Adipose fatty acid composition and gene expression in obesity, and response to chronic marine omega-3 fatty acid supplementation

UNIVERSITY OF Southampton

82

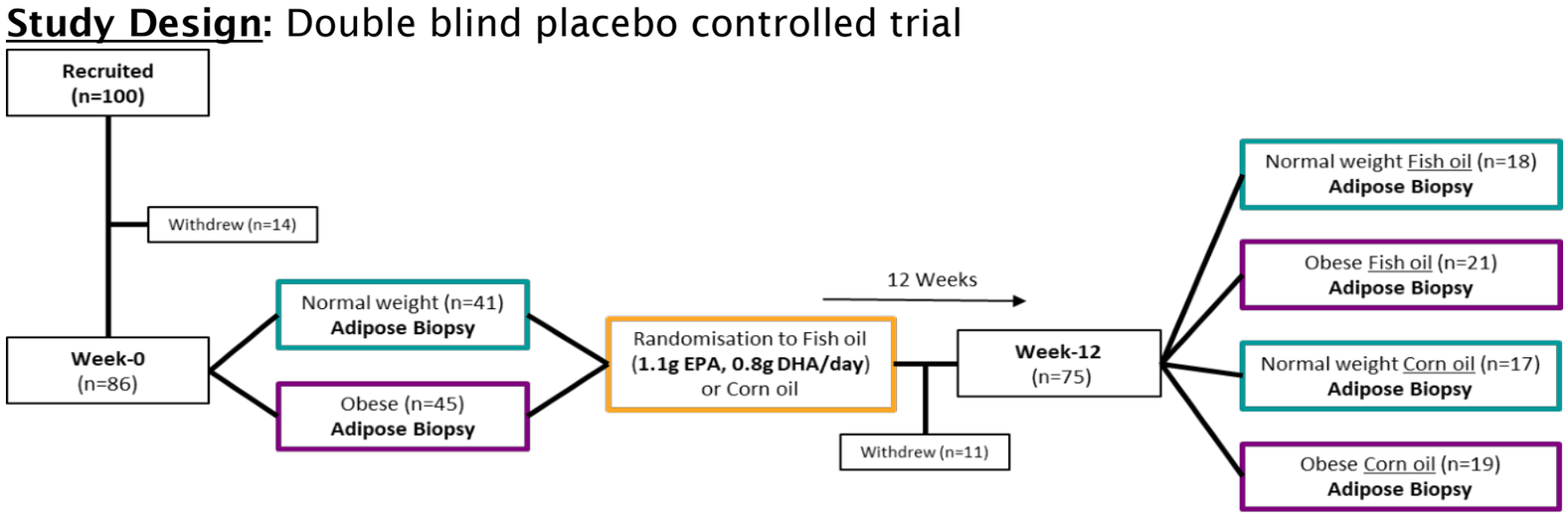
Ethical Approval number 11/SC/0384
Funding by the European Commission

Fisk HL[1], Ayres R[1], Antoun E[1], Childs CE[1] and Calder PC[1].
[1] *Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton, Southampton,*

Introduction:
In the development of obesity, the expression of genes responsible for coordinating processes such as lipid metabolism, adipose tissue (AT) growth, expansion and remodelling, and release of inflammatory molecules become altered. However, such data has come from candidate gene approaches in obesity accompanied by insulin resistance or in visceral AT. The omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) occur naturally in fatty fish and fish oil and have been widely studied for their anti-inflammatory effects. They have been shown to affect the expression of genes involved in in fatty acid (FA) oxidation and lipolysis, adipogenesis, and inflammatory and immune responses. However, investigation into the effects of these on the subcutaneous white AT (WAT) transcriptome, particularly in the context of metabolically healthy obesity is lacking.

Objectives: To investigate whether obesity is associated with an altered WAT FA composition and WAT transcriptome, and whether 12-week fish oil (FO) (EPA+DHA) supplementation is associated with FA and transcriptome responses.

