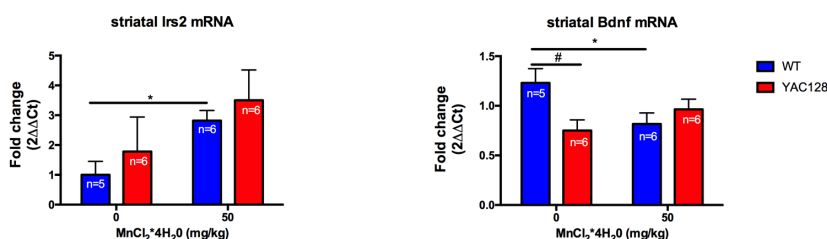


Supplemental Table 1. qRT-PCR validation of top 10 Mn-responsive genes.					
gene ID	Group 1	Group 2	Log2Fold Change	Q-value	Validate
Col3a1	128_H2O	128_Mn	-3.68	0.02	No
Lcp2	WT_H2O	WT_Mn	-2.59	0.01	No
Apold1	WT_H2O	WT_Mn	2.01	0.01	No
Arc	WT_H2O	WT_Mn	1.56	0.01	No
Nr4a2	WT_H2O	WT_Mn	-3.23	0.02	No
Irs2	WT_H2O	WT_Mn	-0.45	0.04	Yes
Ptgds	128_H2O	128_Mn	0.78	0.02	No
Bdnf	WT_H2O	WT_Mn	-2.33	0.01	Yes
Bdnf	128_H2O	128_Mn	1.23	0.03	No
Smoc2	WT_H2O	WT_Mn	-2.27	0.01	No

Supplemental Table 1. qRT-PCR validation of genes of interest identified from striatal RNA sequencing. Genes quantified were Col3A1, Lcp2, Apold1, Arc, Nr4a2, Irs2, Ptgds, Bdnf, Smoc2. Log2Fold Change indicates the log2 fold change after Mn exposure with a negative fold change indicating a greater expression in Mn exposure group. Q-value corresponds to the false discovery rate determined by differential expression software (DESeq2). The Validate column cooresponds to whether differential expression was confirmed for a select gene ID with qRT-PCR from an independent experiment.

Supplemental Figure 1. Striatal Irs2 and Bdnf mRNA in WT and YAC128 pre-manifest exposed to Mn



Supplemental Figure 1. Striatal Irs2 and Bdnf mRNA in 12-week old WT and YAC128 after Mn exposure. Genes quantified were insulin receptor substrate 2 (Irs2) and brain derived neurotrophic factor (Bdnf); Data represented as the mean ± sem and * indicates a Mn effect and # indicates a genotype effect a significance level of p<0.05; n=5-6

