Supplementary Table 1: Key resources table

Antibodies and probes
Anti-NeuN mouse antibody, clone A60, Millipore, MAB377
Anti-GFP polyclonal rabbit antibody, Invitrogen, A6455
Goat anti-mouse IgG (H+L) cross-adsorbed secondary antibody, Alexa Fluor 647, ThermoFisher, A-21235
Goat anti-rabbit IgG (H+L) cross-adsorbed secondary antibody Alexa Fluor 488, ThermoFisher, A-11008
Probe-Mm-Th-C2, ACD, 317621-C2
Probe-Mm-Abhd6, ACD, 532861
Probe-Mm-Slc32a1-C3, ACD, 319191-C3
RNAscope Multiplex Fluorescent Detection Reagent, ACD, 320851
Experimental models: organisms/strains
Abhd6$^{lox/lox}$ on C57Bl/6N background, Zhao et al., 2014, N/A
C57Bl/6NCrl, Charles River, 027
C57BL/6J, Jackson Laboratoires, 000664
Viruses
AAV2/1.hSynapsin.HI.EGFP.WPRE.bGH, Penn Vector Core, AV-1-PV-1696/CS1221
AAV2/1.hSynapsin.HI.GFP.Cre.WPRE.SV40, Penn Vector Core, AV-1-P1848/CS1234
AAV9.TH.eGFP.WPRE.rBG, Penn Vector Core, V1802-1CS
AAV9.rTH.PI.Cre.SV40, Penn Vector Core, V5869R
Commercial assays and reagents
TRIzol, Invitrogen, 15596018
Chloroform, Bioshop, CCL402.1
Random Hexamer Phosphorylated; pd(N)6, GeneLink, 26-4000-10
M-MLV Reverse Transcriptase, Invitrogen, 28025013
dNTP set (100mM), Invitrogen, 10297018
GlycoBlue Coprecipitant, Invitrogen, AM9516
RNAsin Plus RNase Inhibitor, ThermoFisher, PRN2611
Rotor Gene SYBR Green PCR Kit (2000), Qiagen, 204076
SsoAdvanced Universal SYBR Green Supermix, Bio-Rad, 1725274
Tris (1M) pH 8.0, RNase-free, ThermoFisher, AM9855G
MgCl2 (1M), ThermoFisher, AM9530G
Goat serum, Sigma-Aldrich, G9023-10ml
Triton X-100, Sigma-Aldrich, T8787
Vectashield Hardset Antifade Mounting Medium with DAPI, Vector Laboratories, H-1500
2-methylbutane, ACP, M5342-500ML
RNAscope Multiplex Reagent Kit (V1), ACD, 320850
RNAscope Multiplex Reagent Kit (V2), ACD, 323270
RNAscope Wash Buffer Reagents, ACD, 310091
Opal 570 reagent pack, AKOYA biosciences, FR1488001KT
Opal 690 reagent pack, AKOYA biosciences, FP1497001KT
ProLong Gold Antifade Mountant, ThermoFisher, P36934
Pharmacological agents
d-amphetamine, Sigma-Aldrich, A5880
WWL70, Cayman Chemical, 10011213
DMSO, Sigma-Aldrich, 41640-100ML
WIN55,212-2, Cedarlane, BML-CR105-0010
AM251, Tocris Bioscience, 1117
TTX, Tocris Biosciences, 1078
NBQX, Tocris Biosciences, 0373
PTX, Tocris Biosciences, 1128
d-APV, Tocris Biosciences, 0106
Software and algorithms
Prism 9.3.1, GraphPad Software, https://www.graphpad.com
Rotor-Gene Q Series Software 2.3.1, Qiagen, N/A
Med-PC 5.1, Med Associates, N/A
Zen blue 3.4, Zeiss, N/A
ImageJ, NIH, https://imagej.net/ij/index.html
Clampfit 10.3, Molecular Devices, N/A

Mulitquant 2.0.2, SCIEX, N/A
NormFinder, Andersen et al., 2004, https://moma.dk/normfinder-software
EthoVision XT 15.0, Noldus, https://www.noldus.com/ethovision-xt
Oxymax for Windows V5.40, Columbus Instruments, N/A
Wheel Manager Data Acquisition, Med Associates, N/A
Diet
Modified AIN-93G Purified Rodent Diet with 50% Fat Derived Calories from Palm Oil, Dyets Inc., 182101
Dustless precision pellets (20mg) sugar, Bio-Serv, F05550

Supplementary Table 2. List of Primer Sequences

Gene	Forward sequence	Reverse sequence
18s	TAGCCAGGTTCTGGCCAACGG	AAGGCCCCAAAAGTGGCGCA
β-actin	TTCTTGGGTATGGAATCCTGTGGCA	ACCAGACAGCACTGTGTTGGCATA
Cyclophilin	GCTTTTCGCCGCTTGCTGCA	TGCAAACAGCTCGAAGGAGACGC
Abhd6	AGACCAGGTGCTTGATGT	CTCTCCATCACTACCGAAT
Mgll	GTGCCTACCTGCTCATGGAAT	GAGGACGGAGTTGGTCACTTC
Cnr1	GTGCTGTTGCTGTTCATTGTG	CTTGCCATCTTCTGAGGTGTG
Dagla	AGGAACACTTTTAGACGGCG	AAGCTGAGAGCCACCAAGAG
Daglb	AGGATTGGTGGCGACTGT	TGGTCACCTTCCACTGCAT
Faah	GTATCGCCAGTCCGTCATTG	GCCTATACCCTTTTTCATGCCC
Napepld	TTCTTTGCTGGGGATACTGG	GCAAGGTCAAAAGGACCAAA

