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Prolonged exposure to omega 3 fatty acids improves insulin sensitivity and modulates genes involved in insulin signaling pathway in mice

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Background and aims: A growing body of evidence suggests that the amount and type of fat included in the diet contribute to the development of insulin resistance and that the reduction of the tissue n-6/n-3 fatty acid ratio could effectively suppress the development of many chronic diseases, including inflammatory disorders, diabetes and neurodegenerative diseases. The fat-1 transgenic mouse is capable of converting omega-6 (n-6) to omega-3 (n-3) fatty acids, leading to an increase in n-3 fatty acid content with a balanced n-6/n-3 fatty acid ratio in all tissues, independent of diet. In the present study we investigate the effects of n-3 on insulin sensitivity as well as the expression of insulin pathway-related genes in aging mice.

Materials and Methods: The total number of C57BL/6 mice were divided in four study groups: wild-type at age 8 weeks (n=4), fat-1 at age 8 weeks (n=4), wild-type at age 8 months (n=4) and fat-1 at age 8 months (n=4). The tissue fatty acid composition was measured using gas chromatography (GC). After the treatment period, body mass, food intake and the plasma concentration of glucose and insulin were measured. Glucose tolerant testing (GTT), insulin tolerant testing (ITT) and heart gene expression by Real Time PCR was performed in all groups.

Results: Lipid analysis confirmed that n-3 tissue levels of fat-1 mice are much higher than that of wild type mice. Fat-1 mice at 8 months of age showed decreased body weight and food intake, decreased basal glucose and insulin levels and displayed an improvement in glucose tolerance and insulin sensitivity during GTT and ITT, respectively, compared to wild-type mice of the same age. Evidence for increased insulin related genes in the heart tissue of fat-1 mice (age 8 months) was obtained by a 2-fold increase in mRNA levels for insulin receptor (IR) and protein kinase B (Akt) and 3-fold increase in mRNA levels for phosphatidylinositol 3-kinase (PI3K-p85) and nitric oxide synthase (e-NOS) compared with all other groups.

Conclusion: Aged fat-1 mice are more insulin sensitive than the other groups tested in this study, despite the age-related insulin resistance observed in the aged wild type mice. This suggests that a prolonged increase in n-3 fatty acid tissue content with a balanced of the n-6/n-3 fatty acid ratio may be an important approach for the prevention and treatment of insulin resistance and related chronic diseases.

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