Supplementary data：

Table S1. Rat and human primers used for reverse transcriptase-polymerase chain reaction.

Species	Genes	Forward primers (5'-3')	Reverse primers (5'-3')	Annealing
Rat	GAPDH	GCAAGTTCAATGGCACAG	AAGTTCTTCCTGGCCGGTAT	60℃, 30 s
	StAR	GGGAGATGCCTGAGCAAAGC	GCTGGCGAACTCTATCTGGGT	60℃, 30 s
	P450scc	GCTGCCTGGGATGTGATTTTC	GATGTTGGCCTGGATGTTCTTG	60℃, 30 s
	3β-HSD	TCTACTGCAGCACAGTTGAC	ATACCCTTATTTTTGAGGGC	60℃, 30 s
	P450c21	ATGAGCGTGAGTAGACAG	GATGCGTGTCGCATGGTC	60℃, 30 s
	P450c11	CCGCTTGTAGGATGTTGTAG	CAGGCTCTAAGGTGTCCAGT	60℃, 30 s
	HMGCR	CTGGTGAGTTGTCCTTGATG	CCGTGTTTCAGTCCAGTATG	60℃, 30 s
	SREBP2	AGAAGGAGAAAGGCGGACAA	TCTCCTGGCGCAGTTTATGA	60℃, 30 s
	SR-B1	CTTCTGGTGCCCATCATTTA	CCTACAGCTTGGCTTCTTG	60℃, 30 s
	LDLR	GGATCCATGGCAACATCTAC	ACCCTTTCTCTCGGAACA	60℃, 30 s
	ABCA1	AGAGCTAGGTCTCCCTT	CACTGCCCCTGTAATGG	60℃, 30 s
	ABCG1	TCTGACCTTTCCCCTCGAGAT	AGTACACGATGCTGCAGTAGGC	60℃, 30 s
	NLRP3	GAGCCTACAGTTGGGTGAAA	GCTTCCACACCTACCAAGAA	60℃, 30 s
	caspase1	AAGACAAGCCCAAGGTTATCA	AAGAATCCCTCTTCGGAGTTTC	60℃, 30 s
	IL-1β	TCTGACAGGCAACCACTTAC	CATCCCATACACACGGACAA	60℃, 30 s
	GR	CACCCATGACCCTGTCAGTC	AAAGCCTCCCTCTGCTAACC	60℃, 30 s
	SREBP1	CAGTACCCTTGAGGACCTTTG	ATCTCCAGATCTGCCACTAGA	60℃, 30 s
	p300	CAAATGCAGGCATGGGCAAT	TCCTGGTTGTCCTCCCATCT	60℃, 30 s
Human	GAPDH	CCATGGGTGGAATCATATTGGA	TCAACGGATTTGGTCGTATTGG	60℃, 30 s
	StAR	ACAGACTTCGGGAACATGC	TGAGTAGCCACGTAAGTTTGG	60℃, 30 s
	P450scc	AAGTCCACCTTCACCATGTC	TGAGGAATCGTTCTGGGTTG	60℃, 30 s
	SR-B1	TTGATGCCCAAGGTGATG	CCTTATCCTTTGAGCCCTTT	60℃, 30 s
	NLRP3	TTGGTGAATTCTGGCCTTAC	GAGTCCCTCACAGAGTAGTT	60℃, 30 s
	caspase1	GTTCCTGGTGTTCATGTCTC	CTTGGGCAGTTCTTGGTATT	60℃, 30 s
	IL-1β	CATGGGATAACGAGGCTTATG	CCACTTGTTGCTCCATATCC	60℃, 30 s
	GR	GCAGCAGTGAAATGGGCAAA	CAGCAGGTTTGCACTTGATTGT	60℃, 30 s

SREBP1	CACTGAGGCAAAGCTGAATAAAT	TAGGTTCTCCTGCTTGAGTTTC	60℃, 30 s
p300	GGCTGTATCAGAGCGTATTG	TCTTCCTCCTGTTCCAGTT	60℃, 30 s

GAPDH, glyceraldehyde-3-phosphate dehydrogenase; StAR, steroidogenic acute regulatory protein; P450scc, cytochrome P450 cholesterol side chain cleavage; 3β-HSD, 3β-hydroxysteroid dehydrogenase; P450c11, steroid 11β-hydroxylase; P450c21, steroid 21-hydroxylase; HMGCR, 3-hydroxy-3-methylglutaryl coenzyme A reductase; SR-B1, scavenger receptorB1; LDLR, low-density lipoprotein receptor ; ABCA1, ATP-binding cassette protein A1; NLRP3, NOD-like receptor family protein 3; IL-1β, interleukine-1β; GR, glucocorticoid receptor; SREBP1, sterol regulatory element-binding protein 1.