Study Design: Double blind placebo controlled trial



Methods:
The proportional composition of FA in the total lipid extract, and expression of genes in the total RNA extract of abdominal subcutaneous WAT obtained from normal weight (NW) and metabolically healthy obese (OB) individuals at Week-0 and Week-12 following FO (EPA + DHA) or Corn oil intervention, was investigated by gas chromatography and RNA-sequencing (validated by qRT-PCR) respectively.

Results: Week-0

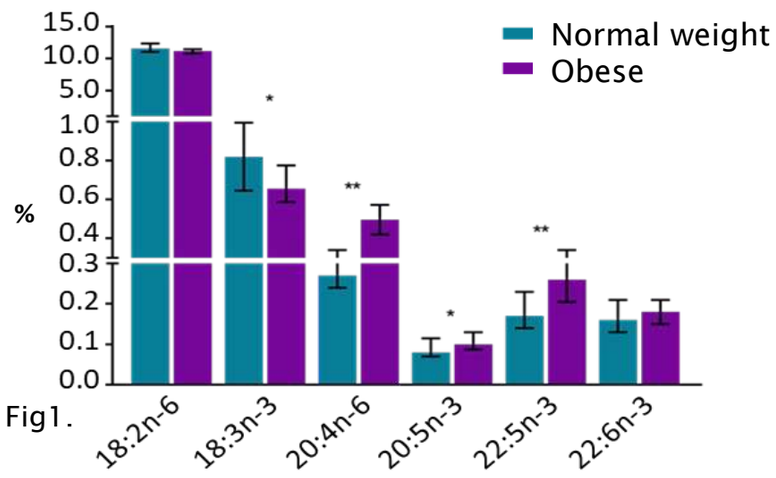


Fig1.

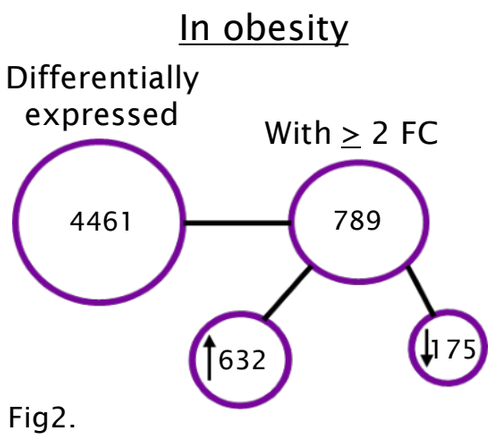


Fig2.

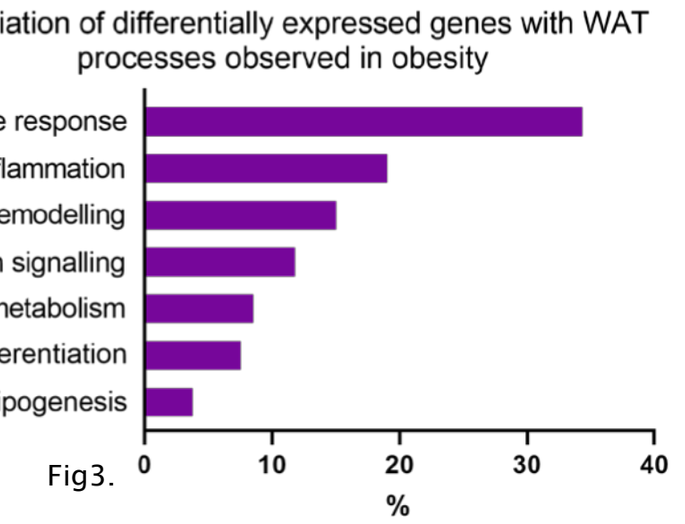


Fig3.

