Saturated and monounsaturated fatty acids differently regulate lipid droplet metabolism, energetics, and autophagy in hepatic cells

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High-fat diets can induce the accumulation of hepatic lipid droplets (LDs), consisting mainly of triacylglycerols (TAG). Numerous studies have shown that LDs generated from mono- or polyunsaturated fatty acids have a protective role in the liver whereas saturated fatty acids induce hepatotoxicity. The different fatty acids showed different abilities to be incorporated into TAG. Therefore, we hypothesized a role for diacylglycerol acyltransferase (DAGT) 1 and DGAT2, enzymes of TAG synthesis, in fatty acid-induced hepatotoxicity. In the present study, we aimed to follow the metabolism of LDs induced by palmitic acid (PA), a saturated fatty acid, and oleic acid (OA), a monounsaturated fatty acid, and the action of these fatty acids on the activity and the expression of DGAT1 /2. Furthermore, we followed the effects of these PA and OA on liver cell energy and autophagy. For this, HuH7 liver cells were treated for 48 h with PA and OA, and confocal microscopy, western blot, and enzyme activity assay were performed. We found that PA, unlike OA, induces hepatotoxicity and cell death. Furthermore, PA induced less TAG accumulation than OA and was more oxidized in mitochondria. PA treatment induced increased endoplasmic reticulum stress, block of autophagy, and reduction in DGAT1 expression, while OA did not affect both DGAT1 and DAGT2 expression. Inhibition of DGAT1 in OA-treated cells induced the formation of LDs like those of PA-treated cells and hepatotoxicity. These results indicate that DGAT1 may play a key role in the different lipotoxicity induced by saturated and monounsaturated fatty acids in the liver.