New View of Human Brain pH: MR Monitoring of Bicarbonate

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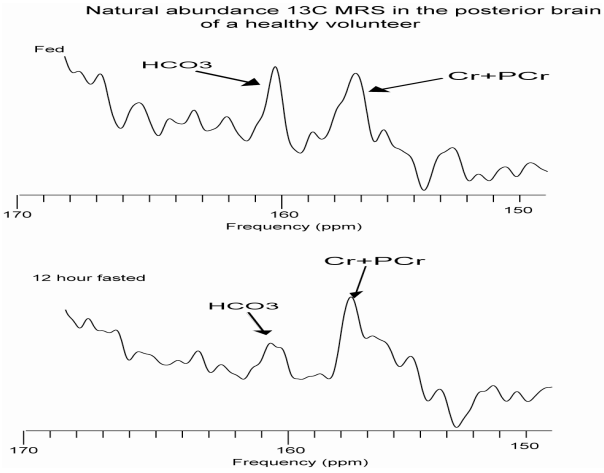
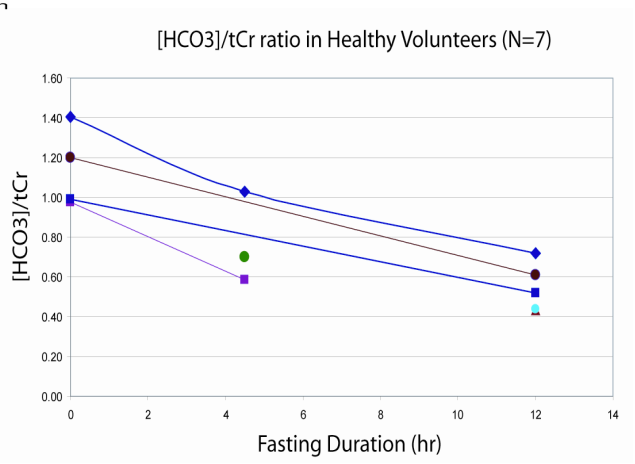
Purpose: Non-invasive assay of bicarbonate concentration in intact human brain, using 13C MRS.

Background: Acid-base homeostasis remains a corner stone of human acute medical care, using determinations of intracellular pH based upon Henderson Hasselbach calculations from HCO3 and pC02 or direct implantation of pH electrodes. Continuous monitoring of blood gas and intra-arterial pH is available in most Hospital Intensive Care Units. MRS promised advances by direct pH assay using the chemical shift of inorganic phosphate (Pi) [1] proved too cumbersome for routine use and anyway, shortcomings in 31P MRS assays emerged. The direct assay of human cerebral HCO3 which is now feasible and simple using natural abundance 13C MRS at 1.5 Tesla, may therefore be of increasing interest.

Human Subjects and Methods: Fourteen 13C MRS brain studies were performed in 7 consecutive normal subjects aged 22 – 47yrs. Subjects were well fed. Repeated examinations were performed after 4.5 and 12 hours of fasting. 13C MRS data acquisition has been described previously [2]. Data was acquired with TR=3sec in 6.5 minute time blocks until SNR for each of the natural abundance resonances of interest exceeded 4:1.

Results: A representative natural abundance 13C spectrum (Figure left) displayed for only 150 -200 ppm, illustrates 4 peaks: The intrinsic resonance at 158 ppm assigned to Creatine plus phosphocreatine is used here as an internal quantitation reference; the neighboring resonance at 161ppm assigned to 'free' intracerebral HCO3, a large 'lipid-glycerol' peak at 172 ppm which is of extra cerebral origin (used as chemical shift reference), and the resonance of total cerebral glutamate (C5) at 182ppm. Since the objective was to quantify cerebral 'bicarbonate' that chemical shift amplitude was compared with Cr + PCr at an assumed total cerebral concentration = 11mM. Physiological modulation of cerebral 13C HCO3: As expected, fasting reduced brain bicarbonate concentration (Figure left) – compare fed with 12 hr fasted in a single individual) and Figure (right) shows comparison of brain bicarbonate assay in 7 individuals subject to fed, fasting 4.5 and 12 hours. Mean cerebral HCO3 are 6.7 ±2.5 mM (N=7) in 12 hr fasted, 8.5 ± 2.5 mM (N=3) in 4.5 hr fasted and 11.6 ± 1.3 mM (N=4) in fed subjects. Paired t-test, P=0.007 for fed vs 12 hr fasting and 0.08 for 4.5 vs 12 hr fasting.





Discussion and Conclusions: The intracellular [HCO3] in human brain is readily modified by diet, moving cerebral pH into "acid" range during fasting as predicted [3]. While normative values for HCO3 of human brain are not available, estimates in animals lie around 14 – 17mM [2]. Calculation of cerebral bicarbonate from Henderson Hesselbach equation, using 31P cytosolic pH = 6.99 provides a value HCO3 = 17mM. Because the present 13C derived values do not match precisely the value expected, based upon arguments of human pH cerebral homeostasis, we speculate that some unmeasured consideration (T1, T2; bicarbonate MR visibility to 13C or compartmentation between glia, neurons, mitochondria and cytosol or CSF and extracellular space) remain to be considered. Nevertheless, it seems probable that natural abundance 13C can provide useful information relevant to human brain homeostasis.

References: [1] R.B. Moon, et al J Biol Chem 248 (1973) 7276-8.[2] Sailasuta et al. JMR 195 (2008) 219- 25 [3] B.K. Siesjo, Experientia 20 (1964) 455-6.

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