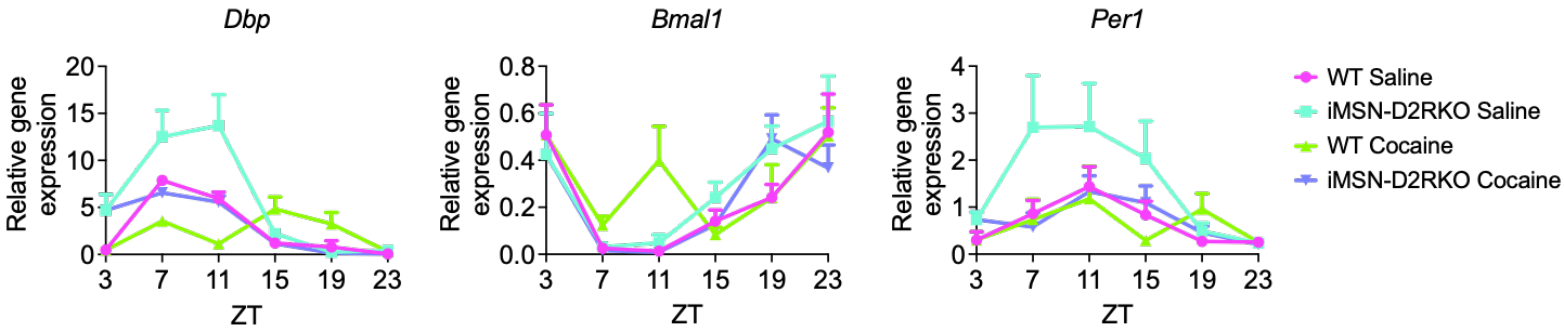

Fig. S1 Rhythmicity of core clock genes. qPCR analysis of Dbp, Arntl (Bmal1), and Per1 in the liver samples used for metabolomics.

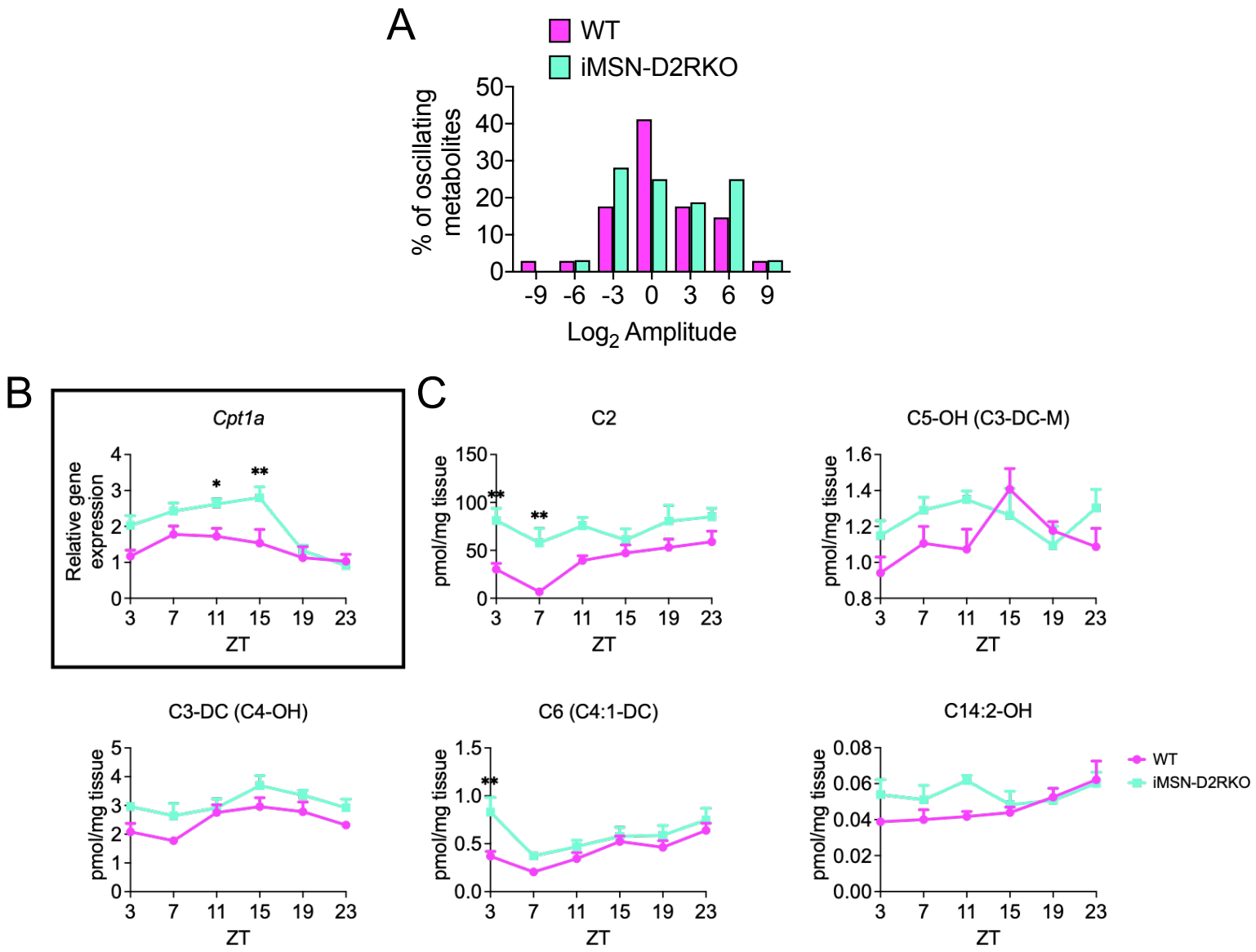

Fig. S2 Analysis of rhythmic metabolites in WT and iMSN-D2RKO mouse liver. A. Analysis of the distribution of amplitude size as a percentage of hepatic oscillating metabolites in WT (pink) or iMSN-D2RKO (blue) mice. **B**. qPCR analysis of Cpt1a gene expression in WT or iMSN-D2RKO mouse livers along the circadian timepoints. **C**. Concentrations of the five acylcarnitines which significantly lost rhythmicity in the iMSN-D2RKO mice compared to the WT mice. *p < 0.05, **p < 0.01. 2-way ANOVA followed by Tukey's multiple comparisons test.