Supplemental Table 2. Untargeted striatal metabolomics after 18-week Mn exposure.							
Compound ID	AVG WT 0	AVG WT 50	AVG HD 0	AVG HD 50	WT 0:WT 50	HD 0:HD 50	Greatest FC
5.90_158.1175m/z	26998.78	15603.01	20252.74	14396.33	1.73	1.41	WT
1.20_327.0077m/z	4352.58	2275.26	3050.33	2672.44	1.91	1.14	WT
1.41_179.1278m/z	2186.66	1498.18	1717.63	1703.03	1.46	1.01	WT
1.29_309.2267m/z	23639.06	8461.77	12342.54	14236.32	2.79	0.87	WT*
1.52_238.1647m/z	3450.96	1014.92	1604.83	2152.82	3.40	0.75	WT*
1.43_183.0765m/z	3400.74	2135.28	3145.08	2362.04	1.59	1.33	WT
6.82_230.1247m/z	3280.54	5154.35	2953.95	4761.32	0.64	0.62	WT
1.24_308.2794m/z	6459.08	3444.45	4140.96	3902.13	1.88	1.06	WT
5.94_216.1707m/z	6001.38	3842.70	4771.58	3071.53	1.56	1.55	WT
2.63_518.2105m/z	14694.58	6448.10	15780.85	8820.49	2.28	1.79	WT
1.22_329.0048m/z	3868.22	2163.18	2895.91	2515.38	1.79	1.15	WT
21.15_175.1189m/z	453692.86	338766.55	490824.01	300601.66	1.34	1.63	WT
1.35_254.1599m/z	5163.46	2257.13	2852.61	3037.03	2.29	0.94	WT*
2.94_186.0185m/z	2305.58	1039.21	1548.16	1799.90	2.22	0.86	WT*
2.16_928.5906m/z	72752.94	108346.09	89739.55	85397.94	0.67	1.05	WT*
14.20_226.1064n	1959626.34	1521127.34	1696726.50	1383319.36	1.29	1.23	WT
1.25_317.2412n	4765.46	2677.39	3240.14	3532.85	1.78	0.92	WT*
14.20_210.0872m/z	16864.21	13016.11	14525.69	11660.22	1.30	1.25	WT
14.20_228.1170m/z	207246.25	162752.99	182823.97	146960.79	1.27	1.24	WT
6.43_144.1019m/z	20517.61	14757.46	16165.61	15441.95	1.39	1.05	WT
1.92_168.0655m/z	38970.84	30789.84	35160.24	33048.15	1.27	1.06	WT
1.94_900.5594m/z	211427.67	265616.13	237084.01	221454.40	0.80	1.07	WT*
1.39_270.1909m/z	6426.86	2490.52	4908.94	4688.78	2.58	1.05	WT
1.79_253.1158m/z	3236.27	1446.04	2055.14	2451.14	2.24	0.84	WT*
1.22_324.2742m/z	2650.89	1047.57	1912.01	1092.41	2.53	1.75	WT
9.08_264.1494m/z	372882.00	413417.40	393359.24	372753.94	0.90	1.06	WT*
1.29_326.2535m/z	16259.70	5997.72	11687.00	11511.35	2.71	1.02	WT
1.24_308.2065m/z	10136.00	6655.33	7930.99	7563.77	1.52	1.05	WT
2.04_167.0815m/z	5142.38	3859.86	4538.88	4197.96	1.33	1.08	WT
1.24_141.1273m/z	750.37	1109.22	1023.92	975.06	0.68	1.05	WT*
1.67_726.5874m/z	430068.74	347694.64	332203.43	283425.91	1.24	1.17	WT
5.28_157.0760m/z	2515.06	3037.90	2760.66	2886.32	0.83	0.96	WT
1.24_97.0648m/z	6637.05	7812.62	7331.37	7438.16	0.85	0.99	WT
8.40_171.0764m/z	27248.38	37048.90	25447.90	32646.56	0.74	0.78	WT
3.20_848.6308m/z	71115.23	90796.08	80014.43	80275.98	0.78	1.00	WT
1.28_266.1960m/z	7540.98	3494.17	4413.93	4271.70	2.16	1.03	WT
1.33_237.1695m/z	15639.31	6318.58	7672.43	9676.24	2.48	0.79	WT*
1.96_746.5118m/z	199932.92	229950.96	191739.18	214080.79	0.87	0.90	WT
1.52_231.1200m/z	4283.33	2796.79	3927.66	3234.54	1.53	1.21	WT
1.25_279.1799m/z	1577.04	367.06	647.22	402.94	4.30	1.61	WT
13.04_268.1401m/z	44491.17	27538.22	34233.18	25351.77	1.62	1.35	WT
1.35_158.1176m/z	1453.25	519.72	674.96	693.85	2.80	0.97	WT*
9.08_262.1386n	4147789.73	4548793.63	4368538.96	4090802.73	0.91	1.07	WT*
1.67_302.2146m/z	21772.84	35754.20	21260.48	30198.13	0.61	0.70	WT
1.39_223.1540m/z	10755.62	4735.18	5389.64	6733.39	2.27	0.80	WT*
1.65_316.2301m/z	49909.15	70305.19	54458.05	69031.92	0.71	0.79	WT
1.75_246.1521m/z	60039.23	95405.75	61697.76	77548.21	0.63	0.80	WT
1.33_235.1902m/z	12303.18	3565.09	8323.59	6809.21	3.45	1.22	WT
1.54_212.1491m/z	76074.11	46458.38	49531.15	59464.26	1.64	0.83	WT*
1.28_266.1728n	11435.10	7581.15	7882.65	7573.84	1.51	1.04	WT
1.29_251.1852m/z	154319.95	62122.83	70692.43	90636.83	2.48	0.78	WT*
1.24_183.1743m/z	1199.39	1754.55	1599.37	1561.86	0.68	1.02	WT*
1.24_367.2466m/z	2563.15	1435.90	1759.43	1862.65	1.79	0.94	WT*
11.19_514.2053n	356442.22	203827.43	321768.16	233627.90	1.75	1.38	WT
3.90_269.0878m/z	607165.27	738316.47	606414.35	782406.85	0.82	0.78	WT
9.40_176.1029m/z	61137.63	49655.55	64128.88	51390.41	1.23	1.25	WT
3.90_137.0458m/z	222530.03	269541.66	225542.88	285390.26	0.83	0.79	WT
1.25_184.1696m/z	952.08	2495.32	1683.05	1984.82	0.38	0.85	WT
2.69_707.4904m/z	51233.90	67596.92	63468.35	58982.16	0.76	1.08	WT*
14.20_181.1083m/z	5467.24	4469.55	4916.79	4041.66	1.22	1.22	WT
1.43_352.2303m/z	6483.51	9440.26	8259.63	8347.30	0.69	0.99	WT
1.94_623.5028m/z	24659.54	32017.21	30768.01	28618.59	0.77	1.08	WT*
1.28_242.1750m/z	4965.99	9183.89	6840.70	7036.19	0.54	0.97	WT
1.54_195.1226m/z	372294.18	233684.58	251879.42	292843.29	1.59	0.86	WT
1.22_461.2654n	222079.76	53603.52	94236.27	98372.88	4.14	0.96	WT*
1.56_133.0858m/z	3100.98	2070.83	2229.39	2600.35	1.50	0.86	WT*
1.75_244.0426m/z	1756.29	3197.25	2562.08	2554.41	0.55	1.00	WT*
1.20_149.0233m/z	14905.21	11407.69	12107.03	13335.99	1.31	0.91	WT*

