THE EFFECT OF THE GLUCOCORTICOID RECEPTOR MODULATOR,SAFIT, ON ACUTE STRESS REACTIVITY IN A RAT MODEL OF ABUSIVE HEAD TRUAMA

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Introduction: Traumatic brain injuries (TBI), particularly as a result of child abuse, are pervasive amongst infants and children and lead to psychosocial and cognitive deficits that persist throughout life. Importantly, as brain-injured infants and toddlers age into adolescence where they face stressful situations, they may not be able to adapt in an appropriate manner. Previous studies in Dr. Raghupathi's lab have demonstrated that maternally separated neonatal rodents subjected to repeated mild TBIs (rmTBI) at post-natal day 11-13 exhibited increased stress-related behaviors when tested in the elevated plus maze (EPM) than non-maternally separated animals subjected to rmTBIs. Separately, it has also been demonstrated that a dysfunction of the glucocorticoid receptor (GR) within the hippocampus may underlie this aberrant response to acute stress. Enhanced activity of FKBP5(a GR co-chaperone protein) has been associated with increased corticosterone effects and blunted negative feedback of the HPA axis. Thus, regulating the HPA axis by inhibiting the GR through inhibition of FKBP5, is thought to relieve some of the behavioral impairments associated with TBIs. One such modulator of the the GR receptor is SaFit, an inhibitor of FKBP5. **Methods:** In the present study, neonatal rats underwent maternal separation for 4 weeks and received a rmTBI on post-natal day 11-13. On post-natal day 41, rats were treated with SaFit 4 hours prior to testing in the EPM. **Results:** Elevated plus maze is a behavioral paradigm that has been shown to be a measure of anxiety in rodents. An increase in open arm activity reflects anti-anxiety behavior. We found confirmatory evidence that neonatal rats sustaining rmTBIs were spending prolonged time in the open arm with a reduction in closed arm time for both the Injured-Vehicle and Injured-SaFit cohorts compared to Sham groups. Administration of SaFit in post-rmTBI rats did not show significantly different behavioral patterns compared to post-rmTBI rats who received only vehicle although it did show a trend in behavior between SaFit injured vs. uninjured. Statistical significance data was revealed between the Sham-SaFit and Injured-Vehicle group, demonstrating that SaFit was significantly beneficial in un-injured rats when ran through the elevated plus maze.