Non-invasive regional brain temperature measurements during and after hypothermia therapy in newborns with suspected hypoxic/ischemic brain injury

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Introduction:

Standard care for newborns with suspicion for hypoxic ischemic encephalopathy (HIE) is therapeutic hypothermia (HT). However, the extent of cooling is not assessed by monitoring brain temperature directly. Instead, esophageal or rectal temperatures are measured and it is not known to what extent these temperatures accurately reflect brain temperature. The goal of this study was to assess brain temperatures directly during and after HT using the same single voxel 1H-MRS technique currently employed to assess brain metabolism in these neonates.

Methods:

Eight newborns with birth asphyxia and suspicion for HIE were examined (i) during HT (using MR-compatible cooling equipment) and (ii) 24 hours after re-warming. The rectal temperature of the patients was continuously monitored. MR spectra of basal ganglia (BG) and parietal grey matter (GM) were acquired using a single voxel PRESS sequence (TR=2s, TE = 35ms; 128 averages). Control data were obtained by a retrospective review of studies obtained from 37 subjects, aged 0-16 years, deemed appropriate controls due to unremarkable MR imaging findings and clinical follow-up. The study was approved by the local IRB. *In vivo* temperatures were determined from the chemical shift difference between the water signal and the NAA peak (**Fig. 1**). For calibration, MR spectra of a NAA model solution were obtained at different temperatures. All studies were carried-out on a clinical 3T system (Philips Healthcare, Best, The Netherlands). iNMR software (Mestrelab Research, Molfetta, Italy) was used to determine the chemical shifts.

Results:

In controls, mean temperatures of BG and of GM were 36.2±1.2 and 36.2±0.8˚C and indistinguishable. Measured mean brain temperatures in patients during and after cooling (34.4±0.9 and 36.7±1.2 ˚C) were slightly higher but generally consistent with temperatures measured by the rectal probe (33.0±0.3 and 36.0±0.5 ˚C) (**Fig. 2**). However, across different brain regions, during cooling, significantly different levels of cooling were achieved. For example, mean temperature during cooling was lower in the BG compared to the GM (33.4±1.1 versus 34.9±1.3˚C, $p<0.05$, Student's t-test). Post-cooling, as in controls, there was no significant difference between the temperatures measured in these brain regions. Outcome in individual patients varied with, tentatively, the dissociation observed between rectal and brain temperature, such that there was a trend toward poorer outcome in the patients for whom there was a larger dissociation between the rectal temperature during cooling and brain temperature, which was warmer.

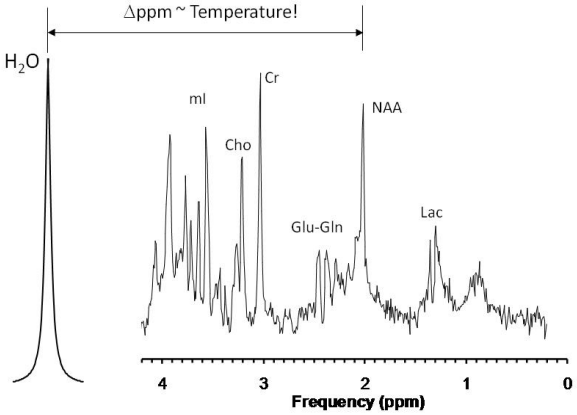

Fig. 1: *MRS of basal ganglia (BG) obtained from a newborn with HIE during cooling. Temperature was measured from the chemical shift difference between NAA and the unsuppressed water signal. Core temperature in this patient was 33˚C (rectal probe) at the time of the study. The measured temperature in the basal ganglia by MR spectroscopy was 35˚C. Post-cooling, ADC signal in the BG decreased and temperature increased to 40 ˚C, well above levels observed in controls. The spectrum above showed a significant lactate peak and overall outcome was poor for this patient.*

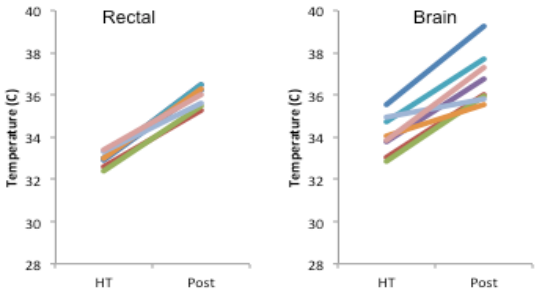

Fig. 2: *Rectal and brain temperatures (average of BG and GM) during and after HT.*

Discussion:

Currently, standard of care for infants suffering perinatal asphyxia is hypothermia therapy, with the goal to provide neuroprotection by lowering brain and core body temperature. Yet, as performed currently, HT is performed without knowledge of the actual brain temperature. Several groups have demonstrated that brain temperatures can be measured accurately with in vivo MR spectroscopy (1-4). While HT has been achieved in all our patients, this preliminary study demonstrates that the extent of cooling may differ in individual subjects and across different brain areas. Thus, in addition to aiding in assessing injury in HIE neonates, measurements of brain temperature from MRS may provide a means for tailoring HT for individual infants and their evolving patterns of injury.

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