Define impact of fasting on human brain acid-base homeostasis using natural abundance 13C and 31P MRS

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Background: It is often assumed, that fasting impacts intracellular brain pH, resulting in acidosis. We recently reported, 13C brain bicarbonate falls significantly ($p \leq 0.007$) after 4 and 12 hours of fasting [1] and predicted significant acidification of the brain. However, results of human and rodent studies for example in ketogenic diets have been mixed. Pan et al [2] argue in favor cerebral alkalinization in brain of fasted humans, based upon elevated intracerebral lactate; working in diabetic ketoacidotic rats Al-Mudallal et al [3] saw no pH change and Glaser et al [4] observed acidification. We have therefore extended our study in the same cohort of subjects using proton-decoupled (dc) 31P MRS to define intracerebral pH during fasting.

Human Subjects and Methods: Using 1.5T GE MR scanner equipped with second rf channel and head coils dual tuned to proton-13C and proton-31P 5 subjects underwent natural abundance 13C MRS in the fed state and after 4 and 12 hours of fasting. 13C MRS data acquisition was described previously [5]. Dc 31P MRS was performed (N=6) in fed state and after 4 and 12 hours of fasting; four of the subjects were among those previously examined with dc 13C MRS. Intracerebral pH was calculated from PCr to Pi chemical shift using [6].

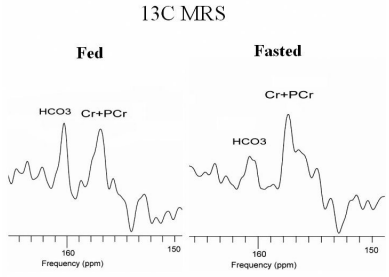

Figure 1. Natural abundance 13C bicarbonate and PCr + Cr in fed (left) and fasted (rate) human volunteer.

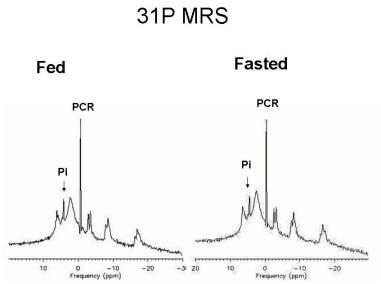

Figure 2. dc31P MR spectrum in fed (left) and fasted (right) in same volunteer.

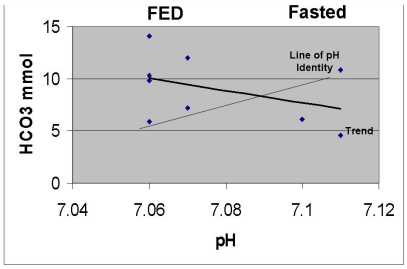

Figure 3. Lack of correlation between intracerebral HC03 and pH in fed and fasted individuals.

Table 1. Effect of fasting on HC03 and pH in normal human subjects.

	Fed	Fasted	Δ	P-value
HCO3	11.4 ± 2.0	7.3 ± 2.4	04.1	0.10
pH	7.07 ± 0.01	7.09 ± 0.02	0.03	0.02
pH paired t-test n=6		*HCO3 paired t-test n=4*		

Results: The striking reduction in intra-cerebral HC03/ PCr + Cr induced by fasting is shown in Figure 1. Fasting did not result in significant change in [PCr] (Figure 2) confirming the prior conclusion that the altered metabolite ratio is exclusively the result solely of the reduction in [HC03]. Fasting was not associated with any reduction in intracerebral pH (Table 1); although the small effect observed was statistically significant, the direction of that change (+0.02 pH Units) was alkalinization rather than the acidification predicted by the significant concomitant reduction in [HC)3]. Finally, there was no correlation between the change in HCO3 and intracerebral pH (Figure 3).

Discussion and Conclusions: According to the Henderson Hasselbalch equation, reduced HCO_3 should have a corresponding decrease in either intracerebral pH or a significant increase in CO_2 in order to maintain pH homeostasis. In severe brain trauma and other medical emergencies, an invasive pC02 probe is frequently used for that purpose. The present data suggests that [HC03] assay may be equally relevant. This 'missing' data may explain some contradictory clinical outcomes when bicarbonate replacement therapy is employed in emergent clinical situations [7].

References: 1) Sailasuta, N and Ross, BD ISMRM 2010. (2) Pan et al. JCBFM 2000 ; 20 :1502-1507. (3) Al-Mudallal et al. Epilepsia 1996 ; 37(3) :258-61. (4) Glaser et al. Diabetes 2005; 54:510–516. (5) Sailasuta et al. JMR 195 (2008) 219- 25. (6) Petroff OA et al. Neurology: 1985; 35: 781-788. (7) Shapiro et al. Am J Physiol Heart Circ Physiol 1989 ; 256 : H1316-1321.

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