



Fig. S1. Graphical abstract.

Table S1. Animal models

	Mice	Diet	Blockade of afferent sympathetic fibers	Follow up period
WT+SCD4W (Control)	C57BL/6JJcl	SCD	No	4 weeks
WT+SCD8W (Control)	C57BL/6JJcl	SCD	No	8 weeks
Sham+CDAA (4W)	C57BL/6JJcl	CDAA	No	4 weeks
Cap+CDAA (4W)	C57BL/6JJcl	CDAA	Yes	4 weeks
Sham+CDAA (8W)	C57BL/6JJcl	CDAA	No	8 weeks
Cap+CDAA (8W)	C57BL/6JJcl	CDAA	Yes	8 weeks
Sham+HFD (4W)	C57BL/6JJcl	HFD	No	4 weeks
Cap+HFD (4W)	C57BL/6JJcl	HFD	Yes	4 weeks
Sham+HFD (8W)	C57BL/6JJcl	HFD	No	8 weeks
Cap+HFD (8W)	C57BL/6JJcl	HFD	Yes	8 weeks
Sham+MC4RKO+SCD (4W)	MC4RKO	SCD	No	4 weeks
Cap+MC4RKO+SCD (4W)	MC4RKO	SCD	Yes	4 weeks
Sham+MC4RKO+SCD (8W)	MC4RKO	SCD	No	8 weeks
Cap+MC4RKO+SCD (8W)	MC4RKO	SCD	Yes	8 weeks
Sham+MC4RKO+HFD (4W)	MC4RKO	HFD	No	4 weeks
Cap+MC4RKO+HFD (4W)	MC4RKO	HFD	Yes	4 weeks
Sham+MC4RKO+HFD (8W)	MC4RKO	HFD	No	8 weeks
Cap+MC4RKO+HFD (8W)	MC4RKO	HFD	Yes	8 weeks
Sham+PH	C57BL/6JJcl	SCD	No	2 days
Cap+PH	C57BL/6JJcl	SCD	Yes	2 days

Table S2. The sequences of primers

Gene name	Forward primer (5' -3')	Reverse primer (5' -3')
<i>Tph1</i>	ACCATGATTGAAGACAACAAGGAG	TCAACTGTTCTCGGCTGATG
<i>Htr2a</i>	AAAGTTCTCTGCTGCGCTTC	CACGCAATGTTAATGCCATC
<i>Htr2b</i>	AAATAAGCCACCTCAACGCCT	TCCCGAAATGTCTTATTGAAGAG
<i>Acaca</i>	GCCTCTCCTGACAAACGAG	TGACTGCCGAAACATCTCTG
<i>Fasn</i>	AAGCGGTCTGGAAAGCTGAA	AGGCTGGGTTGATACCTCCA
<i>Gpat1</i>	CCACAGAGCTGGGAAAGGTT	GTGCCTTGTGTGCGTTTCAT
<i>Cpt1a</i>	AGCTCGCACATTACAAGGACA	CCAGCACAAAGTTGCAGGAC
<i>Mtp</i>	TCTCACAGTACCCGTTCTT	TCTTCTCCGAGAGACATATCC
<i>Pparg</i>	GGTGTGATCTTAACTGCCGGA	GCCCAAACCTGATGGCATTG
<i>Srebp1c</i>	GGAGCCATGGATTGCACATT	GGCCCGGGAAGTCACTGT
<i>Adgre1</i>	TCAAGGACACGAGGTTGCTGA	CCAAGGGGCAATCTGGAA
<i>Ccl2</i>	GGCTCAGCCAGATGCAGTTAA	AGCCTACTCATTGGGATCATCTT
<i>Colla1</i>	ACATGTTTCAGCTTTGTGGACC	TAGGCCATTGTGTATGCAGC
<i>Tgfb1</i>	GGGCTACCATGCCAACTTCTG	GAGGGCAAGGACCTTGCTGTA
<i>Timp1</i>	CCCTGCTCAGCAAAGAGC	TCACTCTCCAGTTTGCAAGG

Table S3. Clinical characteristics of the patients

Clinical characteristics	Control (n=54) Median (min–max)	NAFLD (n=31) Median (min–max)	<i>P</i>
Age	61 (30–75)	60 (18–76)	.7418
Male:Female	27:27	16:15	
Height (m)	1.61 (1.41–1.90)	1.62 (1.41–1.84)	.7046
BW (kg)	56.0 (34.2–111.0)	69.8 (48.2–140.0)	< .0001
BMI (kg/m ²)	22.1 (16.8–30.7)	25.6 (21.1–47.9)	< .0001
AST (U/L)	22 (14–57)	57 (26–166)	< .0001
ALT (U/L)	19 (8–62)	70 (16–267)	< .0001
ALP (U/L)	211 (109–337)	278 (107–510)	< .01
γ-GTP (U/L)	22 (7–159)	78 (19–729)	< .0001
T-Bil (mg/dL)	0.7 (0.4–2.2)	0.8 (0.4–2.9)	.0849
HbA1c (%)	5.6 (4.9–7.6)	6.1 (4.4–9.1)	< .0001
TG (mg/dL)	105 (29–456)	132 (31–464)	.0296
TC (mg/dL)	201 (146–280)	196 (124–282)	.1146
HDL-C (mg/dL)	63 (37–121)	50 (27–108)	.0100
LDL-C (mg/dL)	111 (63–256)	116 (33–177)	.8253
Plt (×10 ⁴ /μL)	23.4 (9.0–37.4)	17.7 (7.8–36.5)	.0066
FIB-4 Index	1.37 (0.45–3.82)	2.26 (0.36–10.47)	.0002
5-HT (ng/mL)	97.3 (27.1–281.4)	64.0 (9.2–254.5)	.0026
Liver CT score	62.61 (49.88–71.54)	40.42 (10.89–63.12)	< .0001
Spleen CT score	47.86 (38.51–59.76)	50.44 (28.84–57.40)	.7335
Liver-to-spleen CT score ratio	1.27 (1.05–1.59)	0.88 (0.22–1.35)	< .0001