Supplementary Table 3. Figure 1 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 1d	*Abhd6* relative expression	n=10 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=5.219, df=17, P<0.0001
Figure 1d	*Mgll* relative expression	n=11 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.3965, df=18, P=0.6964
Figure 1d	*Cnr1* relative expression	n=10 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.422, df=16, P=0.0277
Figure 1e	2-AG (ng/mg)	n=5 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=3.187, df=9, P=0.0111
Figure 1e	Anandamide (ng/mg)	n=4 ABHD6$^{NAc.\ GFP}$, n=4 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.3015, df=6, P=0.7732
Figure 1f	Body weight (% change)	n=8 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Two-way ANOVA, with Sidak's post-hoc multiple comparisons	Two-way ANOVA Interaction: $F_{(27,351)}$=6.642, P<0.0001 Time: $F_{(27,351)}$=10.58, P<0.0001 Group: $F_{(1,13)}$=5.332, P=0.0380 Sidak's multiple comparisons All rows before day 44 adjusted P>0.05 Day 44 t=3.185, df=364, adjusted P=0.0431 Day 46 t=4.335, df=364, adjusted P=0.0005 Day 48 t=3.351, df=364, adjusted P=0.0246 Day 50 t=3.784, df=364, adjusted P=0.0050 Day 52 t=3.507, df=364, adjusted P=0.0142 Day 54 t=3.908, df=364, adjusted P=0.0031 Day 56 t=3.882, df=364, adjusted P=0.0034
Figure 1g	Lean mass (g)	n=10 ABHD6$^{NAc.\ GFP}$, n=12 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.765, df=20, P=0.0120
Figure 1g	Fat mass (g)	n=10 ABHD6$^{NAc.\ GFP}$, n=12 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=3.355, df=20, P=0.0031
Figure 1h	Food intake (kcal)	n=6 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(28,364)}$=0.4826, P=0.9889 Time: $F_{(28,364)}$=1514, P<0.0001 Group: $F_{(1,13)}$=0.6803, P=0.4244
Figure 1i	Feed efficiency	n=6 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.629, df=13, P=0.0208
Figure 1j	Beam breaks	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,\ 336)}$=0.9034, P=0.6450 Time: $F_{(42,336)}$=2.952, P<0.0001 Group: $F_{(1,8)}$=4.261, P=0.0729
Figure 1k	Beam breaks (dark cycle)	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.770, df=8, P=0.1148
Figure 1k	Beam breaks (light cycle)	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.909, df=8, P=0.0196
Figure 1l	Rotations	n=7 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(25,300)}$=0.8558, P=0.6674 Time: $F_{(25,300)}$=12.27, P<0.0001 Group: $F_{(1,12)}$=0.7336, P=0.4085
Figure 1m	Total rotations	n=7 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.8565, df=12, P=0.4085

Supplementary Table 4. Supplementary Figure 1 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Supplementary Figure 1a	*Dagla* relative expression	n=6 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.5603, df=10, P=0.5876
Supplementary Figure 1a	*Daglb* relative expression	n=6 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.1964, df=10, P=0.8483
Supplementary Figure 1a	*Faah* relative expression	n=10 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=5.231, df=16, P<0.0001
Supplementary Figure 1a	*Napepld* relative expression	n=6 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.386, df=10, P=0.0383
Supplementary Figure 1b	Body length (mm)	n=7 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.2329, df=12, P=0.8198
Supplementary Figure 1c	Energy expenditure (kcal/h)	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,336)}$=0.9100, P=0.6337 Time: $F_{(42,336)}$=6.336, P<0.0001 Group: $F_{(1,8)}$=1.407, P=0.2696
Supplementary Figure 1d	Dark cycle energy expenditure (kcal/12hr)	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.170, df=8, P=0.2758
Supplementary Figure 1d	Light cycle energy expenditure (kcal/12hr)	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.200, df=8, P=0.2644
Supplementary Figure 1e	RER	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,336)}$=1.447, P=0.0418 Time: $F_{(42,336)}$=1.758, P=0.0037 Group: $F_{(1,8)}$=4.115, P=0.0770
Supplementary Figure 1f	Dark cycle RER	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.985, df=8, P=0.0824
Supplementary Figure 1f	Light cycle RER	n=4 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.8442, df=8, P=0.4231
Supplementary Figure 1g	Body weight (g)	n=7 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction $F_{(3,36)}$=0.7558, p=0.5263 Time: $F_{(3,36)}$=7.616, p=0.0005 Group: $F_{(1,12)}$=0.5581, p=0.4694

Supplementary Table 5. Figure 2 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 2b	Rewards achieved	n=6 ABHD6$^{NAc.\ GFP}$, n=4 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=3.445, df=8, P=0.0088
Figure 2c	Active lever discrimination (%)	n=6 ABHD6$^{NAc.\ GFP}$, n=4 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.2461, df=8, P=0.8118
Figure 2e	Preference (%)	n=14 ABHD6$^{NAc.\ GFP}$, n=11 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.080, df=23, P=0.0488
Figure 2f	Center time (%)	n=8 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.337, df=14, P=0.2026
Figure 2g	Center entries (%)	n=8 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.181, df=14, P=0.2571
Figure 2h	Velocity (cm/s)	n=8 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.5624, df=14, P=0.5828
Figure 2i	Open arm time (%)	n=8 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.8866, df=15, P=0.3893
Figure 2j	Open arm entries (%)	n=8 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.4195, df=15, P=0.6808
Figure 2k	Velocity (cm/s)	n=8 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.378, df=15, P=0.1883
Figure 2l	Time immobile (%)	n=9 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.9804, df=16, P=0.3415

Supplementary Table 6. Supplementary Figure 2 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Supplementary Figure 2a	Rewards achieved	n=6 ABHD6$^{NAc.\ GFP}$, n=4 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.2942, df=8, P=0.7761
Supplementary Figure 2b	Active lever discrimination (%)	n=6 ABHD6$^{NAc.\ GFP}$, n=4 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.198, df=8, P=0.2653
Supplementary Figure 2c	Velocity (cm/s)	n=9 ABHD6$^{NAc.\ GFP}$, n=9 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.2526, df=16, P=0.8038

