Modulation of Adipose Tissue Content and Composition by Omega-3-fatty acids in a Murine Model of Obesity

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INTRODUCTION

There is renewed interest on the role of omega-3 fatty acids (from fish oil) on metabolic and physiological processes. Dietary omega-3 fatty-acids have been shown to exert influences at cellular and organ level, in some cases leading to a significant modulation of adipose tissue content and distribution [1-5]. However, most of this work has been restricted to healthy control animals, which has limited our understanding of the potential role of omega-3 fatty acids in disease state. In this study we have investigated the effects of omega-3 fatty acid enriched diet on the adipose tissue metabolism in the obob$^{(-/-)}$ mice, a murine model of extreme obesity.

METHODS

Animals and Treatment: Eight control (C57BL/6, 4 weeks old) mice were subdivided into equal groups of four and placed on a fish-oil (FO) enriched diet (12% omega-3-fatty acids) or a normal chow diet (<1% omega-3-fatty acids) for a period of 20 weeks. Eight obese (obob$^{(-/-)}$, 4 weeks old) mice were also subdivided into equal groups of four and placed on either the FO or the chow diet for the same period of time. Bodyweights and percentage adiposity of animals were recorded prior to and at 20 weeks after the start of the FO diet.

MR Scanning: Anaesthesia was induced and maintained by inhalation of 1-2% isoflurane/oxygen mix. Following a 16h fast, whole body ^{1}H MRS spectra, to assess adiposity, were obtained at 4.7T (Varian Ltd, USA): TR 20s, 45^{o} and ns = 4. The total percentage adiposity was calculated by multiplying the lipid peak by 0.38 to correct for the ratio of total body water compared to total fat free mass [6]. Whole body ^{13}C-^{1}H coupled spectra were also obtained (TR=1s, 90^{o}, ns =1000) at 9.4 T (Varian Ltd., USA), to assess adipose tissue composition. Values are quoted as mean±SEM.

RESULTS AND DISCUSSION

Table 1: Bodyweight Data on FO Diet

	t_0 (g)	$t_{20weeks}$ (g)	$t_{20weeks-t0}$ (g)
C57BL/6	12.98±0.74	27.54±2.14	14.56±3.25
Obob$^{(-/-)}$	24.45±0.88	52.89±1.49	28.45±4.29

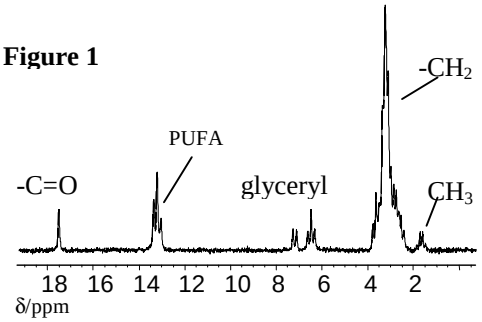
Table 2: Percentage Adiposity on FO Diet

	t_0 (%)	$t_{20weeks}$ (%)	$t_{20weeks-t0}$ (%)
C57BL/6	1.30±0.35	24.98±4.10	23.68±4.23
Obob$^{(-/-)}$	44.33±1.62	55.93±1.73	11.60±2.92

Table 3: ^{13}C Body Composition

	Diet	Omega-3/C=O
C57BL/6	FO	0.81±0.02
Obob$^{(-/-)}$	FO	0.50±0.01
C57BL/6	chow	0.79±0.07
Obob$^{(-/-)}$	chow	0.39±0.02

Figure 1



As expected, a significant increase in bodyweight was observed for both strains of mice after 20 weeks on the FO diet ($p<0.01$, Table 1). Similarly, the relative percentage adiposity was also increased during this period for both strains (Table 2). However, the relative increase in body adiposity was generally lower in the obob$^{(-/-)}$ mice compared to the C57BL/6 mice, suggesting that the gain in bodyweight in the former arises mainly from lean body mass rather than adipose tissue. This finding is consistent with the hypothesis proposed by Webster *et al* [7], of an upper limit for body adiposity for living systems, i.e. the percentage adipose tissue at infinite weight will approach but not be greater than 75%. The lesser increase in adipose tissue in the obob$^{(-/-)}$ mice, suggests that these mice may be approaching a saturation limit for body adiposity. Similar upper limits have been previously observed in human subjects with genetic abnormalities. Evidently, this does not apply to the C57BL/6 mice, as body adiposity at the start and end of the study was well under 50%. Further support for the hypothesis of Webster *et al* comes from the data of the strains fed on the chow diet. The FO diet having the higher fat content led to adiposity in the C57BL/6 mice of 24.99±4.10% after 20weeks as compared to 8.16±3.54% ($p<0.05$) on the chow diet. However, in the obob$^{(-/-)}$ mice, the percentage adiposity was 55.93±1.73% and 60.30±1.33%, (not significantly different) on the FO and chow diet, respectively, suggesting that the saturation limit is being approached.

Through the use of *in vivo* ^{13}C MRS [8] (Figure 1), we were also able to observe that obob$^{(-/-)}$ mice had a significantly different adipose tissue composition compared to controls. Polyunsaturated fats (PUFA) were higher in the C57BL/6 mice than the obob$^{(-/-)}$ ($p<0.001$) on either the FO or the chow diet (Table 3). Apparently, the handling of PUFA differs between the two strains such that the obese mice are less able to incorporate PUFA in adipose tissue and/or are sequestrated for other functions.

CONCLUSION

We have shown that obob$^{(-/-)}$ mice, a murine model of obesity, appears to be differentially influenced by an increase in omega-3 fatty acids in the diet, compared to control and that the modulation of adipose tissue by omega-3 fatty acids may be model specific.

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