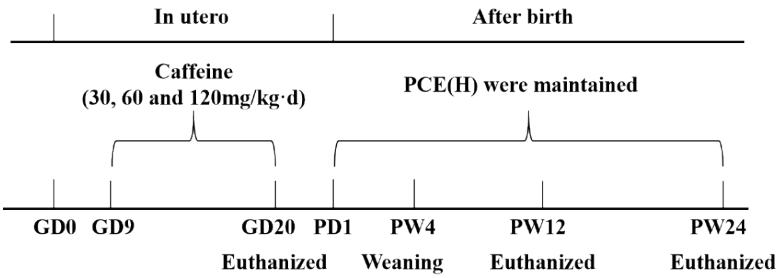

Fig S1. Animal experimental treatment. GD, gestational day; PD, postnatal day; PW, postnatal week; PCE, prenatal caffeine exposure.

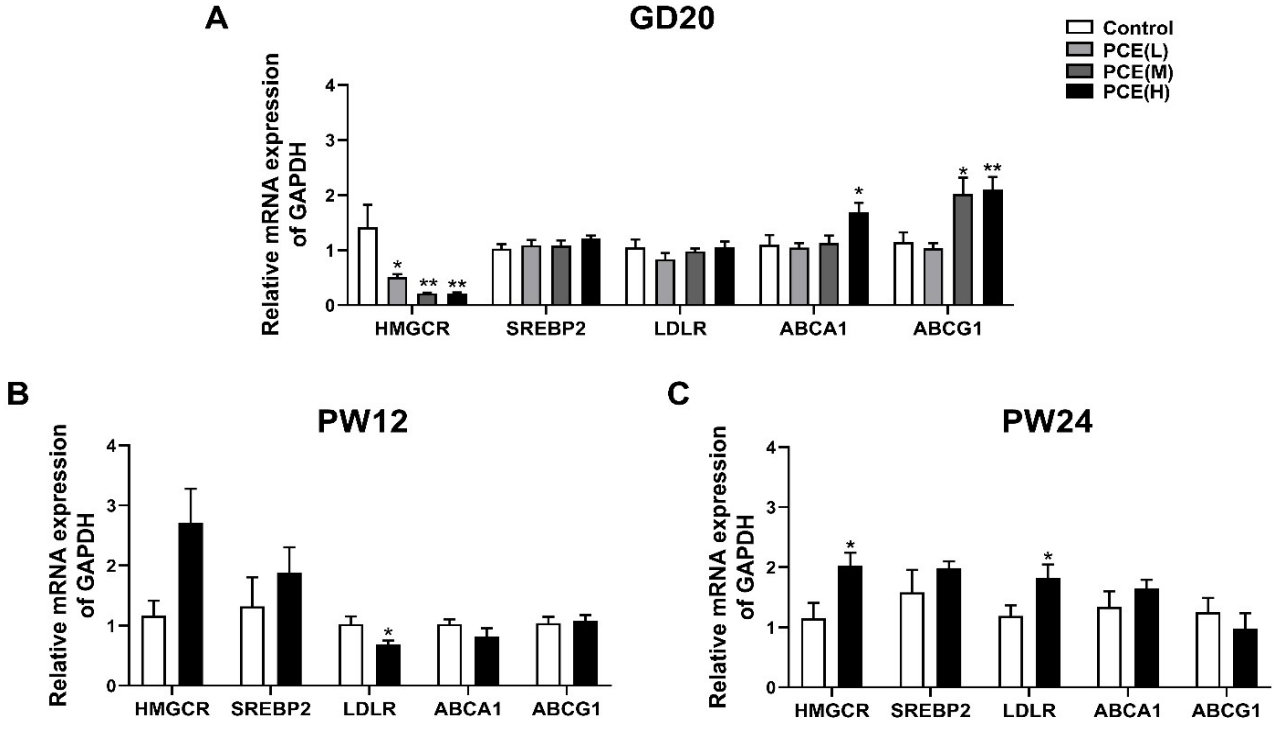

Fig S2. Change in the expression of adrenal cholesterol metabolism genes induced by PCE in female offspring

rats. (A-C) The mRNA expression of cholesterol metabolism genes, including HMGCR, SREBP2, LDLR, ABCA1 and ABCG1 on GD20, PW12 and PW24. Mean ± S.E.M., n = 12 from 12 different litters for RT-qPCR. $^{*}P<0.05$, $^{**}P<0.01$ *vs*. respective controls. PCE, prenatal caffeine exposure; GD, gestation day; PW, postnatal week; HMGCR, 3-hydroxy-3-methylglutaryl coenzyme A reductase; SREBP2, sterol regulatory element-binding protein 2; LDLR, low-density lipoprotein receptor; ABCA1, ATP-binding cassette protein A1; ABCG1, ATP binding cassette G1; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