Supplementary Table 7. Figure 3 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 3a	Body weight (% change)	n=9 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA, with Sidak's post-hoc multiple comparisons	Two-way ANOVA Interaction: $F_{(27,351)}$=33.17, P<0.0001 Time: $F_{(27,351)}$=44.89, P<0.0001 Group: $F_{(1,13)}$=23.25, P=0.0003 Sidak's multiple comparisons All rows before Day 26 adjusted P>0.05 Day 26 t=3.507, df=364, adjusted P=0.0142 Day 28 t=4.293, df=364, adjusted P=0.0006 Day 30 t=4.681, df=364, adjusted P=0.0001 Day 32 t=5.063, df=364, adjusted P<0.0001 Day 34 t=5.730, df=364, adjusted P<0.0001 Day 36 t=5.594, df=364, adjusted P<0.0001 Day 38 t=6.271, df=364, adjusted P<0.0001 Day 40 t=6.446, df=364, adjusted P<0.0001 Day 42 t=6.923, df=364, adjusted P<0.0001 Day 44 t=7.000, df=364, adjusted P<0.0001 Day 46 t=7.574, df=364, adjusted P<0.0001 Day 48 t=7.558, df=364, adjusted P<0.0001 Day 50 t=7.642, df=364, adjusted P<0.0001 Day 52 t=7.535, df=364, adjusted P<0.0001 Day 54 t=7.845, df=364, adjusted P<0.0001 Day 56 t=8.425, df=364, adjusted P<0.0001
Figure 3b	Lean mass (g)	n=13 ABHD6$^{NAc.\ GFP}$, n=13 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.450, df=24, P=0.0219
Figure 3b	Fat mass (g)	n=13 ABHD6$^{NAc.\ GFP}$, n=13 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=5.635, df=24, P<0.0001
Figure 3c	Cumulative food intake (kcal)	n=9 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA, with Sidak's post-hoc multiple comparisons	Two-way ANOVA Interaction: $F_{(28,\ 364)}$=3.544, P<0.0001 Time: $F_{(28.\ 364)}$=1698, P<0.0001 Group: $F_{(1,13)}$=1.520, P=0.2395 Sidak's multiple comparisons adjusted P>0.05 for all rows
Figure 3d	Feed efficiency	n=9 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=5.995, df=13, P<0.0001
Figure 3e	Energy expenditure (kcal/h)	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,462)}$=1.685, P=0.0059 Time: $F_{(42,462)}$=10.88, P<0.0001 Group: $F_{(1,11)}$=0.06399, P=0.8050
Figure 3f	Dark cycle energy expenditure (kcal/12hr)	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.3061, df=11, P=0.7652
Figure 3f	Light cycle energy expenditure (kcal/12hr)	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.1405, df=11, P=0.8908
Figure 3g	RER	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,462)}$=1.489, P=0.0283 Time: $F_{(42,462)}$=1.351, P=0.0752 Group: $F_{(1,11)}$=0.5066, P=0.4914
Figure 3h	Dark cycle RER	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=1.062, df=11, P=0.3110
Figure 3h	Light cycle RER	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.2010, df=11, P=0.8444
Figure 3i	Beam breaks	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(42,462)}$=1.874, P=0.0011 Time: $F_{(42,462)}$=7.431, P<0.0001 Group: $F_{(1,11)}$=6.114, P=0.0310
Figure 3j	Dark cycle beam breaks	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.087, df=11, P=0.0610
Figure 3j	Light cycle beam breaks	n=7 ABHD6$^{NAc.\ GFP}$, n=6 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.318, df=11, P=0.0407
Figure 3k	Rotations	n=6 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(25,275)}$=2.434, P=0.0002 Time: $F_{(25,275)}$=2.693 p<0.0001 Group: $F_{(1,11)}$=5.873, P=0.0338
Figure 3l	Total rotations	n=6 ABHD6$^{NAc.\ GFP}$, n=7 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.423, df=11, P=0.0338

Supplementary Table 8. Supplementary Figure 3 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Supplementary Figure 3a	Cumulative food intake (kcal)	n=9 ABHD6$^{NAc.\ GFP}$ (HFD), n=6 ABHD6$^{NAc\ KO}$ (HFD)	Unpaired t-test	t=1.658, df=13, P=0.1213
Supplementary Figure 3b	Rotations	n=7 ABHD6$^{NAc.\ GFP}$ (chow), n=6 ABHD6$^{NAc.\ GFP}$ (HFD), n=7 ABHD6$^{NAc\ KO}$ (HFD)	Two-way ANOVA	Interaction: $F_{(50,425)}$=2.374, P<0.0001 Time: $F_{(25,425)}$=5.514, P<0.0001 Group: $F_{(2,17)}$=9.083, P=0.0021
Supplementary Figure 3c	Rotations	n=7 ABHD6$^{NAc.\ GFP}$ (chow), n=6 ABHD6$^{NAc.\ GFP}$ (HFD), n=7 ABHD6$^{NAc\ KO}$ (HFD)	One-way ANOVA, with Tukey's post-hoc multiple comparisons	One-way ANOVA Group: $F_{(2,17)}$=9.083, P=0.0021, Tukey's multiple comparisons ABHD6$^{NAc\ GFP}$ vs. ABHD6$^{NAc\ GFP}$ (HFD) q=6.025, df=17, adjusted P=0.0015 ABHD6$^{NAc\ GFP}$ vs. ABHD6$^{NAc\ KO}$ (HFD) q=2.723, df=17, adjusted P=0.1619 ABHD6$^{NAc\ GFP}$ (HFD) vs. ABHD6$^{NAc\ KO}$ (HFD) q=3.408, df=17, adjusted P=0.0675

Supplementary Table 9. Figure 4 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 4b	mIPSC frequency (Hz)	n=21 ABHD6$^{NAc.\ GFP}$, n=17 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=4.122, df=36, P=0.0002
Figure 4c	mIPSC amplitude (pA)	n=21 ABHD6$^{NAc.\ GFP}$, n=17 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.971, df=36, P=0.0053
Figure 4d	sIPSC frequency (Hz)	n=12 ABHD6$^{NAc.\ GFP}$, n=10 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.939, df=20, P=0.0081
Figure 4e	sIPSC amplitude (pA)	n=12 ABHD6$^{NAc.\ GFP}$, n=10 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=3.707, df=20, P=0.0014
Figure 4f	sEPSC frequency (Hz)	n=8 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.03512, df=14, P=0.9725
Figure 4g	sEPSC amplitude (pA)	n=9 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=0.8296, df=15, P=0.4198
Figure 4h	mIPSC frequency (% baseline)	n=10 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(21,336)}$=1.791, P=0.0185 Time: $F_{(21,336)}$=13.90, P<0.0001 Group: $F_{(1,16)}$=4.505, P=0.0497
Figure 4i	mIPSC amplitude (% baseline)	n=10 ABHD6$^{NAc.\ GFP}$, n=8 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(21,336)}$=1.226, P=0.2261 Time: $F_{(21,336)}$=3.524, P<0.0001 Group: $F_{(1,16)}$=0.2018, P=0.6593
Figure 4j	eIPSC amplitude (% baseline)	n=2 ABHD6$^{NAc.\ GFP}$, n=3 ABHD6$^{NAc\ KO}$	Two-way ANOVA	Interaction: $F_{(20,60)}$=0.4473, P=0.9757 Time: $F_{(20,60)}$=21.75, P<0.0001 Group: $F_{(1,3)}$=0.07500, P=0.8020
Figure 4k	mIPSC frequency (Hz)	n=14 ABHD6$^{NAc.\ GFP}$, n=14 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=2.111, df=26, P=0.0446
Figure 4l	mIPSC amplitude (pA)	n=14 ABHD6$^{NAc.\ GFP}$, n=13 ABHD6$^{NAc\ KO}$	Unpaired t-test	t=6.506, df=25, P<0.0001

