Acute Intralipid infusion may improve left ventricular function *via* increases in circulating ketones

N.G. Lawler,[1] S. Nikolic,[2] J. Horne,[3] J. E. Sharman[2] and L. M. Edwards,[1] [1]School of Medicine, University of Tasmania, Hobart 7000, Australia, [2]Menzies Research Institute Tasmania, Hobart 7000, Australia and [3]Central Science Laboratory, University of Tasmania, Hobart 7001, Australia.

Intralipid is an infusible fat emulsion that is regularly used as a component of parenteral feeding. It was recently shown that an acute infusion of Intralipid improves left ventricular function (Holland *et al.*, 2011), although the precise mechanism is unknown. Thus we used an untargeted metabolomics approach to examine the off-target metabolic effects of Intralipid, and to assess whether metabolic changes may explain the acute effects of Intralipid infusion on cardiac function.

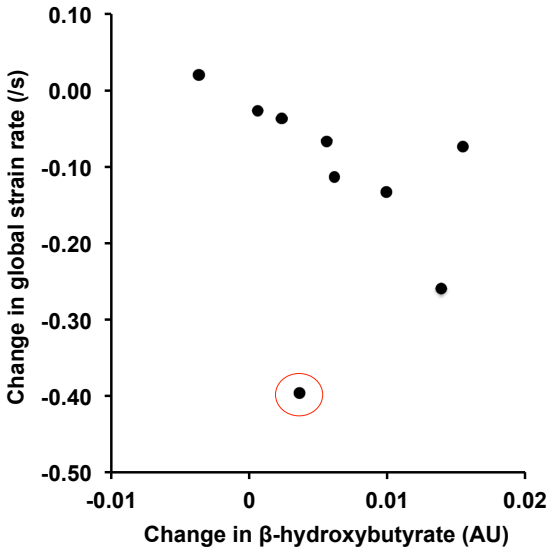
Methods: Ten healthy older men aged 47 ± 3 years (mean ± SE) were infused with either Intralipid (IL) or saline (SAL) on separate days using a blinded randomised crossover design. Venous plasma samples were obtained prior to, and after, 60 minutes of infusion and were stored at −80°C. Metabolites were extracted using a standard methanol / chloroform technique. The resulting fractions were evaporated to dryness in an evacuated centrifuge before being resuspended in appropriate buffers. Proton NMR spectra were acquired from the aqueous fraction using a Varian Inova 400MHz MR spectrometer. Individual free induction decays were Fourier transformed and baseline corrected in NMR manager 12.0 (Advanced Chemistry Development, Toronto, Canada). Spectra were then bucketed and normalized in MATLAB using a custom script. Bucketed spectra were mean-centered and orthogonal signal-corrected before being analysed using PLS discriminant analysis (PLSDA). A single latent variable (LV) PLSDA model was adequate to correctly classify post-IL *vs* post-SAL samples. Left ventricular function was assessed using echocardiography, as described earlier (Holland *et al.*, 2011).

Results: The latent variable was heavily loaded with two peaks that were subsequently identified as β-hydroxybutyrate (BHB, 1.19 ppm) and glucose (4.6 ppm). Given that increased ketones are associated with an improvement in cardiac efficiency (Sato *et al.*, 1995), we correlated individual increases in BHB with reductions in global strain rate post-IL. Although the correlation was not significant, removal of an apparent outlier (Figure) resulted in a significant and strong correlation between increases in BHB and reductions in global strain rate ($r = -0.76$, $P = 0.029$, $n = 8$).

Conclusions: Thus we believe that our data provide new evidence that acute infusion of Intralipid improves left ventricular contractile function *via* an increase in circulating ketones.

Holland DJ, Erne D, Kostner K, Leano R, Haluska BA, Marwick TH, Sharman JE. (2011) *American Journal of Physiology, Heart and Circulation Physiology* **301**: H123-128.

Sato K, Kashiwaya Y, Keon CA, Tsuchiya N, King MT, Radda GK, Chance B, Clarke K, Veech RL. (1995) *FASEB Journal* **9**:651-8.



Relationship between increased serum β-hydroxybutyrate and reduced strain rate after an infusion of Intralipid. Possible outlier is circled in red.