Abnormal brain tissue sodium metabolism on MRI after cardiac arrest in children

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INTRODUCTION

Regional delayed neuronal cell death occurs frequently in children surviving cardiac arrest (CA), especially in the basal ganglia and cortex. Brain tissue sodium (Na) concentration correlates with irreversible injury after focal ischemia, and requires innovative apparatus not included with a traditional scanner. The previously established threshold for tissue viability in stroke is ~ 70 mM and there are no data regarding brain Na MRI after global hypoxia-ischemia and reperfusion. We hypothesized that Na metabolism after CA in children, whose primary etiology is asphyxia and shock, will be deranged in a delayed manner. The long term goal of this preliminary investigation is to assess the role of brain Na MRI in evaluating therapeutic interventions in children with CA and association with patient outcome.

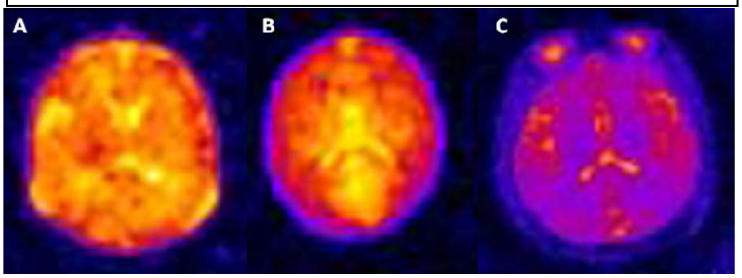
EXPERIMENTS

Brain tissue [Na] was evaluated using a 3.0 T Siemans scanner (FOv 200 x 200 mm, TE 0.5 ms, TR 100 ms, NEX 4, DAT 10 min) in an IRB-approved prospective clinical trial. Tissue [Na] in the cerebrospinal fluid (CSF), right basal ganglia, occipitoparietal cortex, and frontal lobe (voxel size 0.06cc) were quantified using Image J. The frontal lobe is not commonly affected by CA and served as a negative control. Three measurements were taken from each region and averaged. CSF [Na] serves as the standard and is 140 mM. Tissue [Na] is calculated using the following equation: Tissue [Na] = (140 mM * I_{Tissue}/I_{CSF}). Clinical information including age, CA details, and hospital and 6 month outcome were recorded. Hospital outcome was determined using the Pediatric Cerebral and Performance Category (PCPC) score. Six month outcome was determined using the Scales of Independent Behavior (SIB-R) short form using parent interview over the phone.

RESULTS

Brain tissue Na MRI was performed in two children: a 3 year old male with history of cerebral palsy with new asphyxia and a 3 week old male with septic shock, 7 and 5 days after CA, respectively. Both CA subjects had a global increase in brain tissue [Na] compared to the adult control subject (**Fig 1**). Subject 1 had increased intensity chiefly in the occipitoparietal cortex, but also in the basal ganglia, and less in the frontal cortex, corresponding to T2 weighted imaging and lactate presence on MR spectroscopy (**Table 1**). Subject 2 had mildly increased [Na] in the basal ganglia, with normal T2 and negative lactate. The adult control had values that were increased above the established ischemic threshold, but no region had increased [Na] versus another. Subject 1 required total assistance with activities of daily living on hospital discharge, more than before CA; the subject then expired prior to 6 month follow-up of unknown cause. Interestingly, subject 2 was age-appropriate on hospital discharge and at 6 month follow-up.

Figure 1. Na MRI in a 3 yr old child (A), 3 wk old infant (B), and adult control (C). CSF (yellow) has the highest [Na]; blue the lowest.



DISCUSSION

Our study is the first to show abnormally increased tissue [Na] in the brain after CA in children. These findings were seen between 5 and 7 days after CA, and may correspond to delayed or continued Na metabolic derangement, cellular dysfunction, and/or cell death. Limitations to this study are the small number of subjects examined, lack of age-matched control subjects, and acquisition of only one timepoint. It is unknown if brain Na metabolism is age-dependent after global hypoxic-ischemic injury, however, features of cellular injury, death, and restoration are developmentally-dependent, such as anti-oxidant capacity and susceptibility for delayed apoptosis after hypoxia-ischemia.

Table 1. Brain imaging results for the 3 subjects

		Tissue [Na] (mmol)			T2 enhancement		MRS	Outcome at HD	
Subject	D	BG	OP cortex	Frontal Cortex	BG	Cortex	Lactate (BG)	Pre arrest	Post arrest
1	7	91.86	110.79	73.22	Yes	Yes	Yes	Moderate disability	Severe disability
2	5	92.98	80.80	79.01	No	No	No	No disability	No disability
3	NA	97.47	97.49	91.88					

Na, sodium; MRS, magnetic resonance spectroscopy; HD, hospital day; D, day of MRI after arrest; BG, basal ganglia; OP, occipitoparietal; NA, not applicable

CONCLUSION

In children with CA, tissue [Na] was increased in regions of the brain that are most vulnerable to hypoxia-ischemia and reperfusion, representing prolonged or delayed deranged brain tissue Na metabolism.

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