Supporting Information

Altered Cholesterol Biosynthesis Affects Drug Metabolism

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Figure S1

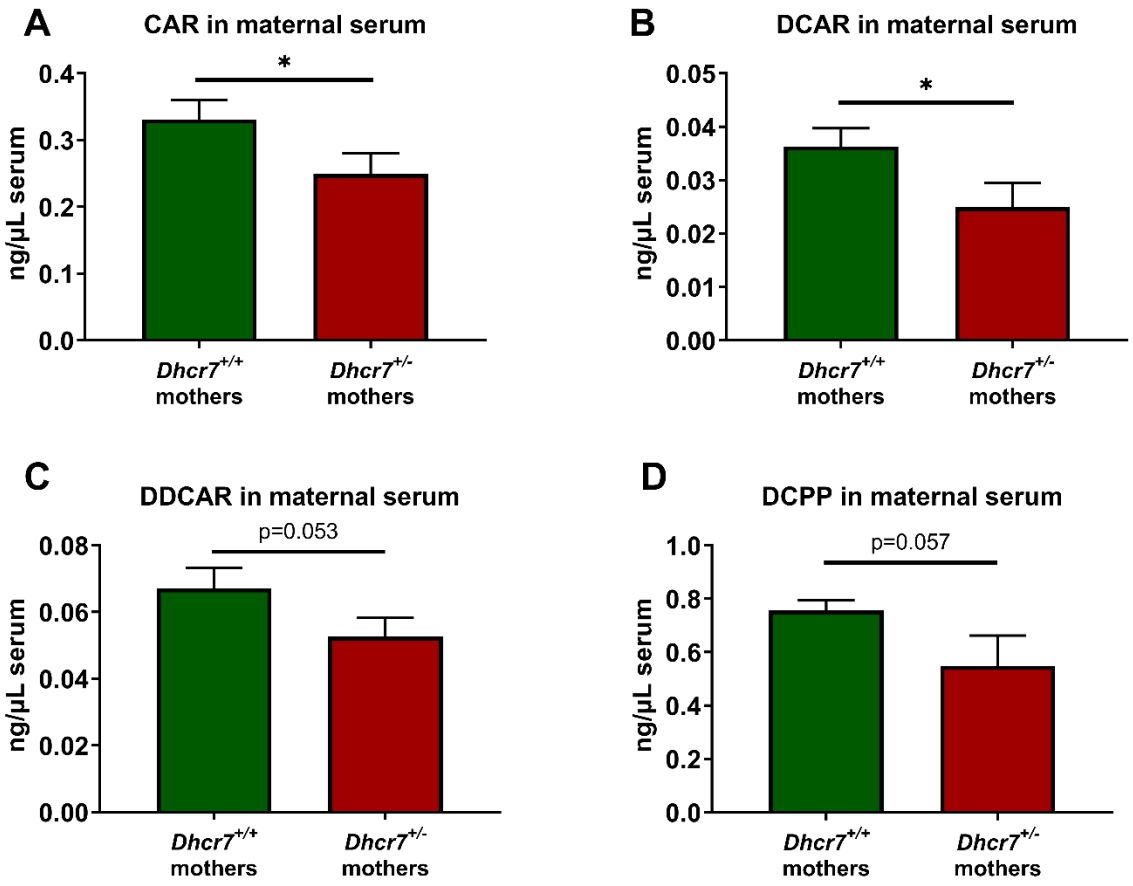

Figure S1. Levels of CAR and its metabolites depend on maternal genotype. The levels of CAR and metabolites were determined in the sera of mothers after delivery of pups. Each column corresponds to the mean ± SEM of three animals analyzed in technical triplicate. Statistical significance (unpaired one-tail *t*-test): *p<0.05.