Supplementary Table 10. Figure 5 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 5c	*Abhd6* relative expression	n=38 $ABHD6^{VTA\ GFP}$, n=26 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=5.111, df=62, P<0.0001
Figure 5d	Body weight (% change)	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(6,90)}$=0.3644, P=0.8996 Time: $F_{(6,90)}$=23.56, P<0.0001 Group: $F_{(1,15)}$=0.6717, P=0.4253
Figure 5e	Cumulative food intake (g)	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(6,90)}$=2.435, P=0.0315 Time: $F_{(6,90)}$=5528, P<0.0001 Group: $F_{(1,15)}$=7.669, P=0.0143
Figure 5f	Feed efficiency	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.7894, df=15, P=0.4422
Figure 5g	RER	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(54,810)}$=0.7757, P=0.8794 Time: $F_{(54,810)}$=15.21, P<0.001 Group: $F_{(1,15)}$=1.889, P=0.1884
Figure 5h	Dark cycle RER	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=1.865, df=15, P=0.0818
Figure 5h	Light cycle RER	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.8289, df=15, P=0.4202
Figure 5i	Beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(55,825)}$=1.146, P=0.2223 Time: $F_{(55,825)}$=8.964, P<0.0001 Group: $F_{(1,15)}$=1.231, P=0.2847
Figure 5j	Dark cycle beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.9291, df=15, P=0.3675
Figure 5j	Light cycle beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=1.178, df=15, P=0.2571
Figure 5k	Body weight (% change)	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(13,195)}$=1.483, P=0.1262 Time: $F_{(13,195)}$=147.8, P<0.0001 Group: $F_{(1,15)}$=0.6316, P=0.4392
Figure 5l	Lean mass (g)	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.3551, df=15, P=0.7274
Figure 5l	Fat mass (g)	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=1.345, df=15, P=0.1987
Figure 5m	Beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(54,810)}$=0.7299, P=0.9270 Time: $F_{(54,810)}$=7.742, P<0.0001 Group: $F_{(1,15)}$=4.818, P=0.0443
Figure 5n	Dark cycle beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=1.767, df=15, P=0.0976
Figure 5n	Light cycle beam breaks	n=10 $ABHD6^{VTA\ GFP}$, n=7 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=2.448, df=15, P=0.0271

Supplementary Table 11. Supplementary Figure 4 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Supplementary Figure 4a	Cumulative food intake (g)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(7,105)}$=2.534, P=0.0189 Time: $F_{(7,\ 105)}$=460.0, P<0.0001 Group: $F_{(1,15)}$=8.568, P=0.0104
Supplementary Figure 4b	24hr cumulative food intake (g)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=2.321, df=15, P=0.0348
Supplementary Figure 4c	Cumulative food intake (g)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(7,105)}$=0.5852, P=0.7667 Time: $F_{(7,105)}$=1076, P<0.0001 Group: $F_{(1,15)}$=0.1479, P=0.7059
Supplementary Figure 4d	Final cumulative food intake (g)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=1.961, df=15, P=0.0687
Supplementary Figure 4e	Energy expenditure (kcal/h)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(55,825)}$=1.299, P=0.0754 Time: $F_{(55,825)}$=16.29, P<0.0001 Group: $F_{(1,15)}$=0.01675, P=0.8987
Supplementary Figure 4f	Dark cycle energy expenditure (kcal/12h)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=0.001040, df=15, P=0.9992
Supplementary Figure 4f	Light cycle energy expenditure	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=0.1616, df=15, P=0.8738
Supplementary Figure 4g	Cumulative food intake (kcal)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(13,195)}$=1.341, P=0.1923 Time: $F_{(13,195)}$=4384, P<0.0001 Group: $F_{(1,15)}$=0.2960, P=0.5944
Supplementary Figure 4h	Feed efficiency	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=1.589, df=15, P=0.1329
Supplementary Figure 4i	Energy expenditure (kcal/h)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(54,810)}$=0.6590, P=0.9723 Time: $F_{(54,810)}$=16.31, P<0.0001 Group: $F_{(1,15)}$=0.1206, P=0.7332
Supplementary Figure 4j	Energy expenditure (kcal/h)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=0.7244, df=15, P=0.4800
Supplementary Figure 4j	Energy expenditure (kcal/h)	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=0.1987, df=15, P=0.8452
Supplementary Figure 4k	RER	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Two-way ANOVA	Interaction: $F_{(54,810)}$=1.069, P=0.3453 Time: $F_{(54,810)}$=5.771, P<0.0001 Group: $F_{(1,15)}$=0.6918, P=0.4186
Supplementary Figure 4l	Dark cycle RER	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=0.8336, df=15, P=0.4176
Supplementary Figure 4l	Light cycle RER	n=10 ABHD6$^{VTA\ GFP}$, n=7 ABHD6$^{VTA\ KO}$	Unpaired t-test	t=1.313, df=15, P=0.2090

Supplementary Table 12. Figure 6 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Figure 6a	Center time (%)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.6640, df=20, P=0.5143
Figure 6b	Center entries (%)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.3393, df=20, P=0.7379
Figure 6c	Open arm time (%)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=1.073, df=20, P=0.2961
Figure 6d	Open arm entries (%)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.06123, df=20, P=0.9518
Figure 6e	Interaction time difference (s)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.6239, df=20, P=0.5397
Figure 6h	Change in rewards achieved (%)	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.6367, df=13, P=0.5354
Figure 6i	Change in active lever responses (%)	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.5550, df=13, P=0.5883
Figure 6j	Pre-fast active lever discrimination (%)	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.3545, df=13, P=0.7286
Figure 6j	Fast active lever discrimination (%)	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.4081, df=13, P=0.6898
Figure 6m	Change in rewards achieved (%)	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=2.186, df=12, P=0.0494
Figure 6n	Change in active lever responses (%)	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=2.442, df=12, P=0.0310
Figure 6o	Pre-fast active lever discrimination (%)	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=1.124, df=12, P=0.2831
Figure 6o	Fast active lever discrimination (%)	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=0.3541, df=12, P=0.7294

