Primary blast injury initiates functional differences in rat brain organotypic hippocampal slices

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I. INTRODUCTION

Traumatic brain injury (TBI) has been diagnosed in over 266,000 members of the US armed forces since 2000 [1]. Common symptoms of these injuries include concussion, loss of spatial navigation and memory loss. Blast-related TBI poses a significant problem for military personnel both in combat and in training. One type of blast loading, primary blast, is caused by the interaction of the shock wave with the skull and brain tissue. This short communication investigates the effect of primary blast loading on functional responses within rat brain organotypic hippocampal slice cultures (OHSCs).

II. METHODS

Rat OHSCs (400 µm thick) were excised from the brains of P7-P10 Sprague-Dawley pups, cultured on Millipore plastic inserts, and fed every two days for 10-14 days. Blast injury was then initiated using a compressed-gas driven shock tube with the plastic culture inserts placed into sterile bags within a fluid-filled receiver directly below the shock tube exit. Cultures were subjected to either a sham injury, or one of two blast conditions: 336 kPa/0.839 ms/86.5 kPa·ms (mild) or 424 kPa/2.307 ms/247.6 kPa·ms (moderate). Four days following injury, cell death was measured by propidium iodide staining.

Functional recordings were acquired four to six days following injury. At the time of recording, slices were placed onto 60-channel microelectrode arrays and perfused with artificial cerebral spinal fluid. Stimuli from 0-200 µA (in 10 µA increments) were applied in specific locations to generate stimulus-response curves. Each electrode's response was fit to a sigmoidal curve, defined by specific parameters with physiological meaning: the maximum amplitude of the evoked response (R_{max}), the current necessary to generate a half-maximal response (I_{50}), and the synchronicity of the firing neurons (m). These parameters were measured in each region of the hippocampus (DG, CA3, and CA1) in response to the two major stimulation pathways (mossy fibers [MF] or Schaffer collaterals [SC]).

III. INITIAL FINDINGS

For all regions measured, I_{50}, in response to MF stimulation, was significantly ($p<0.05$) increased after injury, as compared to sham for both injury groups. In response to SC stimulation, I_{50} in the CA3 region was significantly decreased after only mild injury. At both injury levels following MF stimulation, R_{max} was significantly decreased in the DG and CA1 regions. In the CA3 region, R_{max} only decreased following a moderate injury. In response to SC stimulation, R_{max} decreased for all regions following a severe injury. Following a mild injury, R_{max} only decreased in the CA1. Finally, m significantly decreased in response to MF stimulation at both injury levels in the CA3. In the CA1, only a moderate injury caused a significant decrease. Following SC stimulation, m was significantly decreased for both injury levels in the DG and CA3.

IV. DISCUSSION

Following MF stimulation, excitability was decreased in all regions at both injury levels, accompanied by smaller amplitude signals and decreased synchronicity in regions downstream of the stimulation site. This data is indicative of diminished synaptic communication between pre and postsynaptic neurons and resembles patterns found previously following lateral fluid percussion injury [2]. The response to SC stimulation differed with excitability largely unaffected, but with a similarly decreased response amplitude and decreased synchronicity in upstream regions from the stimulation site. Our data demonstrates that the functional response following primary blast injury, while complex, does significantly change. Future research will include a complete characterization of the functional response following blast injury, correlation amongst functional responses and individual blast parameters, and a time course study on functional changes.

V. REFERENCES

[1] "DoD Worldwide TBI Numbers." *DVBIC*. Online 13 Feb 2013. Accessed 19 Mar 2013.
[2] Cohen, A.S. et al. "Injury-Induced alterations in CNS electrophysiology." *Prog Brain Res.* (161). 2007.