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Liver-adipose tissue communication through mTORC1

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Background/Aims: The mammalian target of rapamycin complex 1 (mTORC1) serves as a nutrient-sensing hub responsible for the switch between anabolism and catabolism. Dysregulation of mTORC1 results in metabolic disorders such as fatty liver, obesity and diabetes. Much is known about the regulation of mTORC1 within the liver, but little is known about how hepatic mTORC1 affects other tissues. Our research focuses on adipose tissue, due to its role in energy storage and its "feedback" relationship with the liver. We studied the role of mTORC1 within the liver-adipose tissue axis using different dietary regimes and knockout mice. Results: Feeding a ketogenic diet strongly activates mTORC1 in adipose tissue and, to a much smaller extend, in the liver. In liver-specific mTORC1 knockout animals, the adipose mTORC1 activation is preserved. These results coincide with our previous research, which shows that even if tissues are subjected to similar dietary conditions, metabolic regulation can differ between those tissues. Some diets show changes in gluconeogenic and lipogenic gene expression in liver but do not show these changes (or show opposite changes) in white adipose tissue, including expression of Pepck, Fasn and Scd1. One possible explanation for the effect of ketogenic diet on adipose tissue might be an increased secretion of the hepatokine fibroblast growth factor 21 (FGF21) that occurs under this diet. We therefore injected mice with recombinant FGF21, resulting in similarly strong activation of mTORC1 in adipose tissue. However, we rejected the hypothesis that hepatic FGF21 is solely responsible for mTORC1 activation, as ketogenic diet in FGF21 knockout mice showed increased adipose mTORC1 activation. Conclusion: The activation of adipose mTORC1 due to a ketogenic diet is neither dependent on hepatic mTORC1 nor solely dependent on increased FGF21 expression. Nutritional regulation of molecular metabolism is not similarly affected amongst investigated tissues.