Supplemental Table 2 continued							
Compound ID	AVG WT 0	AVG WT 50	AVG HD 0	AVG HD 50	WT 0:WT 50	HD 0:HD 50	Greatest FC
1.10_697.3525m/z	6862.375	9051.094	8315.671	8509.889	0.758	0.977	WT
1.47_160.1099n	1704.458	5001.888	3881.520	4668.798	0.341	0.831	WT
1.28_391.2838m/z	394618.424	200947.792	246488.274	291628.150	1.964	0.845	WT*
1.25_265.2007m/z	2265.944	700.762	957.313	1060.248	3.234	0.903	WT*
1.35_196.1180m/z	765.184	383.938	652.978	599.172	1.993	1.090	WT
1.29_268.2116m/z	17559.503	8095.301	9680.637	10272.473	2.169	0.942	WT*
9.43_217.1294m/z	17074.683	13139.937	11318.707	8272.407	1.299	1.368	WT
6.43_335.0540m/z	927.833	2534.931	1936.905	1390.911	0.366	1.393	WT*
1.24_293.1957m/z	7091.098	2617.799	3164.879	3559.521	2.709	0.889	WT*
3.76_828.5507m/z	254574.039	299314.795	255353.548	266692.403	0.851	0.957	WT
2.96_772.5837m/z	509175.038	577611.976	529028.965	553633.995	0.882	0.956	WT
3.90_138.0492m/z	9737.913	12206.694	9982.174	12735.597	0.798	0.784	WT
1.24_280.2480m/z	2998.816	927.758	1347.675	1669.226	3.232	0.807	WT*
1.65_745.4983m/z	8808.045	15647.131	16815.499	12500.552	0.563	1.345	WT*
1.75_232.1365m/z	5447.821	8651.053	5278.242	6263.824	0.630	0.843	WT
1.22_113.0596m/z	3416.746	5159.187	4196.871	4313.636	0.662	0.973	WT
5.63_134.0270m/z	6197.794	8660.948	7500.487	8178.541	0.716	0.917	WT
11.19_257.1025n	5168467.656	4281635.433	4650746.317	4325104.478	1.207	1.075	WT
1.24_128.0837n	5663.440	6766.840	6338.401	6499.344	0.837	0.975	WT
1.79_218.1209m/z	4464.690	6630.298	4111.223	6113.713	0.673	0.672	WT
1.31_313.1625m/z	6463.383	4636.117	5519.570	5280.803	1.394	1.045	WT
1.94_141.0338m/z	4298.405	4876.453	4709.749	4694.120	0.881	1.003	WT*
5.26_205.0971m/z	90579.279	108672.035	102481.465	102433.636	0.834	1.000	WT*
1.24_131.0855m/z	450.832	1592.404	1156.393	1346.353	0.283	0.859	WT*
1.24_454.2647m/z	28438.167	32645.934	30466.109	30111.300	0.871	1.012	WT*
1.33_201.1597m/z	1810.123	676.865	1396.085	740.238	2.674	1.886	WT
9.69_146.0924m/z	49675.539	43737.973	52074.871	42368.420	1.136	1.229	HD
10.10_197.0815n	487345.070	325339.094	664623.769	469203.942	1.498	1.416	WT
1.24_488.3580m/z	4401.468	10172.370	6673.611	4047.363	0.433	1.649	WT*
1.22_363.2255n	71427.887	28973.070	34051.316	41851.126	2.465	0.814	WT*
1.39_209.1383m/z	29405.046	13504.801	15366.319	19138.443	2.177	0.803	WT*
9.08_87.0790m/z	2143.966	2453.697	2325.032	2175.463	0.874	1.069	WT*
1.41_479.4571m/z	914.820	3418.119	2111.360	2321.102	0.268	0.910	WT*
1.22_279.1446m/z	4214.686	1237.057	1475.475	1986.306	3.407	0.743	WT*
1.18_416.2426m/z	2136.719	710.995	716.243	1825.106	3.005	0.392	WT*
1.29_464.3732m/z	7226.235	1562.482	5266.487	3970.409	4.625	1.326	WT
1.25_471.3791m/z	3264.093	15802.252	13858.370	14891.961	0.207	0.931	WT
