Ablation of the Very Long Chain Fatty Acid Elongase ELOVL3 in Mice Leads to Constrained Lipid Storage and Resistance to Diet-induced

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The accumulation of fat in peripheral tissues depends upon the balance between signals determining energy intake and storage generated in regulatory centers within the central nervous system. Recent studies indicate that ablation of the fatty acid elongase ELOVL3 gives rise to alterations in both lipid droplet formation in peripheral tissues and central metabolic regulatory signals. Here we show that *Elovl3*$^{-/-}$ mice are resistant to diet induced obesity despite markedly reduced leptin levels and increased expression of orexigenic peptides in the hypothalamus, a situation that is more exaggerated in female mice. Both female and male knockout mice show reduced hepatic lipogenic gene expression and triglyceride secretion, which is balanced by an augmented lipogenic gene expression in adipose tissue. Despite this, adipose tissue expansion is markedly constrained, implying that very long chain fatty acids produced by ELOVL3 are indispensable for appropriate dietary fatty acid uptake and storage.