Obesity was associated with higher proportions of arachidonic acid, EPA and DPA, and lower α-linolenic acid ($P \leq 0.05$) (Fig1). 632 genes were upregulated and 175 downregulated in obesity (Fig 2). These were associated with immune and inflammatory response ($P \leq 0.05$, FDR ≤ 0.05, FC ≥ 2), tissue expansion and remodelling, and carbohydrate (CHO) and lipid metabolism (Fig3). Immune/inflammatory responses were attributed to by altered regulation of TLRs, NFκB, cytokines including TNFα, IL-1β, and LEP.

Results: Week-12

Differential expression of genes in response to 12-week EPA+DHA supplementation

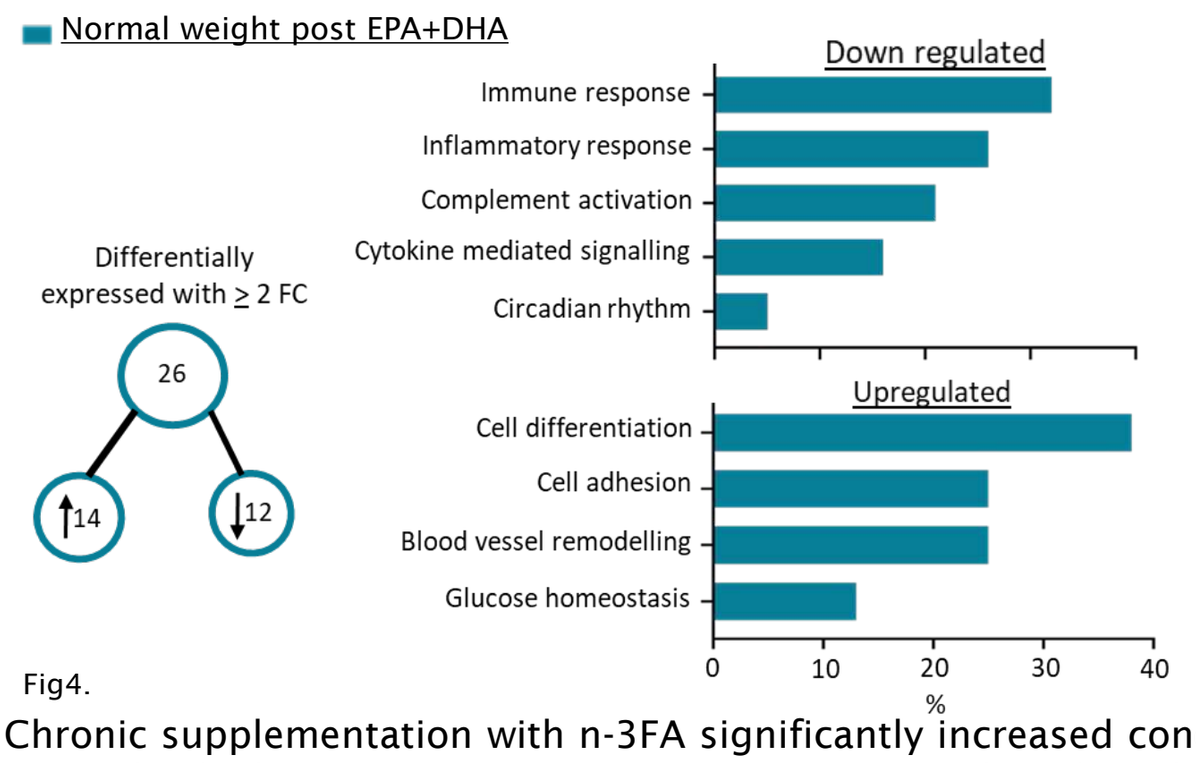


Fig4.

