**Figure 1. Reductions in glucose handling are exacerbated in obese individuals with elevated glucocorticoids.**

Cushing’s and control BMI (A) and HOMA-IR scores (B) stratified by obesity status. Schematic of mouse study design (C). Mouse 6-hour fasted blood glucose levels during insulin tolerance test (D) and prior to insulin injection (basal; E) following 5 weeks of treatment. Mouse glucose infusion rate (GIR; F) and endogenous glucose production (EGP; G) during euglycemic clamp following 3 weeks of dexamethasone or vehicle treatment. Asterisks indicate a significant interaction between diet and treatment.

**Figure 2. Increased glucocorticoids lead to greater severity of hepatic steatosis in obese mice.**

Patient ALT levels (A). Mouse hepatic triglyceride levels (B) and H and E stained liver sections (C) following 6 weeks of treatment. qPCR of hepatic *de novo* lipogenic transcripts (D, E). Asterisks indicate a significant interaction between diet and treatment.

**Figure 3. Dexamethasone-treated reduces fat mass in obese mice.**

Weekly total body mass (A) and fat mass (B) measures via echoMRI in mice over the course of treatment. Inguinal and gonadal adipose tissue weights in 16 hour fasted mice following sacrifice (C). Food consumption measured weekly over the course of treatment (D). Asterisks indicate a significant interaction between diet and treatment.

**Figure 4. Dexamethasone treatment induces lipolysis *in vivo* and *in vitro*.**

Triglyceride levels (A), glycerol released in media (B), qPCR of lipolytic transcripts (C), and western blot of lipolytic proteins (D) from differentiated 3T3-L1 mouse adipocytes following treatment. Serum fatty acid and glycerol levels at basal and following stimulation (isoproterenol or 16hr fast; E) and qPCR of IWAT lipolytic transcripts (F) in 12-week treated, chow-fed mice.

**Figure 5. Obesity exacerbates dexamethasone-induced lipolysis.**

Serum glycerol (A), qPCR of lipolytic transcripts from IWAT (B), and western blot of lipolytic proteins from IWAT (C) in 6-week treated NCD- and HFD-fed mice. Asterisks indicate a significant interaction between diet and treatment.

Supplementary Figures:

H) Glucose turnover rate I) Glucose uptake in tissues