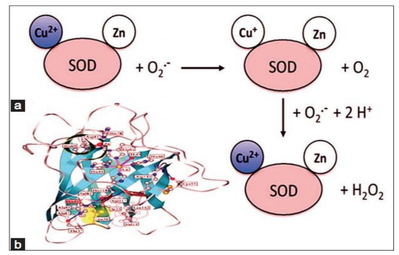

Figure 2:
Diagram illustrating the conversion of ROS into Oxygen and Hydrogen Peroxide by the enzyme, SOD.

Results

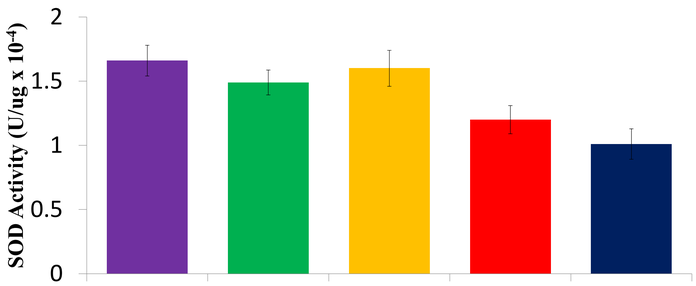

Figure 3:
SOD Activity normalized to protein concentration of brain samples, after 24 hr. following CCI experiments. Samples include left and right (L/R) sides of the brain for mice with (NP) and without (CCI) NP treatment, in addition to a sample control (C) that did not receive damage.

Analysis was conducted using the data collected from the SOD assay experiments, after 24 hours following CCI experiments. From the results provided in Figure 3, brain samples from the left and right sides of the brain following CCI experiments contained higher levels of SOD activity than the control. Additionally, brain samples from the right side of the brain, which did not receive NP treatment had higher levels of SOD Activity, than samples that received treatment.

Discussion

Based on the data collected from these SOD assay experiments, evidence showed that NPs reduced the spread of oxidative stress to the contralateral brain suggested by the reduction of SOD activity in comparison to the injured animals that did not receive NPs. Additional studies are needed in order to confirm the benefits of NPs in reducing the spread of ROS, however, this project offers promise for the promotion of future research.

References

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