Supporting Information

Liu et al. 10.1073/pnas.1309469110

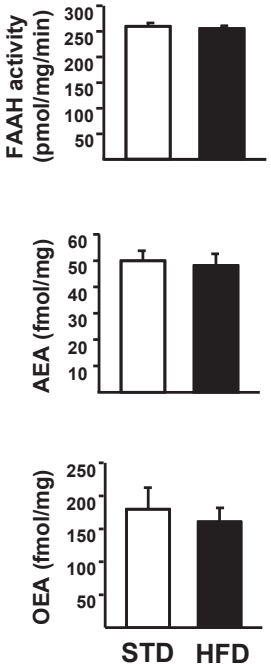


Fig. S1. The levels of arachidonoylethanolamide (AEA), oleoylethanolamide (OEA), and the activity of fatty acid amide hydrolase (FAAH) in whole brain tissue. Note the lack of difference between values in standard diet (STD) and high-fat diet (HFD)–fed mice (n = 4 mice per group).

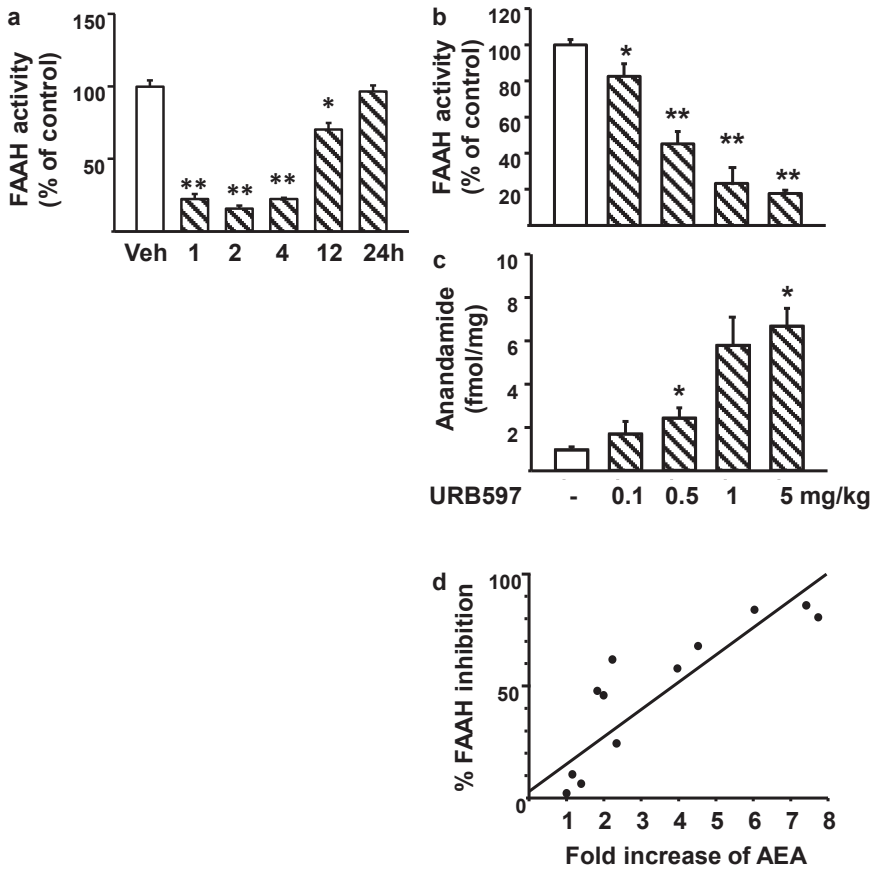


Fig. S2. Inhibition of hepatic FAAH activity and increase in hepatic AEA content in WT mice treated with URB597. (*A*) FAAH activity at various times after acute i.p. treatment with 5 mg/kg URB597. (*B*) FAAH inhibition measured at 2 h following treatment with different doses of URB597. (*C*) AEA levels measured in the same tissue samples as in *B* and *D*: correlation between hepatic FAAH activity and AEA levels. Points represent both parameters measured in individual samples (*$P < 0.05$ and **$P < 0.01$ vs. values in vehicle-treated samples in *A*–*C*). Columns and bars are means ± SE.