Figure S2

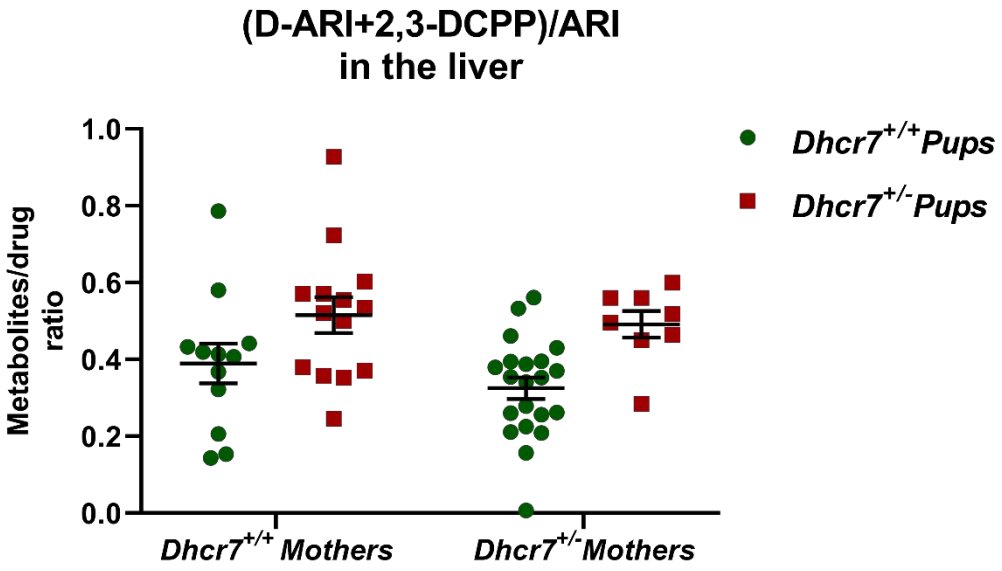

Figure S2. *Dhcr7*$^{+/-}$ mice metabolize ARI faster than WT mice. Aripiprazole turnover was calculated by determining the ratio of drug metabolites over the parent drug. WT and *Dhcr7*$^{+/-}$ pups are depicted in green and red, respectively. Samples were grouped according to both maternal and embryonic genotypes. Bars correspond to the mean ± SEM.

