Interval-Specific, Blood-Brain Barrier Disruption In Vitro After Repetitive Primary Blast Injury

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I. INTRODUCTION

Studies of repetitive brain injury (non-blast) have shown heightened susceptibility to vascular dysfunction and neuropathological changes after the initial insult [1]. However, effects of repetitive primary blast injury on the blood-brain barrier (BBB) are not well understood. This study demonstrates a temporal window of vulnerability to repetitive blast injury in an in vitro BBB model by transendothelial electrical resistance (TEER).

II. METHODS

A mouse brain endothelial cell line (bEnd.3) was used to generate in vitro cultures representing the BBB. Blast injuries (402 kPa overpressure, 0.92 ms duration, and 118 kPa*ms impulse) were delivered in repeated fashion using a shock tube [2]. Cultures were placed in a fluid-filled receiver simulating the surrounding brain and skull. TEER was measured with an Endohm-12 electrode chamber and EVOMX Voltohmmeter (WPI).

III. INITIAL FINDINGS

Following exposure to repeated blast injury separated by 24 hours, TEER of the double injury group decreased to 44 ± 7 %, compared to TEER of 71 ± 4 % in the single injury group and 101 ± 5 % in sham (Fig. 1A). Repeated injury also resulted in delayed recovery of TEER (3 days) compared to cultures exposed to a single blast (1 day; Fig. 1B). After repeated blast delivered 72 hours apart, the double injury group exhibited a consistent 25-30 % difference in TEER compared to age-matched shams on both days 1 and 4 (Fig. 1C).

IV. DISCUSSION

Cultures exposed to repeated blast injury separated by 24 hours exhibited delayed recovery of TEER compared to single injury exposure. An expanded 72 hour inter-injury interval eliminated cumulative effects on TEER depression, as demonstrated by similar differences in TEER between the double injury and sham groups. These results reveal a window of heightened vulnerability to repetitive blast injury in an in vitro BBB model and may suggest a minimum mandatory rest-period to prevent cumulative effects.

V. REFERENCES


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