Effects of a Western diet on fetal organ development and fat deposition using MRI of fetal guinea pigs

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Target Audience: Researchers interested in the use of MRI to detect metabolic disease, particularly with respect to its fetal origins.

Purpose: Exposure to excess nutrients *in utero* as a consequence of maternal obesity or high calorie diet has been shown to increase the risk of metabolic and cardiovascular disease in later life.[1] Adaptations to a nutrient-rich environment during critical development stages *in utero* leads to epigenetic alterations that may progress into postnatal life.[2] It has been hypothesized that as a consequence of increased nutrient availability, fatty acid synthesis in the fetal liver is increased leading to increased fetal fat deposition.[3] It is believed that alterations in fat storage are related to the epigenetic changes that lead to later life disease, and so we sought to identify abnormalities in fetal fat deposition in fetuses exposed to nutrient-rich environments using water-fat MRI.

Methods: Pregnant guinea pigs were used due to their similarity to humans in regard to adipose tissue development during fetal growth.[4] Pregnant guinea pigs (N = 12) were anaesthetized and scanned ~60 days into an ~68 day gestation. Two maternal groups were scanned: a Western Diet group (N = 7) with an increase in fat calories and simple sugars, and a synthetic Control Diet group (N = 5). Imaging was performed at 3T (MR750, GE, Waukesha, WI) using a 32 coil receive array under a protocol approved by the institution's Animal Use Subcommittee. T_1- and T_2-weighted images were acquired with TR/TE/flip angle = 5.1ms/2.4ms/15° and 2000ms/120ms/90°, respectively, with voxel dimensions = 0.875x0.875x0.9mm^3 for both acquisitions. IDEAL water-fat images[5] were also collected for each guinea pig with TR/ΔTE/flip angle = 9.4ms/0.974ms/4° and voxel dimensions = 0.933x0.933x0.9 mm^3. The T_1- and T_2-weighted images were used to segment fetal liver, fetal brain, and total fetal volumes. IDEAL fat-only images (Figure 1a) were used to segment total adipose volumes and visceral adipose volumes. Liver fat fractions were determined using proton density fat fraction (PDFF) maps (Figure 1b).

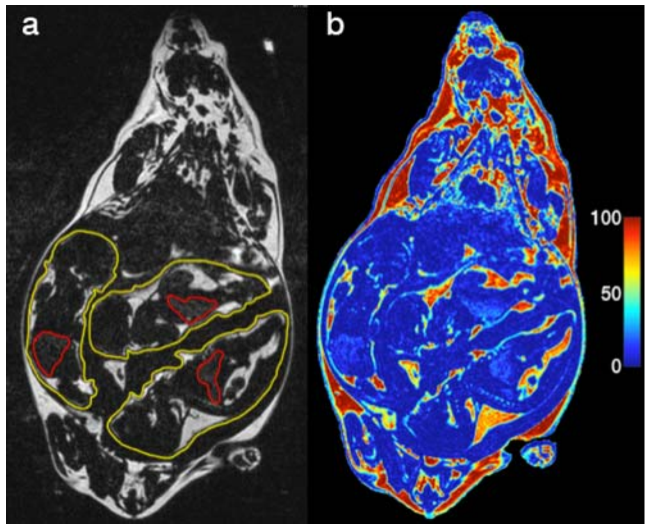

Figure 1: Coronal IDEAL water-fat separated images of a pregnant guinea pig. a) Fat only image with fetuses contoured in yellow and fetal livers in red, and c) Proton density fat fraction (PDFF) map with fat fraction denoted by colour bar.

Results: In total, 16 Western Diet pups and 14 Control Diet pups were scanned. Compared to the Control Diet group, the Western Diet pups were larger (71±14 vs 59±19 cm^3, p= 0.06) and had larger livers (5.5±1.2 vs 4.0±0.9 cm^3, p=0.001), although brain volumes were unchanged (2.1±0.4 vs 1.9±0.4, p=0.36). Western Diet pups had increased fat deposition in the liver compared to controls (25±7% vs 14±9% PDFF, p=0.004), as well as increased adipose tissue volume normalized by total volume (0.18±0.04 vs 0.12±0.05, p=0.009). The fraction of adipose tissue deposited in visceral depots did not significantly differ between groups, although the fraction does look to be decreased in the Western Diet pups (0.18±0.03 vs 0.22±0.04, p=0.15). Furthermore, while adipose tissue volumes correlated well with liver PDFF (Figure 2), the ratio of visceral adipose tissue to total adipose tissue did not (data not shown, R^2 = 0.13).

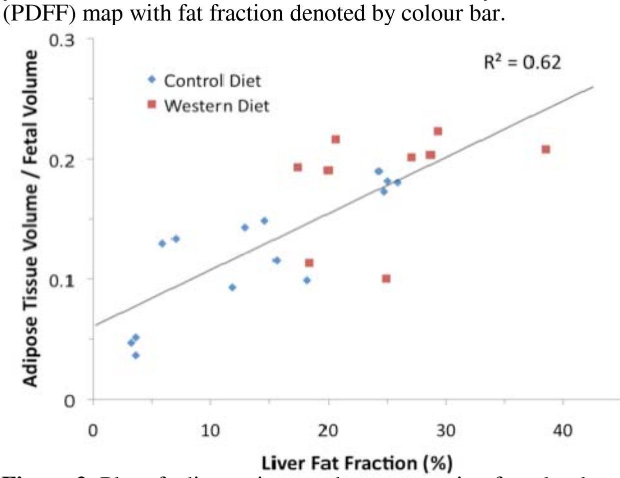

Figure 2: Plot of adipose tissue volume as a ratio of total volume against liver fat fraction. Error bars have been omitted to reduce clutter. Correlation of data is given by the coefficient of determination R^2.

Discussion: The elevated liver PDFF values in the Western Diet pups could be early evidence of non-alcoholic fatty liver disease (NAFLD). NAFLD in adulthood is linked to diabetes, metabolic syndrome, and cardiovascular disease,[6] and so its presence at such an early stage could strengthen this relationship.

Conclusions: This study has demonstrated the capability of MRI in detecting differences in fat deposition between Western Diet pups and healthy controls. The results of this study suggest the possibility of future studies looking at how altered fat deposition relates to epigenetic programming *in utero* and translation to human imaging.

References: 1) Brenseke BM, *et al*. *J Pregnancy* 2013; 2013: 368461, doi:10.1155/2013/368461. 2) Guéant J-L, *et al*. *Eur J Physiol* 2014; 466: 833–850. 3) Godfrey KM, *et al*. *PLoS ONE* 2012; 7(8): e41759. 4) Castañeda-Gutiérrez E, *et al. Am J Clin Nutr* 2011; 94(6 Suppl): 1838S-1845S. 5) Yu H, *et al. Magn Reson Med* 2008; 60(5): 1122–1134. 6) Misra VL, *et al. Curr Gastroenterol Rep* 2009; 11(1): 50–55.

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