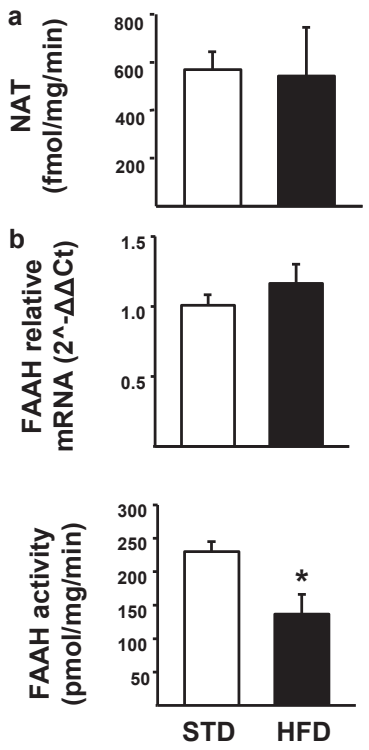
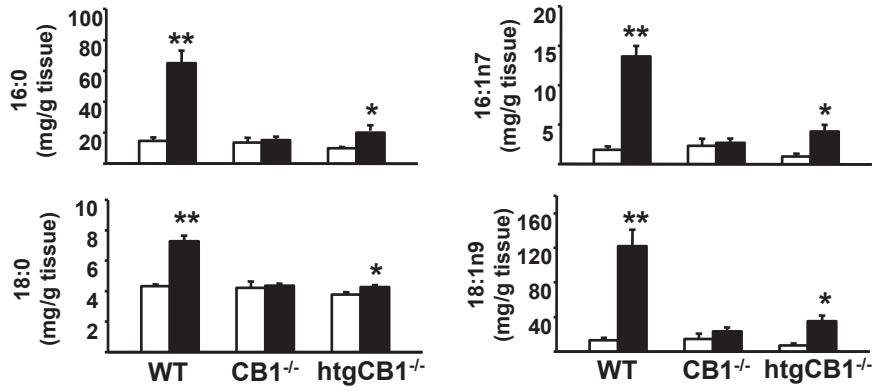


Fig. S3. Effects of HFD on hepatic *N*-acyltransferase (NAT) and FAAH activity and FAAH mRNA levels in lean and diet-induced obese mice. Note that the activity of NAT (the rate-limiting enzyme in AEA biosynthesis) and FAAH mRNA levels in the liver remain unaffected by HFD, whereas FAAH activity is significantly reduced. Assays are described in *Materials and Methods*.



Fold increase of FA by HF					
		16:00	16:1n7	18:00	18:1n9
	WT	4.39	7.54	1.68	9.41
	CB1-/-	1.11	1.17	1.04	1.64
	htgCB1	2.05	4.29	1.13	4.97

Fig. S4. Fatty acid content of the liver of WT, CB1R$^{-/-}$ (global CB1R knockout), and htgCB1R$^{-/-}$ (global CB1R knockout with transgenic reexpression of CB1R in hepatocytes only) mice on an STD (open columns) or HFD (filled columns; n = 6–8 mice per group; *P < 0.05 and **P < 0.005 vs. corresponding STD group).

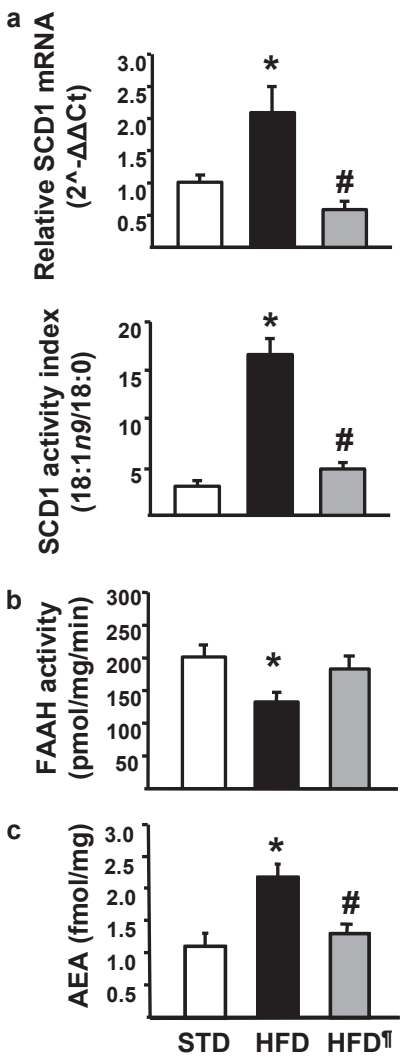


Fig. S5. Increasing dietary monounsaturated fatty acid (MUFA) content abrogates the HFD-induced increases in hepatic stearoyl-CoA desaturase-1 (SCD1) expression and activity (*A*), decreased FAAH activity (*B*), and increased hepatic AEA content (*C*). SCD1 mRNA, SCD1 and FAAH enzyme activities, and AEA levels were measured in liver samples from WT mice maintained for 14 wk on an STD or HFD with 24% or 36% MUFA content (HFD[¶]), as described in *Materials and Methods*. Columns and bars are means ± SEM (n = 6–7; *P < 0.05 vs. value in corresponding STD group; [#]P < 0.05 vs. value in corresponding HFD group).

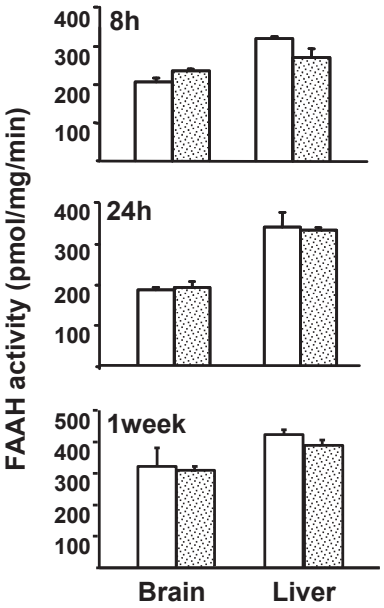


Fig. S6. Oral gavage of mice on STD with 320 mg/d oleic acid fails to affect FAAH activity in brain or liver (n = 6 mice per group).