Table S1.

Diet	Product #, Manufacturer	Physiological Energy (cal/g)	Metabolizable Energy (cal/g)	Fat (% kcal)	NaCl (%)	Na (%)	Protein (% Kcal)	Carbohydrate (% Kcal)
Chow	5L0D, LabDiet	3350	2910	13.5	1	0.4	28.5	58.0
NaCl	5001, LabDiet/In house	3250	2823	13.5	4	1.6	28.5	58.0
HF	D12492, Research Diets	5240	N/A	60	0.350	0.13	20	20
HF/NaCl	D06111102, Research Diets	5030	N/A	60	4	1.6	20	20

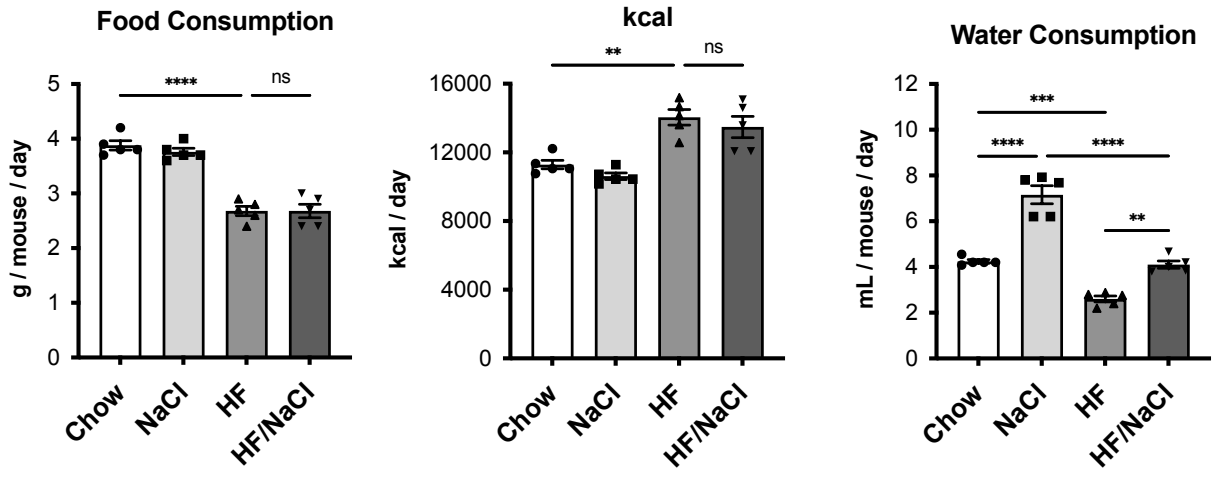

Figure S1. Food consumption, kcal intake and water consumption on diets. Average food and water consumption were measured during weeks 1 through 4 on salt and fat adjusted diets. N = 5 per group.