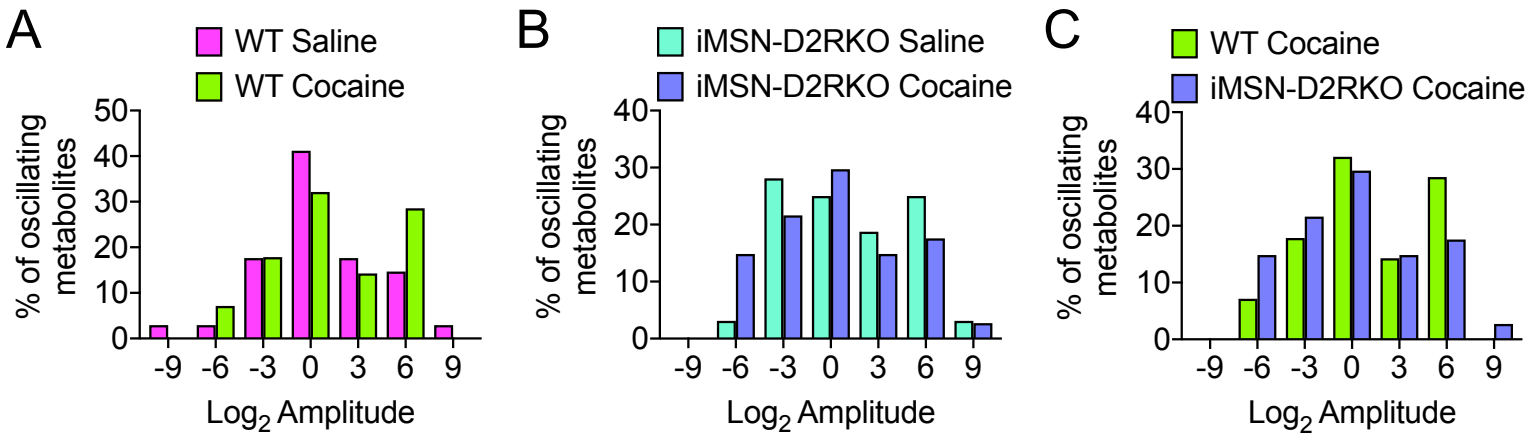

Fig. S3 Cocaine fails to alter metabolite amplitudes. A. Analysis of the distribution of amplitude size as a percentage of hepatic oscillating metabolites in WT treated with Saline (pink) or Cocaine (green). **B.** Analysis of the distribution of amplitude size as a percentage of hepatic oscillating metabolites in iMSN-D2RKO treated with Saline (blue) or Cocaine (purple). **C.** Analysis of the distribution of amplitude size as a percentage of hepatic oscillating metabolites in WT (green) or iMSN-D2RKO (purple) mice after Cocaine treatment.

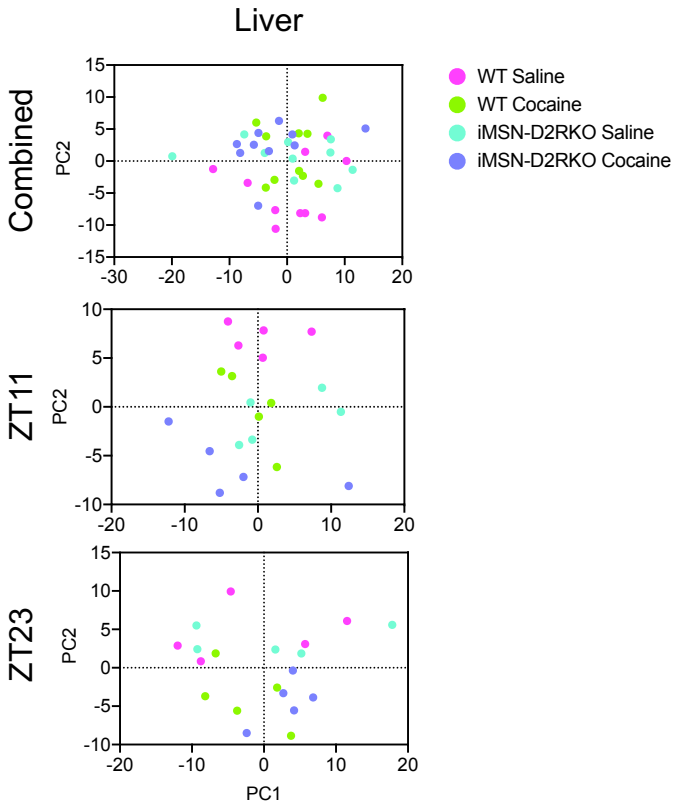

Fig. S4 Principal component analysis of metabolomic data from liver. Principal components for the combined ZT11 and ZT23 (top) datasets of each condition, WT Saline, WT Cocaine, iMSN-D2RKO Saline and iMSN-D2RKO Cocaine treated were analyzed in the liver. PCA plots for the ZT11 datasets (center) and ZT23 datasets (bottom) of each condition, WT Saline, WT Cocaine, iMSN-D2RKO Saline and iMSN-D2RKO Cocaine treated were analyzed in the liver.