Supplementary Tables

Supplementary Table 1. Two-way ANOVA for brain sterols for vehicle-treated, 12 week and 42-week old female wild-type (WT) and YAC128 (HD) mice. Lanosterol (LAN), 7-dehydrocholesterol (7DHC), 8-dehydrocholesterol (8DHC), Desmosterol (DES), and Cholesterol (CHOL); For each tissue, each sterol was assessed using a 2-way ANOVA and main effect (HD or Age) or interaction effect (HD x Age), f-statistic and p-value are reported; Statistical significance is set at p<0.05 and in **bold**. Holm-Sidak's multiple comparisons post-hoc test was performed for significant main or interaction effects.

Supplementary Table 2. Two-way ANOVA for brain sterols for Mn-treated, 12 week and 42-week old female wild-type (WT) and YAC128 (HD) mice. Lanosterol (LAN), 7-dehydrocholesterol (7DHC), 8-dehydrocholesterol (8DHC), Desmosterol (DES), and Cholesterol (CHOL); For each tissue, each sterol was assessed using a 2-way ANOVA and main effect (HD or Age) or interaction effect (HD x Age) F-statistic and p-value are reported; Statistical significance set at p<0.05 and in **bold**. Holm-Sidak's multiple comparisons post-hoc test was performed for significant main or interaction effects.

Supplementary Table 1. ANOVA for sterols in vehicle-treated, young and old female WT and HD mice

Tissue	Sterol	HD	Age	HD x Age
Striatum	LAN	**F (1, 34) = 5.50; P = 0.02**	F (1, 34) = 1.38; P=0.25	**F (1, 34) = 6.48; P=0.02**
	7DHC	F (1, 34) = 0.86; P = 0.36	F (1, 34) = 0.00; P = 0.98	F (1, 34) = 0.18; P = 0.67
	8DHC	**F (1, 34) = 3.8;1 P = 0.05**	F (1, 34) = 0.64; P = 0.43	**F (1, 34) = 3.84; P = 0.05**
	DES	**F (1, 34) = 7.56; P = 0.01**	F (1, 34) = 0.85; P = 0.36	**F (1, 34) = 7.56; P = 0.01**
	CHOL	F (1, 34) = 0.01; P = 0.92	F (1, 34) = 0.01; P = 0.92	**F (1, 34) = 20.6; P = 0.01**
Cortex	LAN	F (1, 34) = 2.82; P = 0.10	F (1, 34) = 0.86; P = 0.36	F (1, 34) = 0.50; P = 0.48
	7DHC	F (1, 34) = 1.92; P = 0.17	F (1, 34) = 0.25; P = 0.62	F (1, 34) = 0.35; P = 0.56
	8DHC	**F (1, 34) = 3.93; P = 0.05**	F (1, 34) = 0.27; P = 0.61	**F (1, 34) = 4.39; P = 0.04**
	DES	F (1, 34) = 0.41; P = 0.53	**F (1, 34) = 4.77; P = 0.04**	F (1, 34) = 0.84; P = 0.37
	CHOL	F (1, 34) = 0.01; P = 0.92	F (1, 34) = 1.97; P = 0.17	F (1, 34) = 0.53; P = 0.47
Cerebellum	LAN	F (1, 34) = 3.50; P = 0.07	F (1, 34) = 0.10; P = 0.75	F (1, 34) = 0.03; P = 0.87
	7DHC	F (1, 35) = 0.10; P = 0.75	F (1, 35) = 1.06; P = 0.31	F (1, 35) = 0.03; P = 0.87
	8DHC	F (1, 34) = 0.14; P = 0.71	F (1, 34) = 0.59; P = 0.45	F (1, 34) = 2.20; P = 0.15
	DES	F (1, 33) = 3.63; P = 0.07	**F (1, 33) = 8.72; P = 0.01**	F (1, 33) = 0.11; P = 0.74
	CHOL	F (1, 34) = 0.96; P = 0.33	F (1, 34) = 1.65; P = 0.21	F (1, 34) = 0.37; P = 0.55

