Mechanisms of cerebral edema in abusive head trauma

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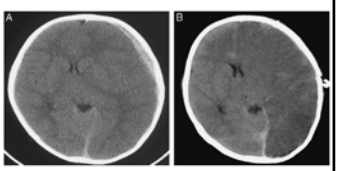
Disclosures

- The speaker has no conflicts of interest to disclose

Introduction

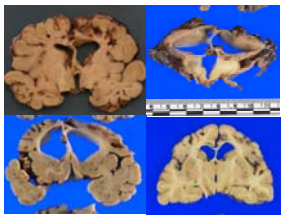
- Brain swelling in the acute phase of SBS/AHT is often pronounced and proceeds rapidly
- Asymmetrical hemispheric hypodensities ("Big Black Brain") suggests a level of complexity
- "The pathophysiological mechanisms…remain unknown."
  - Costine-Bartell et al, *J Neurotrauma* 2019;36:815-833



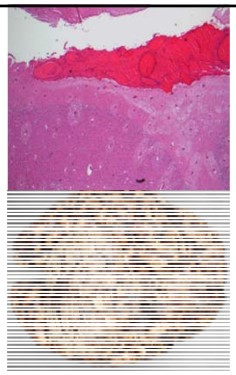
Duhaime and Durham. Progress in Brain Research 2007;161:293-302

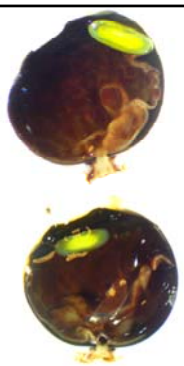
Introduction

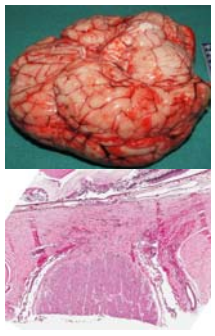
- Long term sequelae are often extensive among survivors of SBS/AHT, with widespread ischemic brain injury

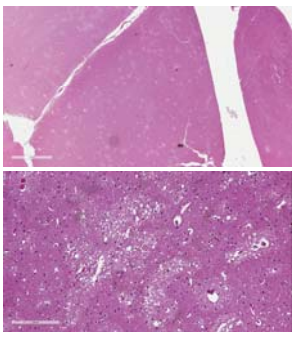


From: *The Daily Times*, Blount County, Tennessee









Methods

- Case material
  - 16 decedents
    - 9 deaths due to homicidal blunt force trauma
      - Age range 2.5 months to 16 months
      - Survival from 0 to 38 hours
    - 7 deaths due to asphyxia
      - Age range 0.5 months to 6 months
      - All decedents found dead
  - Autopsies including brain examination (gross and microscopic) performed in all cases

Methods

- Formalin-fixed, paraffin embedded sections with H&E staining
- Immunohistochemistry
  - IgG
  - Albumin
  - SUR1
  - Trpm4
  - Aquaporin 4
- Rationale
  - IgG and albumin - microvascular injury
  - SUR1 and Trpm4 work in concert to form a nonselective cation channel that upregulates in hypoxia, ischemic stroke, traumatic brain injury – contributing to oncotic edema
  - Aquaporin 4 is expressed in terminal astrocytic processes and facilitates water transport into and out of the central nervous system

HHS Public Access

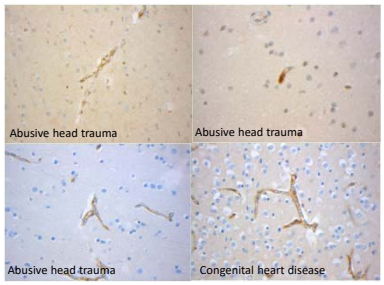
Author manuscript

Sur1-Trpm4 Cation Channel Expression in Human Cerebral Infarcts

Age (months)	Cause of death	Duration of survival	SDH
12	Blunt force trauma	12	Y
12	Blunt force trauma	0	Y
4	Blunt force trauma	?	N
12	Blunt force trauma	0	Y
1	Asphyxia	0	N
16	Blunt force trauma	0	N
6	Asphyxia	0	N
4	Blunt force trauma	48	Y
2.5	Blunt force trauma	0	Y
11	Blunt force trauma	36	N
1	Asphyxia	0	N
0.5	Asphyxia	0	N
0.7	Unknown	0	N
1	Blunt force trauma	24	Y
1	Asphyxia	0	N
5	Asphyxia	0	N
10	Complications of prematurity	0	N
3	Unknown	0	N
3	Asphyxia	0	N
0	Congenital heart disease	2	N

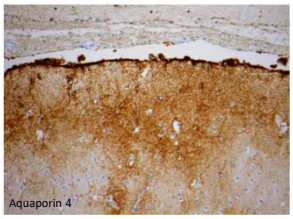
Results

- SUR1 – equivocal
- Trmp-4 - no differences

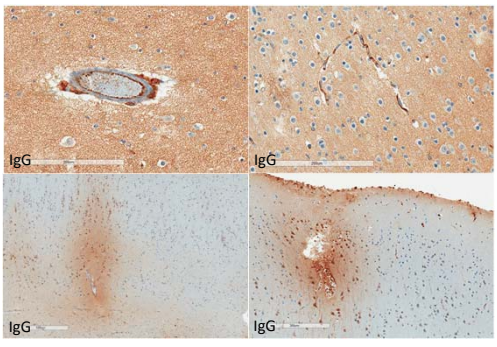


Results

- Aquaporin 4 – no differences

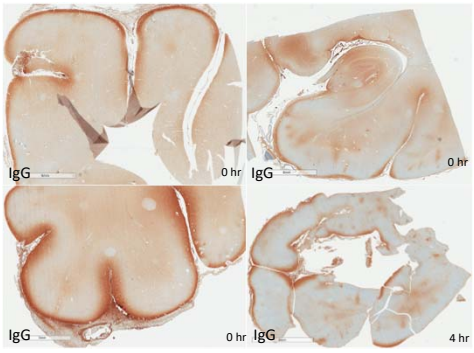


Results



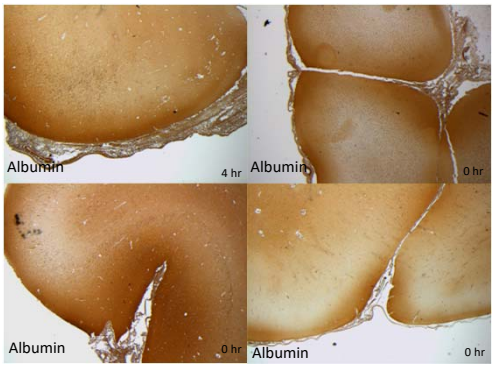
Results

Abusive head trauma



Results

Abusive head trauma



	Subpial, perivascular IgG	Subpial, perivascular albumin	SUR-1-Trpm4 up regulation
Blunt force trauma with subdural hematoma	+++	+++	+/-
Blunt force trauma without subdural hematoma	+	+	+/-
Asphyxia	+/-	+/-	+/-

(Breach of the blood brain barrier appears to precede channelopathy)

Conclusions

- Pathophysiology of brain injury in AHT/SBS is unknown, and not adequately explained by transient global ischemia, increased intracranial pressure, or traumatic axonal injury
- Evidence of SUR1-Trmp4 ion channel up regulation was equivocal; no evidence of aquaporin-4 involvement.
  - Process likely too rapid for channelopathy as a primary process
- Subpial and perivascular IgG, albumin suggest microvascular injury or dysfunction beyond bridging vein rupture
  - Structural damage?
  - Vasospasm?