Dynamic brain lactate responses to visual stimulation in humans during normoglycemia and hyperglycemia: A 1H-MRS study

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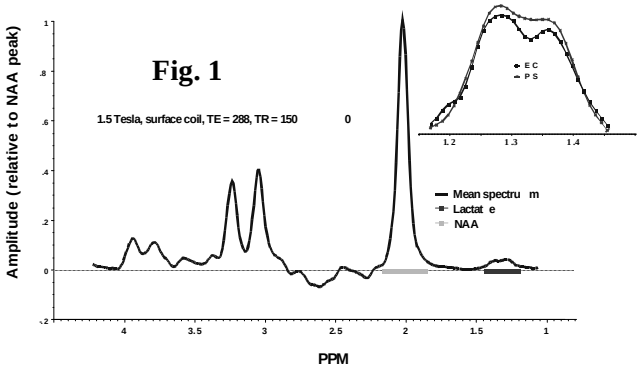
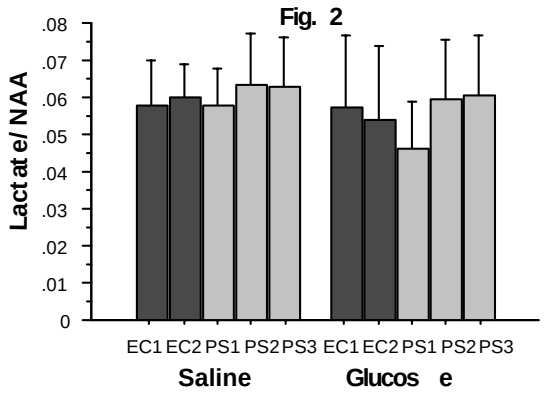
Lactate has an unexpectedly prominent role in brain metabolism. Astrocytic glycolysis and lactate release are triggered by the uptake of glutamate following synaptic activity. Active neurons take up both lactate and glucose for oxidative metabolism (Pellerin et al 1998). Lactate concentration changes biphasically following neuronal activation, with an initial transient decrease followed by a sustained increase (Hu and Wilson 1997). The initial decrease may reflect neuronal consumption of existing lactate while the subsequent increase may result from compensatory overproduction of lactate by astrocytes.

1H-MRS measures of regional brain lactate responses have been used to characterize normal and clinical populations, including dyslexia, panic disorder, mitochondrial disorders, hearing loss, and sleep deprivation. However, the timecourse of brain lactate responses has received little study with 1H-MRS. Mangia et al (2003) showed an early decrease in lactate during visual stimulation in humans with 1H-MRS and suggested is was due to a relative hypoglycemia in brain parenchyma. This study uses 1H-MRS to characterize the timecourse of activity-stimulated brain lactate responses and examine the effects of blood glucose level.

Six fasting subjects were studied twice, while receiving 155 ml over 29 minutes of either 21% glucose (32.5 grams) or normal saline intravenously. Proton spectra were acquired from a 30 cc voxel placed coronally in the primary visual cortex using a 3 inch surface coil and a PRESS sequence at 1.5T, TE=288, TR=1500, reps=192. MRS acquisitions lasted 372 seconds and were obtained in three conditions: 1) EC1 = prior to i.v. infusion, with eyes closed; 2) EC2 = beginning after 10 minutes of i.v. infusion, with eyes closed; 3) two consecutive acquisitions beginning after 17 minutes of infusion, while viewing a radial checkerboard stimulus with a pattern-reversal flicker rate of 8 Hz. Spectra acquired during photic stimulation were analyzed in three separate time periods: PS1= the first minute; PS2= minutes 2 thru 6; PS3= minutes 7 thru 12. Metabolite peaks were quantified with MRUI (MRUI 2003).



The lactate doublet centered at 1.32 ppm (inset in Figure 1) was visible in all scans. The temporal resolution for lactate using this method was one minute.Blood glucose was 94 and 85 mg/dl before and after saline infusion and 96 and 192 mg/dl before and after glucose infusion. Lactate/NAA changed significantly over the five time periods, collapsed across infusion conditions ($F = 4.3$, $df = 4, 20$, $P = .011$; Figure 2). Lactate/NAA decreased non-significantly during the first minute of photic stimulation and then increased significantly. The initial decrease from EC1 to PS1 was significantly greater during hyperglycemia than normoglycemia (paired $t = 2.6$, $df=5$, $p < .05$). There was no effect of hyperglycemia on the sustained increase in Lactate/NAA. Lactate/NAA was significantly lower during the first minute than the subsequent 10 minutes of photic stimulation.



Conclusions: The initial decrease in lactate during continuous visual stimulation lasted no longer than the one minute temporal resolution of this method. The subsequent increase was sustained through 11 minutes of stimulation. The initial decrease in lactate during neuronal activation is not contingent upon a relative hypoglycemia in brain parenchyma, as suggested my Mangia et al (2003). Studies of activity-stimulated increases in regional brain lactate in clinical populations are unlikely to be confounded by variations in blood glucose within the normal range.

Hu Y, Wilson GS (1997)*J Neurochem* 69:1484-90.

Mangia S, Garreffa G, Bianciardi M, Giove F, Di Salle F, Maraviglia B (2003) *Neuroscience* 118:7-10.

MRUI (2003): Magnetic Resonance User Interface.

Pellerin L, Pellegri G, Bittar PG, et al (1998) *Dev Neurosci* 20:291-9.