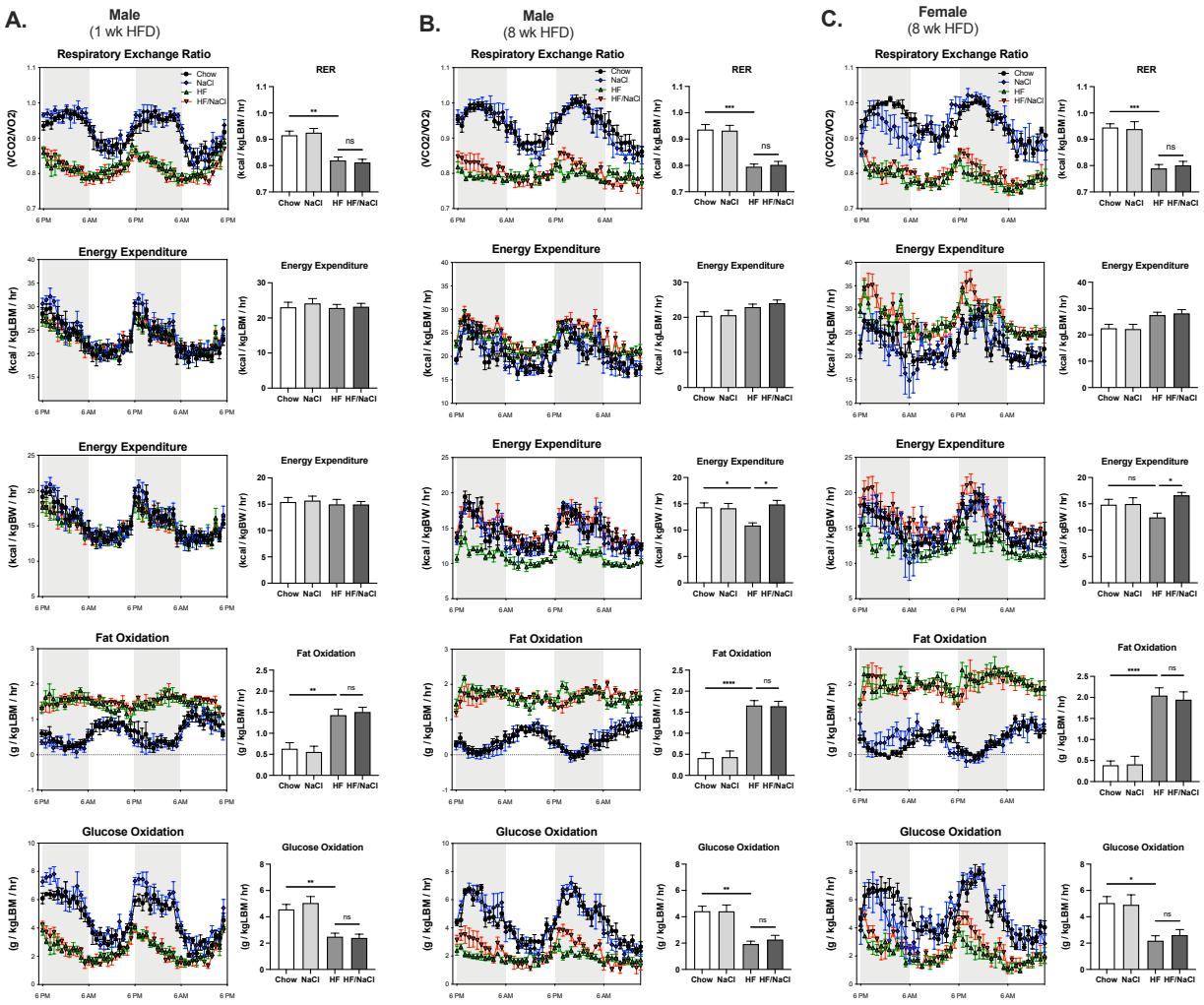

Figure S2. Metabolic rate and energy substrate utilization on diets. Respiratory exchange ratio (RER), energy expenditure, fat oxidation, and glucose oxidation of (A) male mice at 1 wk on diet (B) male mice at 8 wk on diet and (C) female mice at 8 wk on diet. N = 4 per group.

Supplemental Methods

Body Composition

Body composition analysis of body fat, lean mass, and free fluid was determined using an NMR-based analyzer (Minispec LF90II, Bruker Optics) and was performed by the University of Michigan Animal Phenotyping Core. Conscious mice were placed individually in a measuring tube with measurements lasting less than 2 minutes. The machine was checked daily using a reference sample (canola seeds) as recommended by the manufacturer.

Indirect Calorimetry

Indirect calorimetry measurements were performed by the University of Michigan Animal Phenotyping Core by blinded personnel. During the indirect calorimetry, mice were individually housed, and whole body oxygen consumption (VO2), carbon dioxide production (VCO2), spontaneous motor activity and food intake were measured using an integrated open-circuit calorimeter (CLAMS, Columbus Instruments). Mice were weighed before measurements and were placed in individual sealed chambers with free access to food and water and measured continuously for 72 hours. The energy expenditure, glucose oxidation, and fat oxidation were calculated using the following formulas: Energy Expenditure: $3.91VO_2+1.10VCO_2$, Glucose Oxidation: $1.69VO_2-1.69VCO_2$, Fat Oxidation: $4.57VCO_2-3.23VO_2$.

Gene expression analysis

Relative mRNA expression was determined using quantitative reverse transcription–polymerase chain reaction. Total RNA was extracted from tissues using TRIzol reagent and purified using an RNeasy Mini Kit (Qiagen) with an on-column DNase digestion. RNA (1 ug) was reverse transcribed to cDNA with an Applied Biosystems kit and quantitative reverse transcription–polymerase chain reaction was performed using a 7900HT fast real-time PCR system (Applied Biosystems). The relative mRNA expression was quantified by the comparative method and normalized to the housekeeping genes HPRT or L32.

Statistical analysis

A Shapiro-Wilk normality test was used to determine if data were normally distributed. For normally distributed data with equal variance, values are presented as mean ± SEM, and statistical comparison of mean values between multiple groups was performed by Student's t test , one-way ANOVA with a Tukey's post-test, or two-way ANOVA with a Tukey's post-test as indicated in the text. Data that were not normally distributed were analyzed with the nonparametric Mann-Whitney test. All statistical analysis of data was performed in GraphPad Prism (version 7; GraphPad Software, Inc). $P < 0.05$ was considered significant.