# Pyruvate to lactate metabolism with age in normal mice measured by hyperpolarized 13C

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**Introduction:** Dynamic nuclear polarization (DNP) has been proven to increase $^{13}C$ NMR signal for more than 10,000 fold, allowing investigations of $^{13}C$ metabolic exchanges in vivo[1,2]. In this study, we apply this technique to investigate the changes in pyruvate to lactate conversion across maturation in mice.

**Methods:** 3 normal mice were scanned starting on postnatal day 18 and repeated every 10 days. Some time points were delayed due to equipment or scheduling issues. Mice were anesthetized with 1.5% isoflurane and 1 L/min oxygen during scans. All experiments were conducted on a vertical 14.1T (Agilent) 600WB NMR spectrometer with 55mm 1000mT/m gradients and a 40mm diameter $^{1}H$ and $^{13}C$ dual-tuned coil. C1 labeled $^{13}C$ pyruvate was polarized using an Oxford Hypersense™ DNP instrument and 150μL of the dissolution mixture containing 160mM pyruvate was injected into the tail vein through a catheter over a span of 12 seconds. **Data acquisition:** Data were acquired on a 24 mm × 24 mm × 5 mm slab centered on the brain, with 2D chemical-shift imaging acquired using center-out 8x8 phase encoding with 128 spectral points. The acquisition was started simultaneously with the pyruvate injection and repeated every 4s (3s TR with 1s delay between each repetition) for a total of 60s with constant flip angle of 10°. A T2-weighted image was acquired as an anatomical reference. **Data processing:** A 5Hz Lorentzian apodization was applied to each free-induction decay before Fourier transforming the data. Maximum intensity of pyruvate and lactate was recorded at each time point for each pixel. We choose the six pixels matched by the location from the T2 anatomical image for calculation of pyruvate and lactate. To normalize polarization levels and compare lactate signals with age, lactate signal was divided by the total carbon signal in the slab at each time point.

**Results and Discussion:** Fig 1(a) shows the comparison of normalized lactate signals changes with age. At P19, a significant higher lactate level can be observed. At around P30, the lactate level stabilizes. Although absolute pyruvate signals fluctuate with age, as shown in Fig 1(b), due to differences in polarization level, lactate signal seems to be independent to the level of polarization or the pyruvate level.

Another observation can be seen from Fig 1(a) is that there is a slight delay of lactate signal reaching peak height as the mouse ages, while pyruvate signal reaches peak intensity at the approximately the same time for all ages. This may suggest a slower conversion to lactate as the mouse matures due to decreased metabolism rate.

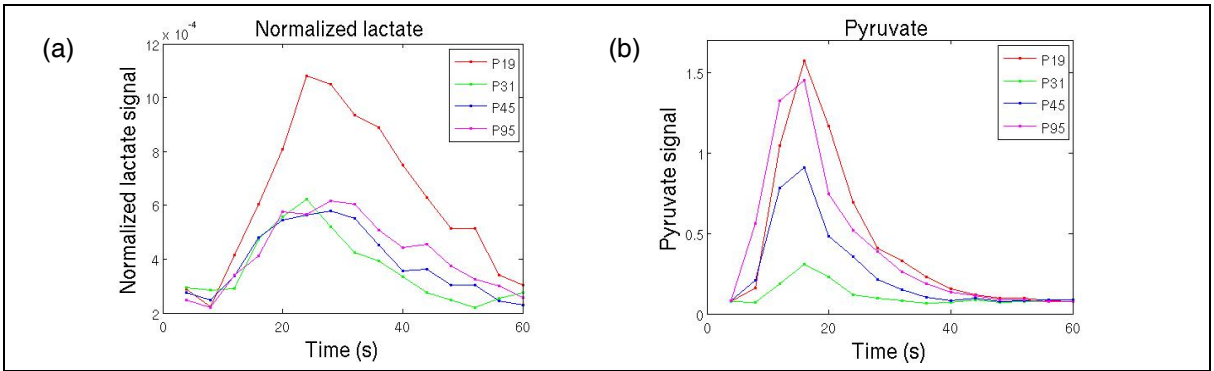


Fig1. Selected normalized lactate intensity (a) and absolute pyruvate intensity (b) with age.

**Reference:** 1. Ardenkjaer-Larsen J, et al. (2003) *Proc. Natl. Acad. Sci. USA* 100, 10158-10163.
2. Golman K, et al. (2006) *Proc. Natl. Acad. Sci. USA* 103, 11270-11275.