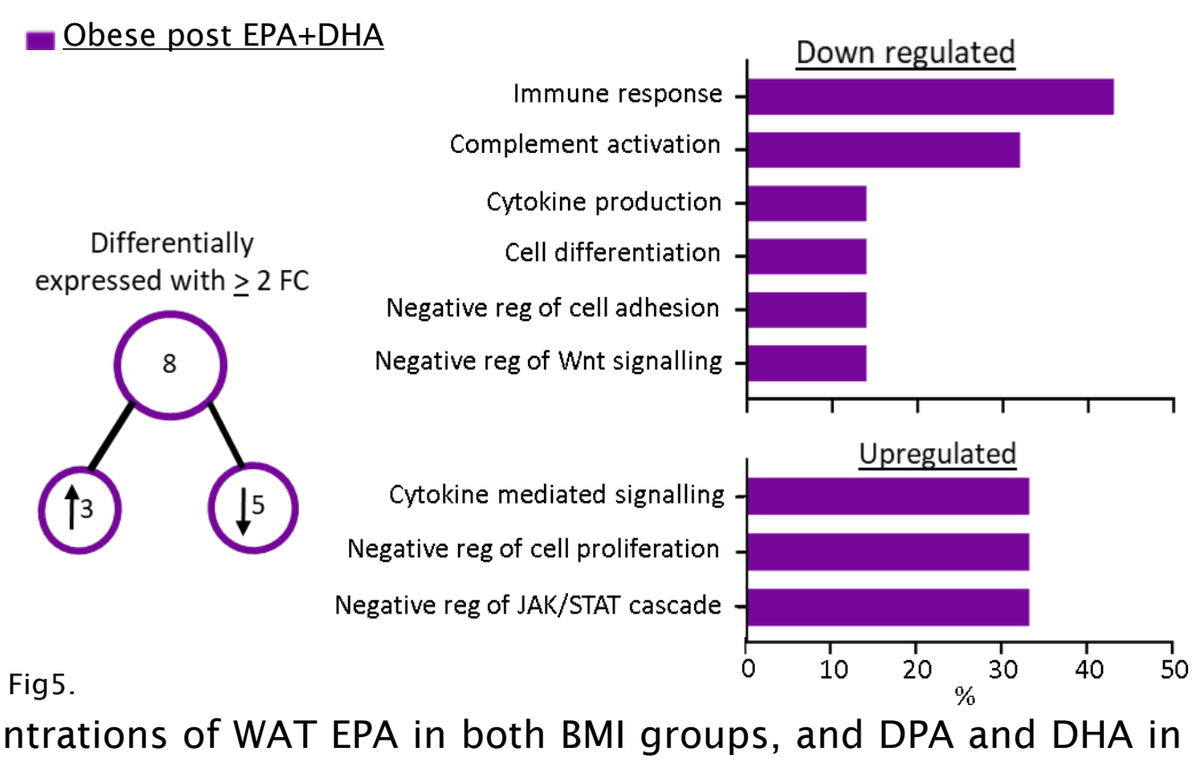


Fig5.

Chronic supplementation with n-3FA significantly increased concentrations of WAT EPA in both BMI groups, and DPA and DHA in NW individuals ($P \leq 0.05$) (data not shown). N-3FA also altered the expression of a number of genes associated with immune, inflammatory, and remodelling processes in both BMI groups (Fig4. and Fig5.) with the majority of changes observed in NW individuals ($P \leq 0.05$).

Discussion and conclusions: Obesity was associated with higher % of adipose AA, EPA and DPA, and higher expression of genes associated with immune and inflammatory responses, energy homeostasis and tissue development. EPA+DHA were incorporated into AT to a similar extent in NW and OB individuals in response to intervention. This resulted in altered expression of genes involved in immune and inflammatory responses in both groups but a greater number of genes were affected in NW individuals. These data report a significantly altered AT transcriptome in metabolically healthy obesity and by n3-FA, and may suggest resistance to the effects of n3-FA in obesity. The transcriptome profile is consistent with data displayed in poster 81 detailing an altered lipid mediator profile in obesity suggestive of enhanced inflammation, tissue expansion and remodelling, and differential metabolism of EPA+DHA in response to intervention.