1.73_443.2937m/z	22266.421	14005.117	18942.177	20100.783	1.590	0.942	WT*
3.84_313.1251m/z	12602.028	16894.638	13616.374	20406.589	0.746	0.667	WT
1.22_412.2527m/z	8177.801	6070.017	7366.378	6115.854	1.347	1.204	WT
2.31_778.5371m/z	101687.175	140917.018	121183.729	124966.484	0.722	0.970	WT
2.29_808.5122m/z	115336.199	146263.231	107083.010	134580.096	0.789	0.796	WT
1.24_112.0888n	5971.550	8965.427	7399.422	8294.467	0.666	0.892	WT
2.98_746.5686m/z	4233286.333	4736709.605	4406638.062	4616203.011	0.894	0.955	WT
1.39_226.1650m/z	23380.628	11712.158	13337.121	16211.213	1.996	0.823	WT*
1.29_240.1804m/z	13432.029	6835.886	7896.671	8022.742	1.965	0.984	WT*
1.22_400.3054m/z	3917.591	5965.635	4719.311	4086.649	0.657	1.155	WT*
4.70_113.0538m/z	3362.090	3683.593	3295.669	3432.231	0.913	0.960	WT
1.25_164.1200n	2285.053	3943.990	2940.586	3288.897	0.579	0.894	WT
1.54_372.2928m/z	19837.213	31238.068	23232.887	22793.083	0.635	1.019	WT*
1.24_170.1539m/z	2341.436	8264.296	5554.054	7528.346	0.283	0.738	WT
3.81_336.0842m/z	20200.318	23666.550	19696.860	20167.263	0.854	0.977	WT
9.08_524.2778n	1095652.354	1288754.866	1247976.704	988651.636	0.850	1.262	WT*
1.90_152.0705m/z	4663.711	1116.112	4664.447	2614.342	4.179	1.784	WT
1.75_267.1312m/z	7197.148	4675.804	5071.088	6548.131	1.539	0.774	WT*
1.24_180.1513n	8811.778	23201.079	16935.637	21334.204	0.380	0.794	WT
3.90_541.1568m/z	2118962.034	2479498.550	2051983.791	2629311.789	0.855	0.780	WT
9.80_265.0850m/z	3789.276	4705.365	3202.509	4842.577	0.805	0.661	WT
1.94_102.0549m/z	4077.580	3368.988	3661.118	3912.024	1.210	0.936	WT*
1.24_237.1848m/z	3584.176	5733.001	4699.332	5232.055	0.625	0.898	WT
1.81_81.0170m/z	4313.516	2132.246	3608.062	4652.441	2.023	0.776	WT
1.22_417.3681m/z	2752.837	11543.750	6295.396	8026.112	0.238	0.784	WT
1.24_105.0698m/z	995.765	1285.222	1106.749	1233.656	0.775	0.897	WT
1.98_116.0706m/z	2499.654	1863.631	1987.355	2117.449	1.341	0.939	WT*
1.22_266.2112m/z	2075.864	8042.023	5572.083	7451.564	0.258	0.748	WT
2.55_192.0864m/z	7587.170	5247.695	6530.082	7167.829	1.446	0.911	WT*
1.81_79.0212m/z	94836.543	48768.704	82445.184	102404.085	1.945	0.805	WT*
1.45_110.0601m/z	628.696	539.519	625.155	644.923	1.165	0.969	WT*

Supplemental Table 2. Untargeted striatal metabolomics after 18-week Mn exposure in manifest WT and YAC128 mice. Compound ID is the unique identifier (specifically, the retention time and mass to charge ratio) for each compound. AVG columns represent the average abundance level for each compound. WT_0:WT_50 and HD_0:HD_50 are the fold change after Mn exposure. Greatest FC indicates which genotype has the greater fold change and an * indicates metabolites that were observed to be altered in opposing directions after Mn treatment (i.e. metabolite increased in WT and decreased in HD).