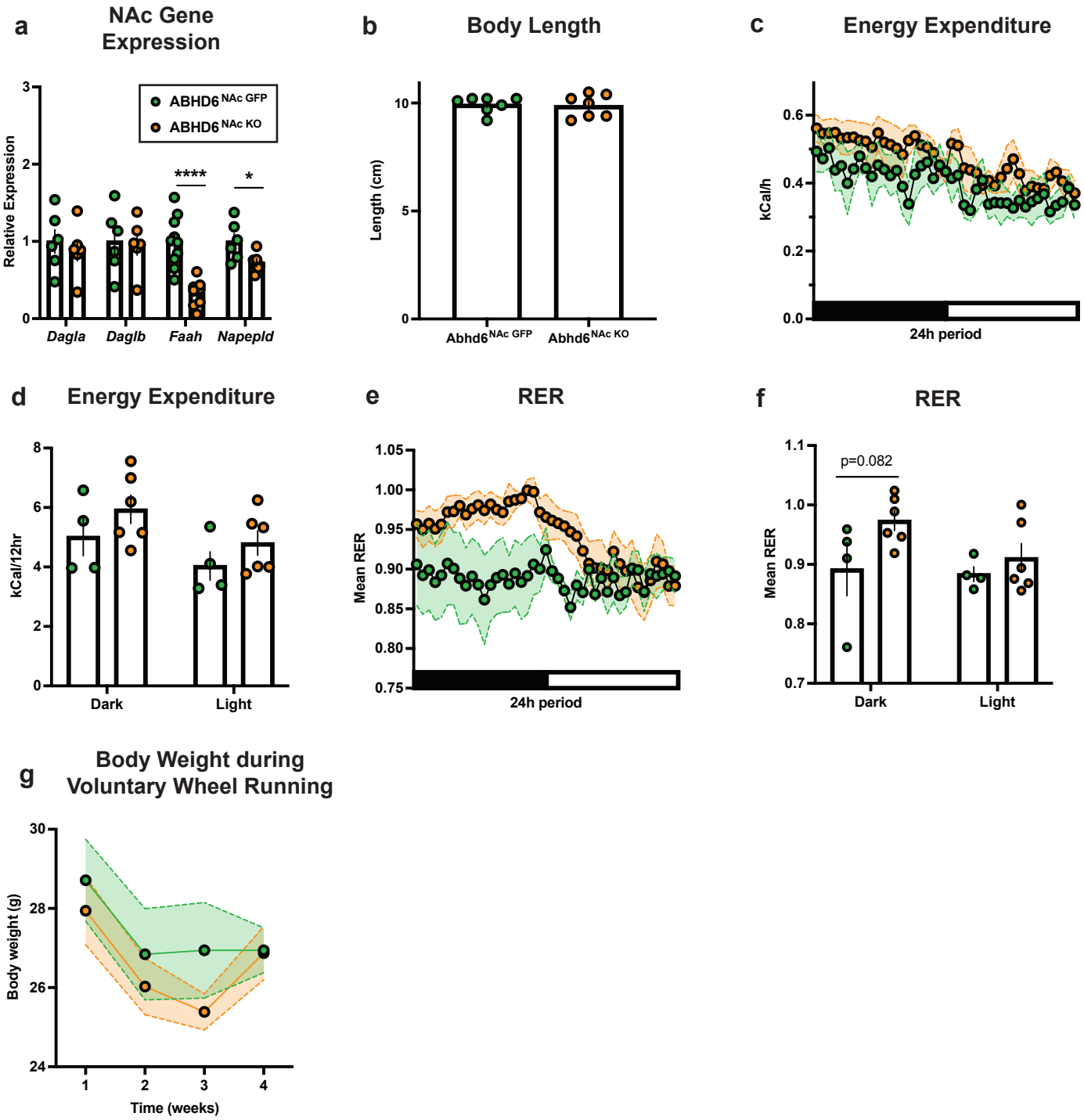
Supplementary Table 13. Supplementary Figure 5 statistics

Figure panel	Response variable	n	Statistical analysis	Result
Supplementary Figure 5a	Velocity (cm/s)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.6297, df=20, P=0.5360
Supplementary Figure 5b	Velocity (cm/s)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.3054, df=20, P=0.7632
Supplementary Figure 5c	Demo preference (%)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.2838, df=20, P=0.7795
Supplementary Figure 5d	Velocity (cm/s)	n=12 $ABHD6^{VTA\ GFP}$, n=10 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.2546, df=20, P=0.8016
Supplementary Figure 5e	Pre-surgery mean rewards achieved	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.6793, df=13, P=0.5089
Supplementary Figure 5f	Active lever discrimination (%)	n=9 $ABHD6^{VTA\ GFP}$, n=6 $ABHD6^{VTA\ KO}$	Unpaired t-test	t=0.9896, df=13, P=0.3404
Supplementary Figure 5g	Pre-surgery mean rewards achieved	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=0.6933, df=12, P=0.5013
Supplementary Figure 5h	Pre-surgery active lever discrimination (%)	n=7 $ABHD6^{TH\ GFP}$, n=7 $ABHD6^{TH\ KO}$	Unpaired t-test	t=0.08657, df=12, P=0.9324