BW, body weight; BMI, body mass index; AST, alanine aminotransferase; ALT, aspartate transaminase; ALP, alkaline phosphatase; γ-GTP, γ-glutamyl transferase; T-Bil, total bilirubin; HbA1c, hemoglobin A1c; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Plt, platelet; FIB-4, Fibrosis-4; 5-HT, 5-hydroxytryptamin. The values represent median (minimum–maximum), Mann–Whitney U test.

Table S4. Effect of autonomic neural signal transduction and HTR2A antagonist administration on the serum biochemical factors in mice

	Control	Sham+CDAA 4 W	Cap+CDAA 4 W	Sham+HFD 4 W	Cap+HFD 4 W	MC4RKO+ Sham+SCD 4 W	MC4RKO+ Cap+SCD 4 W	MC4RKO+ Sham+HFD 4 W	MC4RKO+ Cap+HFD 4 W	HFD 4 W, Sar (-)	HFD 4 W, Sar (+)
AST (U/L)	142.3 (41.6)	340.2 (109.9)	418.5 (17.4)	423.0 (85.9)	286.2 (99.4)	152.5 (39.9)	106.0 (11.0)	164.8 (41.3)	100.0 (19.7)	205.0 (16.7)	158.0 (7.6)
ALT (U/L)	32.3 (8.5)	99.0 (9.0)	189.0 (30.4) **	162.0 (25.6)	108.0 (22.0)	31.3 (3.4)	21.5 (1.7)	92.4 (17.4)	43.5 (11.1)	33.5 (4.9)	26.3 (1.7)
ALP (U/L)	131.9 (40.2)	400.5 (40.9)	607.5 (80.9)	477.0 (196.2)	400.5 (59.7)	243.3 (15.6)	217.6 (10.5)	144.9 (22.6)	118.2 (15.1)	218.0 (8.2)	192.0 (9.9)
TC (mg/dL)	60.9 (6.2)	67.5 (6.0)	76.5 (8.3)	139.5 (12.9)	85.5 (16.2) *	74.3 (4.9)	76.7 (1.4)	162.7 (5.6)	133.8 (5.8) *	138.5 (7.9)	146.0 (2.1)
TG (mg/dL)	50.1 (4.8)	58.5 (4.5)	72.0 (5.7)	103.5 (4.5)	63.0 (5.7) **	57.7 (7.8)	46.0 (9.9)	84.5 (18.4)	91.8 (12.5)	73.7 (12.4)	50.0 (8.4)

	Sham+CDAA 8 W	Cap+CDAA 8 W	Sham+HFD 8 W	Cap+HFD 8 W	MC4RKO+ Sham+SCD 8 W	MC4RKO+ Cap+SCD 8 W	MC4RKO+ Sham+HFD 8 W	MC4RKO+ Cap+HFD 8 W	MC4RKO+ HFD 4 W, Sar (-)	MC4RKO+ HFD 4 W, Sar (+)
AST (U/L)	334.8 (48.0)	459.0 (81.7) *	432.0 (100.5)	351.0 (41.8)	142.2 (28.9)	163.4 (30.1)	169.3 (39.2)	169.3 (36.8)	164.8 (41.3)	174.4 (23.9)
ALT (U/L)	166.5 (29.1)	175.5 (18.1)	139.5 (20.2)	193.5 (23.6)	29.3 (2.3)	43.3 (12.5)	141.5 (24.9)	59.3 (14.8) **	92.4 (17.4)	97.2 (18.0)
ALP (U/L)	661.5 (53.4)	643.5 (50.9)	496.8 (58.3)	626.4 (84.3)	188.7 (11.4)	178.6 (10.1)	189.5 (33.6)	149.5 (26.7)	216.8 (17.2)	241.3 (10.6)
TC (mg/dL)	108.0 (6.9)	81.0 (9.9)	58.5 (8.3)	148.5 (6.0) ***	73.5 (4.4)	76.0 (2.9)	180.1 (17.6)	155.3 (12.0)	153.0 (8.1)	144.0 (4.0)
TG (mg/dL)	58.5 (4.5)	67.5 (6.0)	117.0 (5.7)	90.0 (9.0)	47.3 (8.0)	76.4 (5.9) *	100.3 (10.1)	52.8 (7.4) ***	84.5 (18.4)	68.0 (11.7)

AST, alanine aminotransferase; ALT, aspartate transaminase; ALP, alkaline phosphatase; TC, total cholesterol; TG, triglyceride; Sar, sarpogrelate. The values represent mean (SD) (n = 6 for each group), Significance of the difference was evaluated using Welch's *t*-test. (**P* < .05, ***P* < .01, ****P* < .001 vs Sham group).