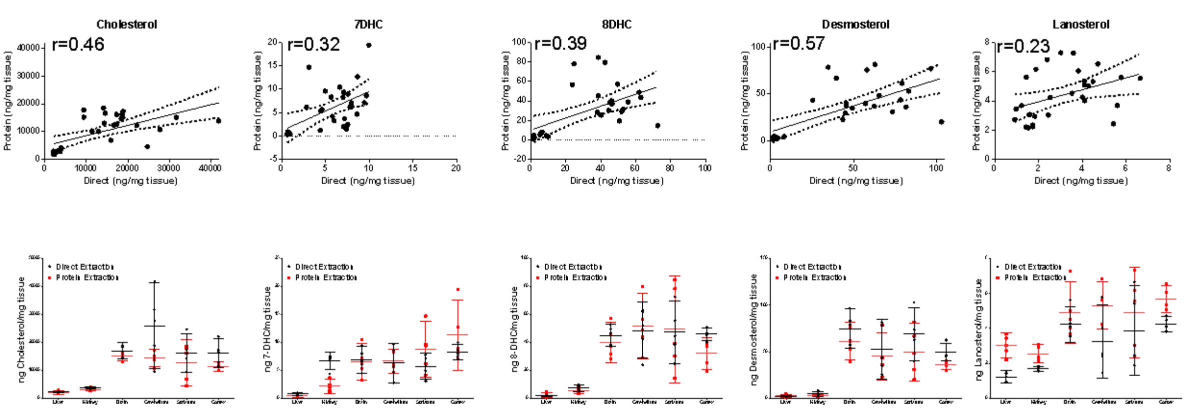
Supplementary Table 2. ANOVA for sterols in Mn-treated, young and old female WT and HD mice.				
Tissue	Sterol	HD	Age	HD x Age
Striatum	LAN	F (1, 30) = 0.01; P = 0.90	F (1, 30) = 3.32; P = 0.08	F (1, 30) = 1.27; P = 0.27
	7DHC	F (1, 28) = 1.04; P = 0.32	F (1, 28) = 0.02; P = 0.90	F (1, 28) = 0.27; P = 0.61
	8DHC	F (1, 30) = 2.32; P = 0.14	F (1, 30) = 1.72; P = 0.20	**F (1, 30) = 8.27; P = 0.01**
	DES	F (1, 30) = 0.25; P = 0.62	F (1, 30) = 3.39; P = 0.08	**F (1, 30) = 8.51; P = 0.01**
	CHOL	F (1, 30) = 0.16; P = 0.70	F (1, 30) = 0.50; P = 0.49	**F (1, 30) = 8.64; P = 0.01**
Cortex	LAN	F (1, 30) = 0.57; P = 0.45	**F (1, 30) = 4.59; P = 0.04**	F (1, 30) = 0.96; P = 0.33
	7DHC	F (1, 30) = 2.14; P = 0.15	F (1, 30) = 3.24; P = 0.08	F (1, 30) = 0.28; P = 0.60
	8DHC	F (1, 30) = 3.23; P = 0.08	F (1, 30) = 3.72; P = 0.06	F (1, 30) = 2.53; P = 0.12
	DES	F (1, 30) = 1.23; P = 0.28	F (1, 30) = 0.42; P = 0.52	F (1, 30) = 2.01; P = 0.17
	CHOL	F (1, 30) = 0.09; P = 0.76	F (1, 30) = 0.75; P = 0.39	F (1, 30) = 1.09; P = 0.30
Cerebellum	LAN	**F (1, 30) = 20.2; P = 0.01**	**F (1, 30) = 8.27; P = 0.01**	F (1, 30) = 0.30; P = 0.59
	7DHC	**F (1, 29) = 5.82; P = 0.02**	F (1, 29) = 2.25; P = 0.14	F (1, 29) = 3.58; P = 0.07
	8DHC	**F (1, 29) = 4.96; P = 0.03**	F (1, 29) = 2.52; P = 0.12	F (1, 29) = 0.12; P = 0.73
	DES	**F (1, 30) = 6.69; P = 0.01**	**F (1, 30) = 13.2; P = 0.01**	F (1, 30) = 1.90; P = 0.18
	CHOL	F (1, 30) = 2.17; P = 0.15	F (1, 30) = 0.01; P = 0.99	F (1, 30) = 0.01; P = 0.95

Supplementary Figures

Supplementary Figure 1. Validation that extracting sterols from protein lysate is similarly efficient as extracting sterols from whole tissue. Significant correlations were determined for extraction of sterols analyzed across all tissues (r=0.0.65, p<0.0001, n=30: 5 samples for each tissue: liver, kidney, whole brain, cerebellum, striatum and cortex). Data were determined to be normal and significant positive correlation with Pearson statistic shown in the top-right hand corner for each individual sterol analyzed (A-E). Average +/- 95% CI is shown for each tissue with whole tissue extract (black circle) and extraction from protein lysate (red square). Comparison of each tissue and matched sample indicated no statistical difference between the two samples (2-way ANOVA, P>0.3209); however, extracting cholesterol (F) from whole tissue is more efficient (P=0.0102) and extracting lanosterol (J) from protein lysate is more efficient (P=0.0007). No statistical significant difference was determined for the other sterols analyzed: (I) desmosterol (P=0.0552), (G) 7-DHC (P=0.7182), (H) 8-DHC (P=0.5682).

Supplementary Figure 2. Sterols in female 12 week old and 42 week old Mn-treated wild-type (WT) and YAC128 (HD) mice in the A) striatum, B) cortex, and C) cerebellum. 12 week old WT mice in empty blue (n=6), 12 week old HD mice in empty red (n=11), 42 week old WT mice in solid blue (n=7) and 42 week old HD mice in solid red bars (n=10). Data represents the mean ± s.e.m. An asterisk (*) indicates a p-value <0.05, ** indicates p-value <0.01.

Supplementary Figure 1



Supplemental Figure 2