

## Anti-Adipogenic effect of n-3 Polyunsaturated Dietary Fat

P-W. So<sup>1</sup>, W-S. Yu<sup>1</sup>, R. Davies<sup>1</sup>, H. G. Parkes<sup>2</sup>, G. Frost<sup>3</sup>, J. D. Bell<sup>1</sup>

<sup>1</sup>Molecular Imaging Group, Imaging Sciences department, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, London, United Kingdom, <sup>2</sup>Wellcome Trust High Field Laboratory, Department of Medical Physics and Bioengineering, University College London, London, United Kingdom, <sup>3</sup>Department of Dietetics, Hammersmith Hospital, Imperial College London, London, United Kingdom

### INTRODUCTION

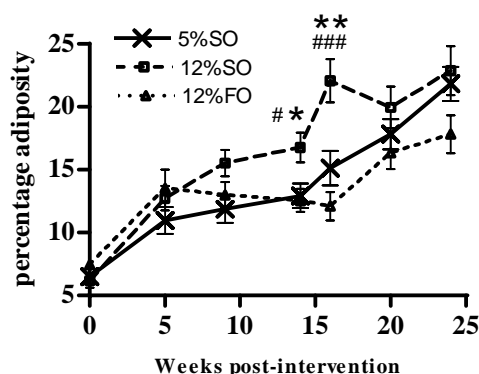
Consumption of high fat diets is known to induce obesity; however, the effect of extended maintenance on diets containing different types of dietary lipid on adipose tissue (AT) metabolism remains to be fully elucidated. In this study, we focus on the effects of dietary supplementation of high levels of two types of polyunsaturated fatty acids (PUFA): *n-6* and *n-3* fatty acids, found in soya and fish oil, respectively. Available data on the effects of different PUFA on adiposity are contradictory [1-3], and probably dependent on the method of adiposity assessment and duration of the study. In this study, both bodyweight and whole body <sup>1</sup>H MRS will be collected, the former and latter being indirect and direct methods, respectively, of assessing adiposity.

### METHODS

**Animals and Treatment:** C57BL/6 mice were obtained (4 weeks old, Harlan UK), weighed and percentage adiposity measured by MRS (see below). The mice were then randomly allocated into 3 groups and placed on 5% soya oil (5%SO), n=17; 12% soya oil (12%SO), n=18 and a 12% fish oil (FO) enriched diet, n=17, for a period of 24 weeks. Bodyweights and food intake were recorded weekly and daily, respectively. Percentage adiposity was assessed prior to and during week 5, 9, 14, 20 and 24 following onset of dietary intervention. Whole body <sup>13</sup>C-<sup>1</sup>H coupled MRS was also performed at week 25 post-intervention to measure lipid composition of total AT.

**MR Scanning:** Anaesthesia was induced and maintained by inhalation of 1-2% isoflurane/oxygen mix. Whole body <sup>1</sup>H MRS was performed at 4.7T (Varian Inc, USA): TR = 20s, 45° and 4 averages, and percentage adiposity calculated according to [2]. Whole body <sup>13</sup>C-<sup>1</sup>H coupled spectra were also obtained (TR=1s, 90°, 1000 averages) at 9.4 T (Varian Inc., USA) and the ratio of the PUFA and C=O resonances measured. Values are quoted as mean±SEM.

Fig. 1



\*, \*\*: P<0.05 and 0.01, respectively, for 5%SO and 12%SO  
#, ###: P<0.05 and 0.001, respectively, for 12%SO and 12%FO

Table 1

| Diet  | Monosaturated/C=O | PUFA/C=O               |
|-------|-------------------|------------------------|
| 5% SO | 85.9±7.05         | 34.0±8.2 <sup>@</sup>  |
| 12%SO | 81.4±4.1          | 42.8±3.3 <sup>@@</sup> |
| 12%FO | 69.3±6.5          | 70.6±6.1               |

<sup>@</sup> and <sup>@@</sup>: P<0.05 and 0.01, respectively, compared to 12%FO

### CONCLUSION

In this study we have shown that the amount and the type of dietary fats can modulate the development of fat depots in mice fed high fat diets. Furthermore, *n-3* PUFAs appear to have a leptogenic effect by reducing the overall AT content rather than through a reduction in dietary intake.

### RESULTS AND DISCUSSIONS

Significant differences in bodyweights were observed between groups despite the fact there was no significant differences in their cumulative food intake. Bonferroni multiple comparisons testing showed that bodyweights were significantly higher in the 12%SO groups compared to the 12%FO (P<0.05) at weeks 16 and 17. Similarly, whole-body adiposity (<sup>1</sup>H MRS) was significantly different at weeks 14 and 16 post-dietary manipulation between the two soya diets, and between the 12%SO and 12%FO diets (Fig. 1). Whole body *in vivo* <sup>13</sup>C MRS revealed that lipid unsaturation levels were significantly higher in the 12%FO mice compared to both soya oil diet groups. Conversely, levels of monounsaturated fatty acids in the mice on the soya oil diets were higher compared to those on the 12%FO, although significance was not reached (Table 1).

The results from this study show that body adiposity appear to be influenced not only by the relative fat content of the diet but also its fatty acid composition. As expected, adiposity was greater in the 12%SO mice compared to the 5%SO mice. However, adiposity of the former mice was also greater than that for the 12%FO mice, suggesting that the latter may have a leptogenic effect. The 12%FO diet consists of high levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), while the SO diet consisted predominately of linoleic acid (54%) and oleic acid (24%). This is clearly reflected in the *in vivo* <sup>13</sup>C MRS measurements of AT composition reported in this study. Previous studies have shown that EPA and DHA can limit adipocyte hypertrophy and thus may affect body adiposity [4]. Our results appear to support these findings and suggest that *n-3* PUFA may reduce body adipose tissues through anti-adipogenic effects.

### REFERENCES

1. Gafo *et al.*, 2001, Brit J Nutr, 86, 371.
2. Dullloo *et al.*, 1995, Metabolism, 44, 273.
3. Tsuboyama-Kasaoka *et al.*, 1999, Biochem Biophys Res Commun, 257, 879.
4. Hill *et al.*, 1992, Intl J Obesity, 16, 321.

**Acknowledgements:** The authors would like to acknowledge the Biological Imaging Centre facilities provided by The Wellcome Trust and the MRC for funding the project.