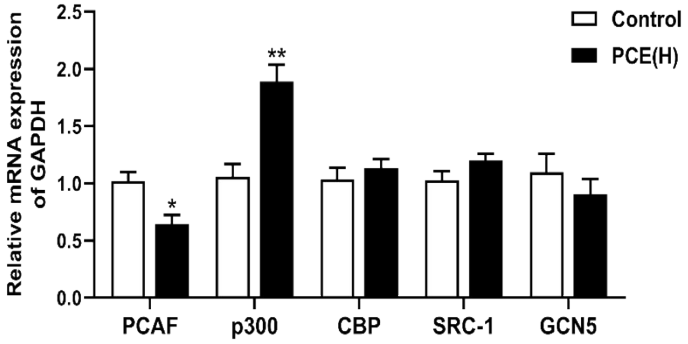

Fig S3. Change in the expression of adrenal histone acetylases induced by PCE in female fetal rats. Mean ± S.E.M., n = 12 from 12 different litters for RT-qPCR. $^{*}P<0.05$, $^{**}P<0.01$ *vs*. respective controls. PCE, prenatal caffeine exposure; PCAF, P300/CBP-associating factor, CBP, cAMP-response element (CRE)-binding protein; SRC-1, steroid receptor coactivator-1; GCN5, related N-acetyltransferases.

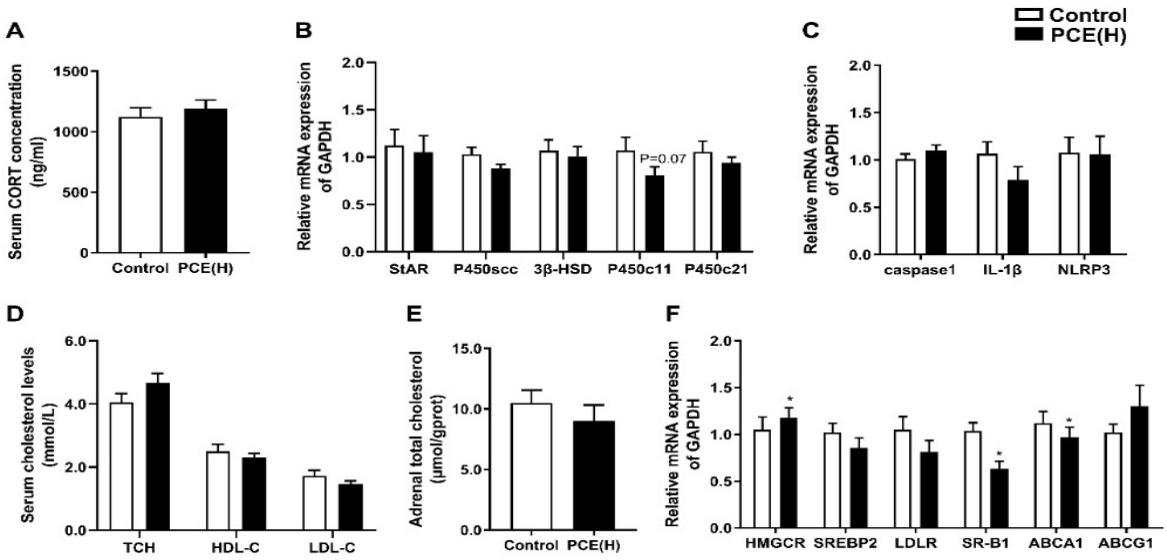

Fig S4. Effects of PCE on steroidogenic function, pyroptosis and cholesterol metabolism in adult male offspring. (A) The concentration of serum corticosterone in PW12; (B) The mRNA expression of steroidogenic enzymes in PW12, including StAR, P450scc, 3β-HSD, P450c21 and P450c11; (C) The mRNA expression of NRLP3, caspase1and IL-1β in PW12. (D) The concentration of serum TCH, HDL-C and LDL-C in PW12; (E) The content of adrenal TCH in PW12; (F) The mRNA expression of cholesterol metabolism genes in PW12, including HMGCR, SREBP2, LDLR, SR-B1, ABCA1and ABCG1. Mean ± S.E.M., n = 12 from 12 different litters for RT-qPCR. $^{*}P<0.05$, $^{**}P<0.01$ *vs*. respective controls. PW, postnatal week; PCE, prenatal caffeine exposure; StAR, steroidogenic

acute regulatory protein; P450scc, cytochrome P450 cholesterol side chain cleavage; 3β-HSD, 3β-hydroxysteroid dehydrogenase; P450c11, steroid 11β-hydroxylase; P450c21, steroid 21-hydroxylase; NLRP3, NOD-like receptor family protein 3; IL-1β, interleukine-1β; TCH, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; HMGCR, 3-hydroxy-3-methylglutaryl coenzyme A reductase; SREBP2, sterol regulatory element-binding protein 2; LDLR, low-density lipoprotein receptor; SR-B1, scavenger receptor-B1; ABCA1, ATP-binding cassette protein A1; ABCG1, ATP binding cassette G1.