Supplementary Table 14. Figure 7 statistics

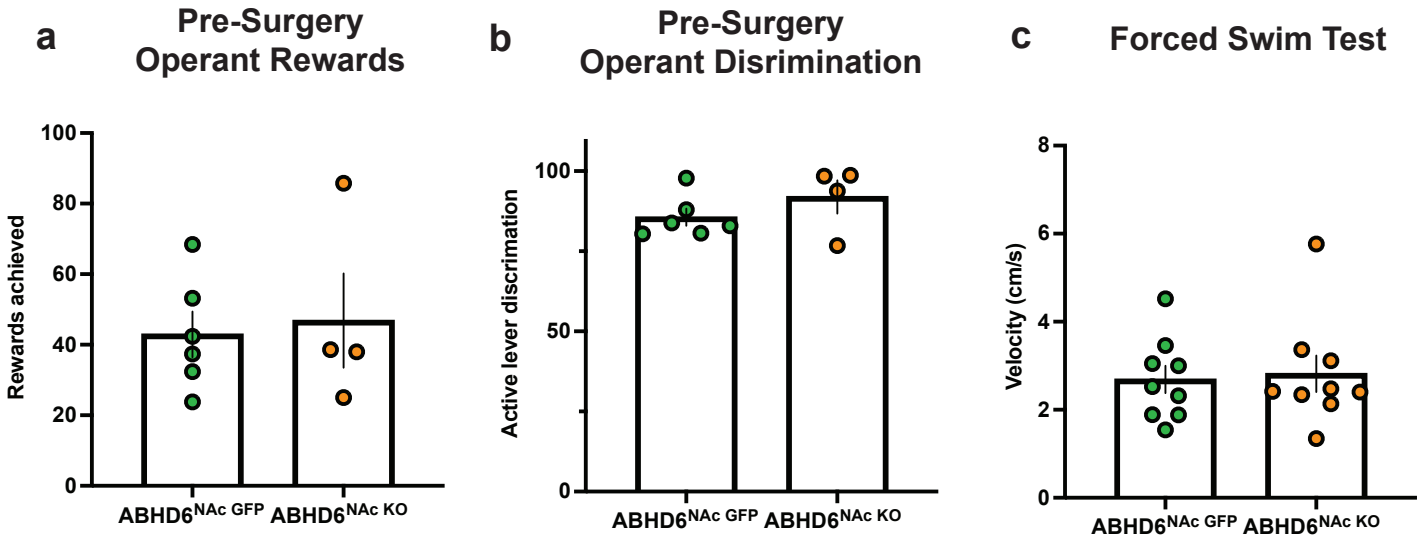
Figure panel	Response variable	n	Statistical analysis	Result
Figure 7a	Body weight (% change)	n=9 vehicle, n=10 WWL70	Two-way ANOVA, with Sidak's post hoc multiple comparisons	Two-way ANOVA Interaction: $F_{(11,187)}$=4.300, P<0.0001 Time: $F_{(11,187)}$=121.2, P<0.0001 Group: $F_{(1,17)}$=13.44, P=0.0019 Sidak's post hoc All rows before Day 12 adjusted P>0.05 Day 12 t=3.270, df=204, adjusted P=0.0150 Day 14 t=3.419, df=204, adjusted P=0.0091 Day 18 t=3.407, df=204, adjusted P=0.0095 Day 21 t=3.814, df=204, adjusted P=0.0022 Day 24 t=4.074, df=204, adjusted P=0.0008 Day 26 t=4.196, df=204, adjusted P=0.0005 Day 28 t=4.459, df=204, adjusted P=0.0002
Figure 7b	Final body weight (% of initial)	n=9 vehicle, n=10 WWL70	Unpaired t-test	t=2.674, df=17, P=0.0160
Figure 7c	Cumulative food intake (kcal)	n=9 vehicle, n=9 WWL70	Two-way ANOVA, with Sidak's post hoc multiple comparisons	Two-way ANOVA Interaction: $F_{(11,176)}$=3.591, P=0.0001 Time: $F_{(11,176)}$=3668, P<0.0001 Group: $F_{(1,16)}$=6.289, P=0.0233 Sidak's multiple comparisons All rows before day 21 adjusted P>0.05 Day 24 t=3.129, df=192.0, adjusted P=0.0241 Day 26 t=3.181, df=192.0, adjusted P=0.0204 Day 28 t=3.164, df=192.0, adjusted P=0.0215
Figure 7d	Total food intake (kcal)	n=9 vehicle, n=9 WWL70	Unpaired t-test	t=2.330, df=16, P=0.0332
Figure 7e	Energy expenditure (kcal/h)	n=6 vehicle, n=6 WWL70	Two-way ANOVA, with Sidak's post hoc multiple comparisons	Interaction: $F_{(53,530)}$=1.520, P=0.0129 Time: $F_{(53,530)}$=11.80, P<0.0001 Group:,$F_{(1,10)}$=4.707, P=0.0552 Sidak's multiple comparisons Row 3 t=3.383, df=540, adjusted P=0.0407 All other rows adjusted P>0.05
Figure 7f	Dark cycle energy expenditure (kcal/12hr)	n=6 vehicle, n=6 WWL70	Unpaired t-test	t=1.826, df=10, P=0.0978
Figure 7f	Light cycle energy expenditure (kcal/12hr)	n=6 vehicle, n=6 WWL70	Unpaired t-test	t=2.514, df=10, P=0.0307
Figure 7g	RER	n=6 vehicle, n=6 WWL70	Two-way ANOVA	Interaction: $F_{(53,530)}$=0.7902, P=0.8558 Time: $F_{(53,530)}$=1.323, P=0.0693 Group: $F_{(1,10)}$=4.798, P=0.0533
Figure 7h	Dark cycle RER	n=6 vehicle, n=6 WWL70	Unpaired t-test	t=1.821, df=10, P=0.0986
Figure 7h	Light cycle RER	n=6 vehicle, n=6 WWL70	Unpaired t-test	t=1.744, df=10, P=0.1118
Figure 7i	Beam breaks	n=5 vehicle, n=5 WWL70	Two-way ANOVA	Interaction: $F_{(53,424)}$=1.148, P=0.2318 Time: $F_{(53,424)}$=4.205, P<0.0001 Group: $F_{(1,8)}$=4.630, P=0.0636
Figure 7j	Dark cycle beam breaks	n=5 vehicle, n=5 WWL70	Unpaired t-test	t=1.681, df=8, P=0.1313
Figure 7j	Light cycle beam breaks	n=5 vehicle, n=5 WWL70	Unpaired t-test	t=2.580, df=8, P=0.0326
Figure 7k	Center time (%)	n=8 vehicle, n=8 WWL70	Unpaired t-test	t=0.8933, df=14, P=0.3868
Figure 7l	Center entries (%)	n=8 vehicle, n=8 WWL70	Unpaired t-test	t=0.1653, df=14, P=0.8711

Supplementary Figure 1



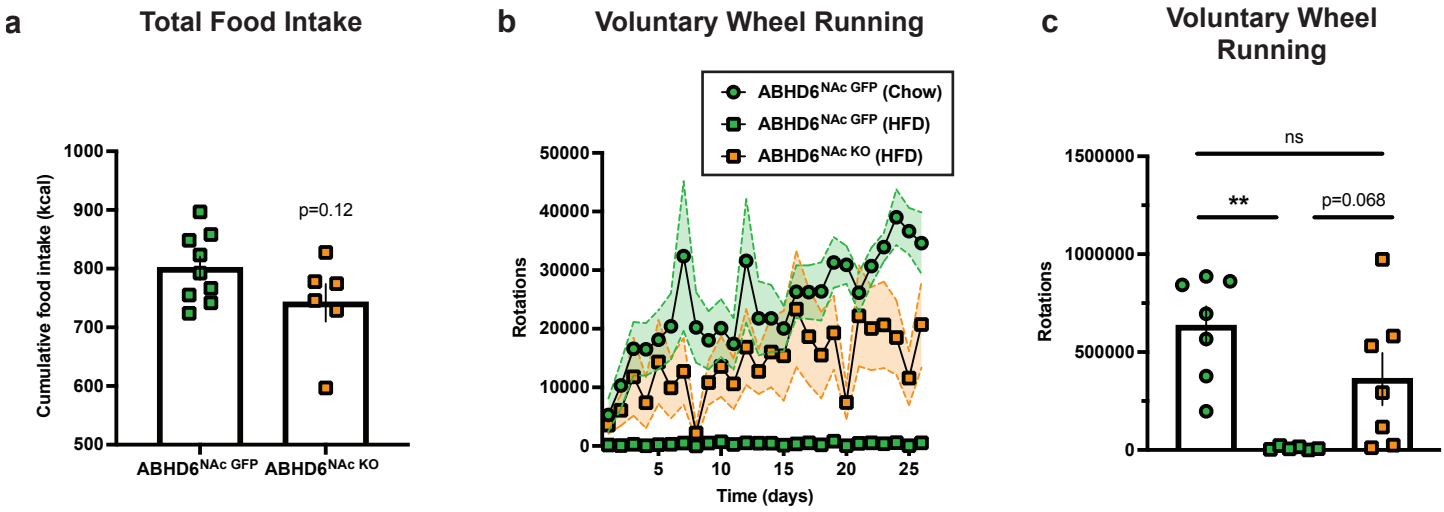
Supplementary Figure 1. NAc gene expression, body length, and metabolism. Related to Figure 1. **a** NAc gene expression for *Dagla* (ABHD6$^{NAc\ GFP}$: n=6, ABHD6$^{NAc\ KO}$: n=6), *Daglb* (ABHD6$^{NAc\ GFP}$: n=6, ABHD6$^{NAc\ KO}$: n=6), *Faah* (ABHD6$^{NAc\ GFP}$: n=10, ABHD6$^{NAc\ KO}$: n=8), and *Napepld* (ABHD6$^{NAc\ GFP}$: n=6, ABHD6$^{NAc\ KO}$: n=6), **b** Body length (ABHD6$^{NAc\ GFP}$: n=7, ABHD6$^{NAc\ KO}$: n=7). **c** Energy expenditure (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6). **d** Energy expenditure in (**c**) during dark (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6) and light cycle (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6). **e** Respiratory exchange ratio (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6). **f** RER in (**e**) during dark (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6) and light cycle (ABHD6$^{NAc\ GFP}$: n=4, ABHD6$^{NAc\ KO}$: n=6). **g** Body weight during wheel-running access (ABHD6$^{NAc\ GFP}$: n=7, ABHD6$^{NAc\ KO}$: n=7). Data represented as mean, with error bars/shaded areas ± SEM. Unpaired t-test (**a, b, d, f**), two-way ANOVA group x time interaction (**c, e, g**).

