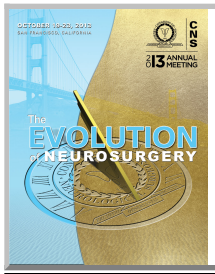

Acute Vascular Response to Penetrating Brain Injury and Associated Metabolic Consequences

Stephen Shelby Burks; Markus Spurlock; Shoji Yokobori; Shyam Gajavelli; Julio C. Diaz; M. Ross Bullock MD, PhD
Miami Project to Cure Paralysis
University of Miami Dept. of Neurological Surgery

Introduction

Penetrating traumatic brain injury (PTBI) has received national attention with coverage of violence. It often has the worst outcomes among head injuries. Little is known about vascular response following PTBI; dedicated imaging studies are not regularly pursued (1). Using a rat model of PTBI, penetrating ballistic brain injury (PBBI), we are investigating vascular response and glucose uptake (2). Based on very poor GCS scores seen in humans with PTBI, we hypothesize that vascular dysfunction will occur in both ipsilateral and contralateral cortices leading to global metabolic failure (1).

Methods

Male Sprague-Dawley rats allocated to control (n=5); PBBI groups (n=6-10).
1)PBBI model: Burrhole made in the right frontal skull. Computed-inflatable probe inserted and inflated (140psi/40ms) (2).
2)Vascular imaging: At 2.5h, 24h and 7 days after PBBI red fluorescent lectin perfused via the ascending aorta, brains rendered transparent and imaged using Ultramicroscopy. Labeling quantified by 3D volume reconstructions.
3)14 C-2-deoxy Glucose (2-DG) autoradiography: 2.5h post PBBI, radioactive 14C-2-deoxy-D-glucose (50μCi) administered. Serial blood samples taken over 45 minutes and estimated using scintillation counter. Sections exposed to X-ray and signals analyzed using densitometry.

Results

Compared to control, decreased overall mean volume of vascular labeling observed in the ipsilateral compared to contralateral hemisphere of injured rats; PBBI ipsilateral 27.39 μm^3 and contralateral 65.34 μm^3 versus 92.43 μm^3 in controls. Additionally, at 2.5h post PBBI a drastic global decrease of glucose utilization observed. Global glucose uptake in injured rats was 44.9 ±0.5μmol/100g/min (Mean±SEM), while controls were 75.2±0.9 μmol/100g/min; p <0.0001 Lowest glucose uptake seen at lesion core and it improved gradually and radially along dorso-ventral and rostro-caudal axes.

Conclusions

Decreased luminal volume of cerebral vasculature is present in injured brains and correlates with lowered glucose uptake. These features likely contribute to global impairment in metabolism and underlies the ensuing pathology. Further studies are needed to separate mitochondrial versus vascular dysfunction (3,4).

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of vascular malfunction in penetrating brain injury, 2) Discuss, in small groups the possible etiologies of vascular volume reduction as well as its relative importance on neuronal metabolism, 3) Identify effective prevention and screening measures for vascular dysfunction in penetrating brain injury.

References

1. Bell RS, Ecker RD, Severson MA 3rd, Wanebo JE, Crandall B, Armonda RA. The evolution of the treatment of traumatic cerebrovascular injury during wartime. Neurosurg Focus. 2010 May;28(5):E5. PubMed PMID: 20568945

2. Murakami Y, Wei G, Yang X, Lu XC, Leung LY, Shear DA, Tortella FC. Brain oxygen tension monitoring following penetrating ballistic-like brain injury in rats. J Neurosci Methods. 2012 Jan 15;203(1):115-21. PMID: 21983109
3. Lactate, not glucose, up-regulates mitochondrial oxygen consumption both in sham and lateral fluid percussed rat brains. Levasseur JE, Alessandri B, Reinert M, Clausen T, Zhou Z, Altememi N, Bullock MR. Neurosurgery. 2006 Nov;59(5):1122-30 PMID:17143246
4. Vespa PM, McArthur D, O'Phelan K, Glenn T, Etchepare M, Kelly D, Bergsneider M, Martin NA, Hovda DA. Persistently low extracellular glucose correlates with poor outcome 6 months after human traumatic brain injury despite a lack of increased lactate: a microdialysis study. J Cereb Blood Flow Metab. 2003 Jul;23(7):865-77. PubMed PMID: 12843790.