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LONG-TERM EFFECTS OF TRAUMATIC BRAIN INJURY ON EMOTION AND COGNITION IN ATHYMIC NUDE RATS

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Introduction

Traumatic Brain Injury (TBI) is an alteration in brain function caused by an external force. An estimated of 1.7 million head injuries occur every year in the United States. Around 40% of TBI patients suffer long-term disabilities in cognition, emotion, sensation and movement. Following initial TBI, secondary brain injury progress for days and weeks, thus offering a window of opportunity for therapeutic interventions, and the stem cell therapy is an alternative for neuronal repair and functional recovery. Nevertheless, preclinical testing depends on the selection and characterization of appropriate animal models. We suggest that 2 months post-TBI is the minimum period needed to evaluate human cell transplant efficacy and safety. A 2 month survival and assessment period would allow sufficient time for differentiation and functional outcome characterization of appropriate animal models. We reviewed few papers have studied functional outcome at a minimum of 2 months post-TBI. We reviewed published TBI literature and found that only 10% of papers evaluated functional outcome 22 months post-TBI and only 8.6% showed functional deficits 22 months post-TBI. The aim of the present study was, to evaluate long-term deficits on emotional and cognitive behaviors in a Controlled Cortical Impact (CCI) injury model in Athymic Nude Rats (ATN). ATN rats are immuno-deficient, which gives an opportunity to use human stem cells for transplantation.

Materials and Method

Surgery

Male ATN rats were anesthetized, using a stereotaxic coordinates. A craniotomy of 6 mm diameter was performed using a trephine over the left cortex. Once the craniotomy was performed, CCI was delivered to the left parietal cortex using a 5mm rounded tip, 2.5 mm depth and 4.5m/s velocity and 500 ms duration.

Behavior

Novel Place Recognition (NPR) and Novel Object Recognition (NOR)

Nine weeks post-injury, sham and injured rats were trained and tested NPR and NOR.

Elevated Plus Maze

Ten weeks post-injury, sham and injured animals were tested on the EPM to evaluate anxiety. Animals were placed in the intersection of the four arms of the elevated plus maze and their behavior was recorded for 5 min.

Morris Water Maze (MWM)

Thirteen weeks post-injury animals performed acquisition and reversal of MWM. Animal was placed in four different start positions. MWM assesses spatial learning and memory.

Results

Novel place recognition was affected in TBI rats. They explored less time in novel than familiar place. Novel object recognition was not affected. TBI rats in EPM spent more time in open arms than closed arms. This behavior suggest less anxiety and more risk behaviors in TBI animals. Injured rats, during MWM showed deficits in spatial acquisition, reversal learning and reference memory. Contextual CTA was not affected in TBI rats. TBI rats showed deficits in NPR, MWM, EPM after 2 months post-injury, which could indicate that these tasks can be used to evaluate long-term deficits in TBI rats and assess long-term cell transplant efficacy.

Conclusion

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Figure 1. Stereotaxic Coordinates (A) and CCI Injury Device (B). Figure 1B From Snyder et al (2007) and modified by L López-Velázquez.