Supplementary Figure 2



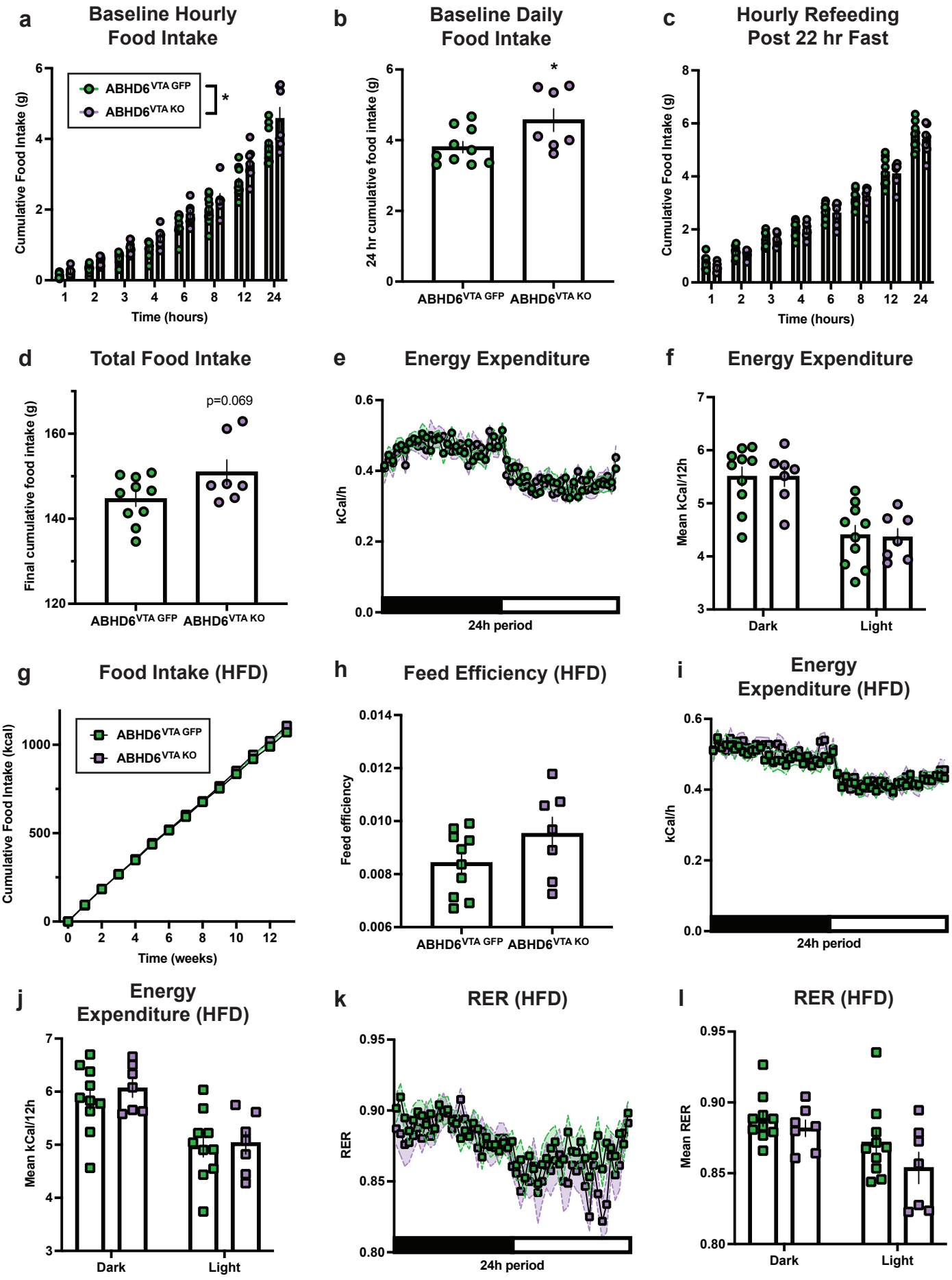
Supplementary Figure 2. Pre-surgery operant behaviour and forced swim test velocity. Related to Figure 2. **a** Pre-surgery operant rewards achieved at fixed ratio 5 (ABHD6$^{NAc\ GFP}$: n=6, ABHD6$^{NAc\ KO}$: n=4). **b** Pre-surgery operant active lever discrimination at fixed ratio 5 (ABHD6$^{NAc\ GFP}$: n=6, ABHD6$^{NAc\ KO}$: n=4). **c** Velocity during forced swim test (ABHD6$^{NAc\ GFP}$: n=9, ABHD6$^{NAc\ KO}$: n=9). Data represented as mean, with error bars areas ± SEM. Unpaired t-test (**a-c**).