Figure S3

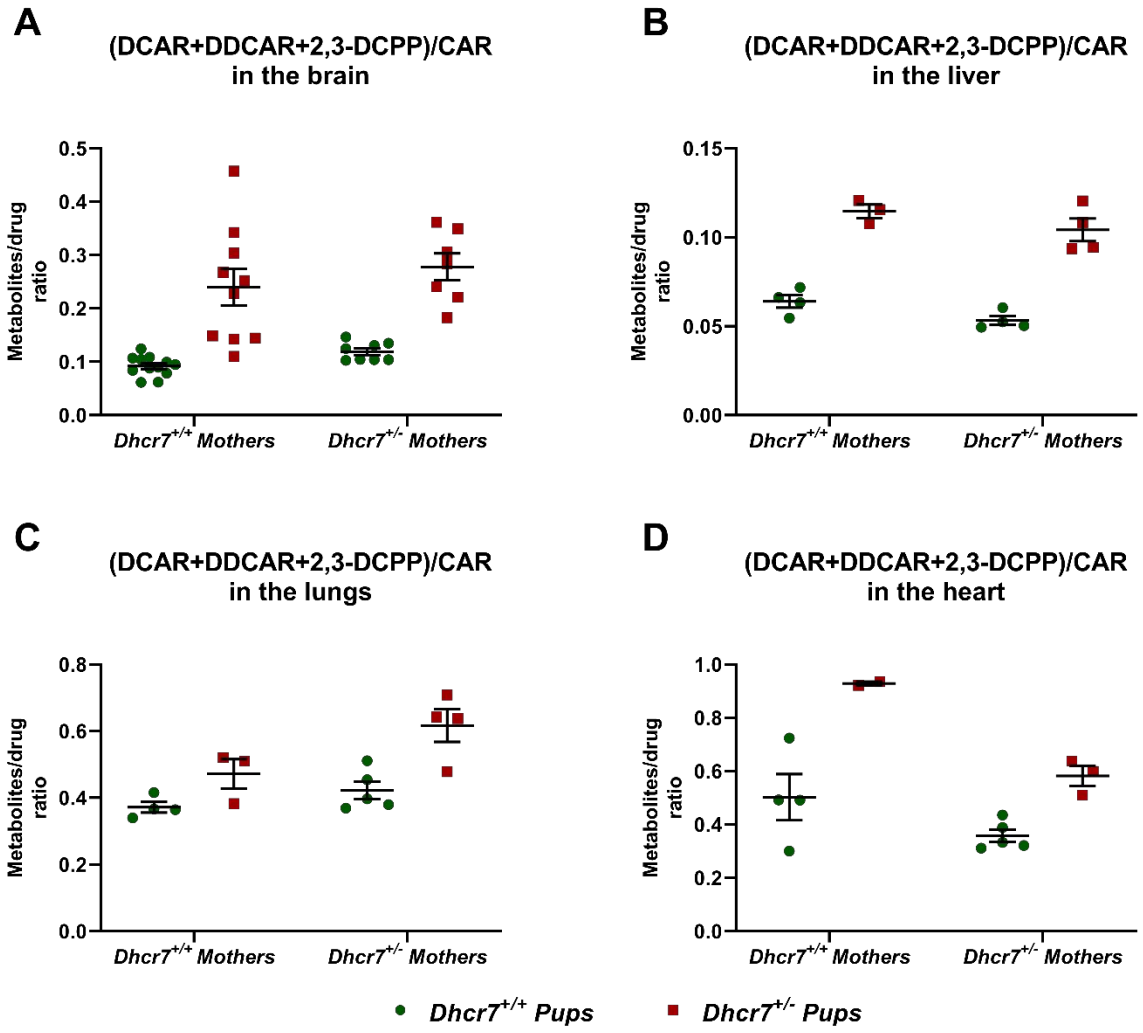

Figure S3. *Dhcr7*$^{+/-}$ mice metabolize CAR faster than WT mice. Cariprazine turnover was calculated by determining the ratio of drug metabolites over the parent drug. WT and *Dhcr7*$^{+/-}$ pups are depicted in green and red, respectively. Samples were grouped according to both maternal and embryonic genotypes. Bars correspond to the mean ± SEM.

Figure S4

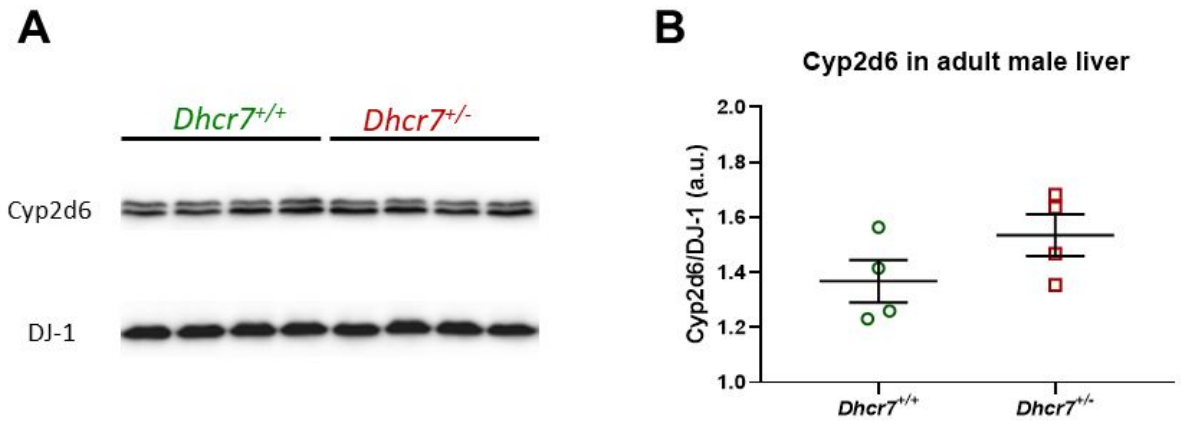

Figure S4. Cyp2d6 protein expression is increased in the liver of adult male *Dhcr7*$^{+/-}$ mice. **A)** Western blot for Cyp2d6. Expression of housekeeping protein DJ-1 was used as a loading control. Each lane corresponds to liver samples from different animals. **B)** Optical density quantification of bands, with Cyp2d6 normalized to DJ-1. The values on **panel B** are shown as averages ± SEM of four biological replicates.

Table S1. ANOVA analysis of ARI turnover in P0 livers.

#	Comparison	ARI
1	Embryonic genotype: *Dhcr7*$^{+/+}$ *vs Dhcr7*$^{+/-}$	**0.0013**
2	Maternal genotype: *Dhcr7*$^{+/+}$ *vs Dhcr7*$^{+/-}$	0.3086
3	Two-way interaction: maternal *Dhcr7 vs* embryonic *Dhcr7* genotypes	0.6365

Table S2. ANOVA analysis of CAR turnover in different tissues of P0 mice.

#	Comparison	Brain	Liver	Lungs	Heart
1	Embryonic genotype: *Dhcr7*$^{+/+}$ *vs Dhcr7*$^{+/-}$	**<0.0001**	**<0.0001**	**0.0013**	**0.0003**
2	Maternal genotype: *Dhcr7*$^{+/+}$ *vs Dhcr7*$^{+/-}$	0.1450	**0.0361**	**0.0166**	**0.0021**
3	Two-way interaction: maternal *Dhcr7 vs* embryonic *Dhcr7* genotypes	0.8042	0.9716	0.2039	0.1196

Rows **#1-2** denote statistical significance for single variables; **#3** reports probability for the two interacting factors; values highlighted in bold denote $p<0.05$. No statistical difference was observed between male and female animals.