Supplementary Figure 3



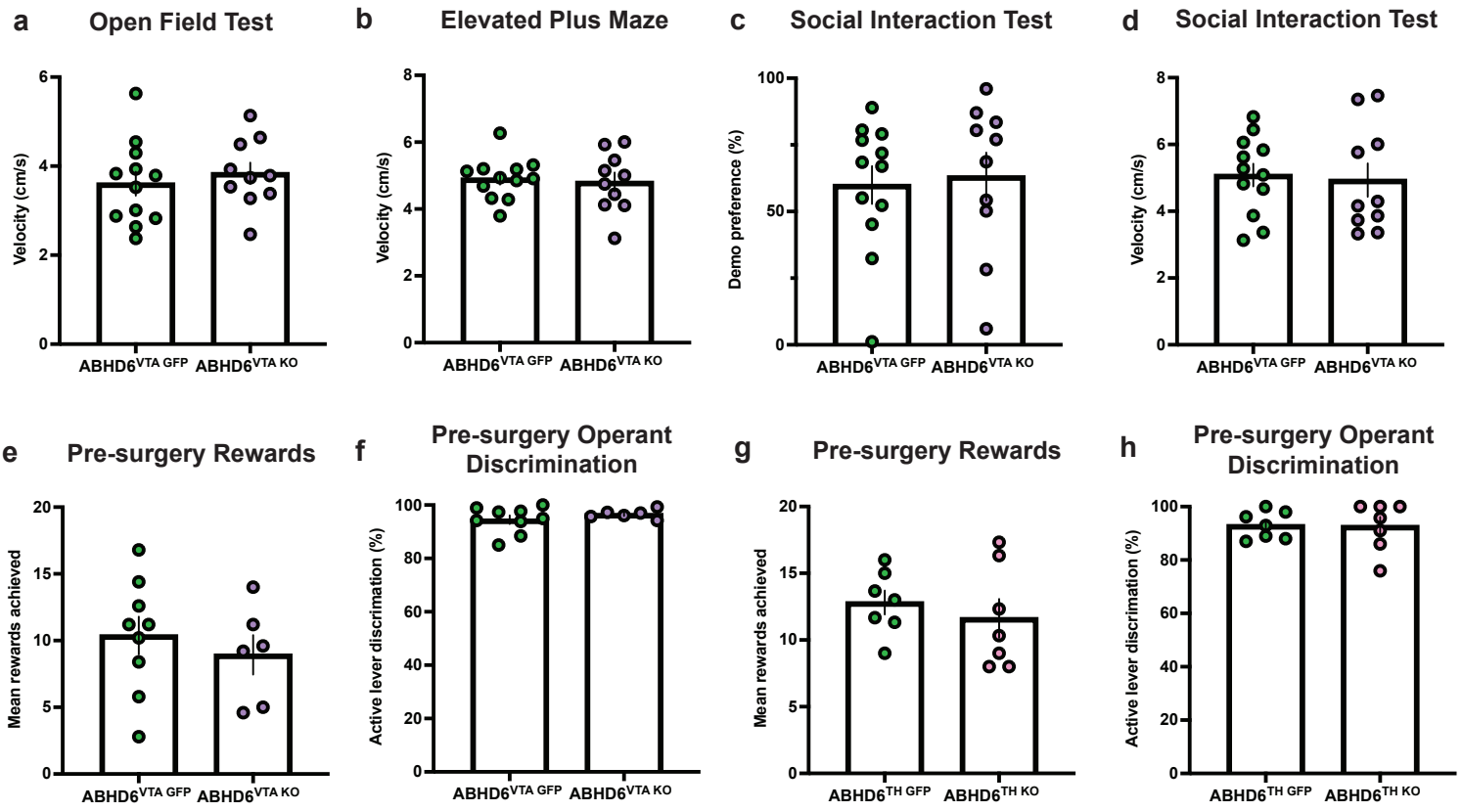
Supplementary Figure 3. Feeding and wheel-running behaviour on HFD. Related to Figure 3. **a** Total food intake on HFD (ABHD6$^{NAc\ GFP}$: n=9, ABHD6$^{NAc\ KO}$: n=6). **b** Wheel running behaviour on chow or high-fat diet (ABHD6$^{NAc\ GFP}$ (chow): n=7, ABHD6$^{NAc\ GFP}$ (HFD): n=6, ABHD6$^{NAc\ KO}$ (chow): n=7). **c** Total wheel-running behaviour in (**b**) on chow or HFD (ABHD6$^{NAc\ GFP}$ (chow): n=7, ABHD6$^{NAc\ GFP}$ (HFD): n=6, ABHD6$^{NAc\ KO}$ (chow): n=7; group main effect p=0.0021). Data represented as mean, with error bars/-shaded areas ± SEM; **p<0.01, ***p<0.001. Unpaired t-test (**a**), two-way ANOVA group main effect (**b**), one-way ANOVA with Tukey post hoc correction (**c**).

Supplementary Figure 4



Supplementary Figure 4. Feeding, body weight, and metabolism on chow and HFD. Related to Figure 5. **a** Baseline hourly food intake over 24 hr period on chow diet ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **b** Total daily food intake over 24 hr baseline period on chow diet ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **c** Refeeding hourly food intake over 24 hr baseline period following a 22 hr fast period ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **d** Total cumulative food intake over 6 weeks on chow diet ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **e** Energy expenditure ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **f** Energy expenditure in (**e**) during dark ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7) or light cycle ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **g** Food intake on HFD ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **h** Feed efficiency on HFD ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **i** Energy expenditure on HFD ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **j** Energy expenditure in (**i**) during dark ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7) or light cycle ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **k** Respiratory exchange ratio on HFD ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). **l** RER in (**k**) during dark ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7) or light cycle ($ABHD6^{VTA\ GFP}$: n=10, $ABHD6^{VTA\ KO}$: n=7). Data represented as mean, with error bars/shaded areas ± SEM; *$p<0.05$. Unpaired t-test (**b, d, f, h, j, l**), two-way ANOVA group x time interaction (**c, e, g, i, k**), two-way ANOVA group main effect (**a**).

Supplementary Figure 5



Supplementary Figure 5. Velocity and social behaviour in the social interaction test and presurgery operant behaviour. Related to Figure 6. **a** Velocity (ABHD6$^{VTA\ GFP}$: n=12, ABHD6$^{VTA\ KO}$: n= 10). **b** Velocity (ABHD6$^{VTA\ GFP}$: n=12, ABHD6$^{VTA\ KO}$: n= 10). **c** Demonstrator mouse interaction preference (ABHD6$^{VTA\ GFP}$: n=12, ABHD6$^{VTA\ KO}$: n= 10). **d** Velocity (ABHD6$^{VTA\ GFP}$: n=12, ABHD6$^{VTA\ KO}$: n= 10). **e** Mean pre-surgery rewards achieved during progressive ratio operant test (ABHD6$^{VTA\ GFP}$: n=9, ABHD6$^{VTA\ KO}$: n=6). **f** Mean pre-surgery active lever discrimination during progressive ratio operant test (ABHD6$^{VTA\ GFP}$: n=9, ABHD6$^{VTA\ KO}$: n=6). **g** Mean pre-surgery rewards achieved during operant test (ABHD6$^{TH\ GFP}$: n=7, ABHD6$^{TH\ KO}$: n=7). **h** Mean pre-surgery active lever discrimination during operant test (ABHD6$^{TH\ GFP}$: n=7, ABHD6$^{TH\ KO}$: n=7). Data represented as mean, with error bars ± SEM. Unpaired t-test (**a-h**).