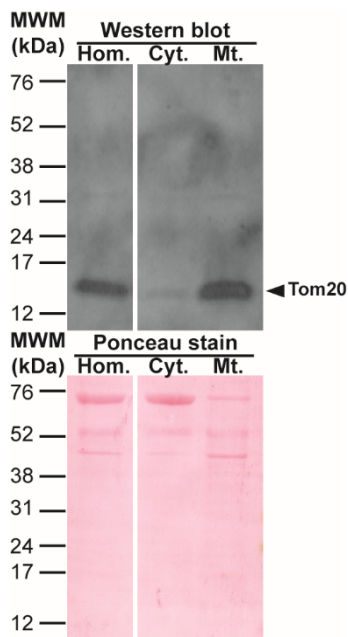


**Figure S1. Visualization of hippocampal primary neuronal cultures.** Primary neurons were cultured *in vitro* for 7 days and then fixed and stained to observe general morphology. Neurons were incubated with antibodies against  $\beta$ III-tubulin (green) or Tom20 (red). Left panel, wild-type (WT) neurons. Right panel, transgenic (Tg) neurons. Scale bar, 200  $\mu$ m.

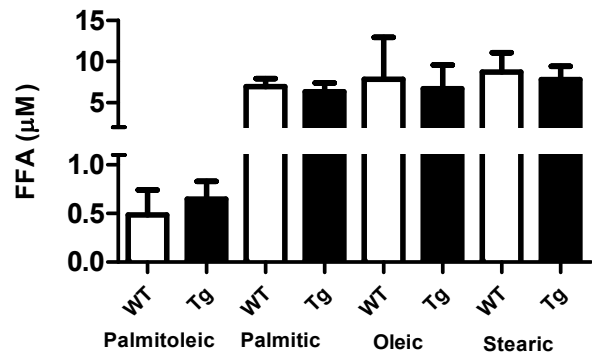


**Figure S2. Quality control of the mitochondrial fraction used for LC-MS/MS global lipidomics.** Upper panel, representative Western blotting of neuronal homogenates (Hom.), cytosolic (Cyt.) and mitochondrial (Mt) fractions immunoreacted with anti-Tom20 showing enrichment of mitochondria in Mt fraction used to assess lipidomics. Lower panel, protein content detected in each lane by Ponceau staining.

**Table S1**

**Detectable free fatty acids and relative quantification in primary neurons of WT and Tg rats**

	FFA (μM)			
	Palmitoleic	Palmitic	Oleic	Stearic
<b>WT</b>	0.99	5.70	2.40	4.50
	0.17	8.90	3.10	12.55
	0.30	6.20	18.00	9.10
<b>Tg</b>	0.99	6.65	7.55	9.55
	0.36	8.00	11.15	9.30
	0.59	4.30	1.40	4.60
<b>t</b>	0.50	0.42	0.19	0.31
<b>α</b>	0.63	0.69	0.85	0.76



Three independent hippocampal primary neuronal cultures/genotype were performed using 10-12 embryos/culture. Free fatty acids (FFAs) row data from 3 biological samples (2 technical replicates) are provided in micromolar as extracted and do not represent the endogenous concentration. Inset, bars show mean ± SEM. A multiple t-test comparison was carried out in Prism between WT and Tg samples, but no significant ( $p < 0.05$ ) differences were observed for any of the detected FFAs.

**Table S2. Complete list of lipid names and relative quantification in mitochondrial extracts of WT and Tg neurons**

Lipid short name	Retention time (min)	Nominal mass	WT Average	Tg Average	P value WT vs Tg
plasmeyl-PE 36:4	13.7	722	17272843	9522255	0.001
CerP 42:4	13.7	722	17272843	9522255	0.001
PE 37:6	13.8	748	20311364	8825412	0.002
PC 20:0	15.5	624	17433948	28166667	0.005

DGDG 15:0	15.3	653	8904623	2098453	0.005
PC 34:1	13.9	818	49591234	30354157	0.007
PC 33:2	14.3	744	5410326	2372405	0.008
DG 34:1	15.3	612	12199583	3434804	0.009
PC 27:1	16	706	9165131	3124040	0.009
PI 38:4	8.3	885	11002317	2425867	0.010
DG 40:6	16	686	3415746	7078109	0.011
DG 38:4	15.3	662	8574788	3396817	0.012
CL 76:11	13.5	748	618420	249091	0.015
PE 36:2	14.2	744	16467800	5415078	0.015
PE 38:5	13.2	766	4311464	1382650	0.016
N-(15Z-tetracosenoyl)-sphing-4-enine	16	649	7726961	3056306	0.017
SM 40:1	15.3	788	3608982	856401	0.017
PC 40:6	13.7	834	6210569	2631169	0.020
PC 38:3	13.7	834	6210569	2631169	0.020
plasmenyl-PE 38:5	14.1	748	11115329	4972135	0.022
plasmenyl-PE 38:4	14.4	750	15223092	7415644	0.022
PE 37:5	14.4	750	15223092	7415644	0.022
plasmenyl-PE 38:6	13.4	746	8044789	2688952	0.023
PC 35:1	14.3	832	5422453	1324633	0.024
PC 36:1	14.7	846	15504496	7321780	0.027
PC 31:1	14.2	718	4301416	1764297	0.028
SM 36:1	13.8	732	13781411	7057502	0.028
PC 24:5	14	596	12313579	5660959	0.029
SM 34:1	11.5	704	9417851	2640561	0.032
SM 42:2	15.3	814	15735150	3656935	0.032
DG 38:6	15.5	658	3945400	6472196	0.033
PC 36:4	12.3	840	3581675	1699059	0.033
PC 36:8	14.3	774	15329783	3976324	0.034
plasmenyl-PE 34:1	14.5	700	21975474	8715185	0.036
PE 34:1	14.2	718	15109566	6876348	0.037
PC 36:2	14	844	15628949	6869951	0.041
PE 39:8	13.5	772	7644586	1865859	0.042
CerP 45:0	13.5	772	7644586	1865859	0.042
PC 31:4	13.9	734	102427232	56158573	0.043
PC 33:0	14.3	806	3811169	931700	0.043
PC 38:5	13.8	792	38201446	19646277	0.044
PC 35:5	14.7	788	39993681	19676793	0.046
PC 32:5	13.4	746	23122794	5452865	0.046
PE 36:1	14.9	746	16563712	7650983	0.047
PC 35:6	14	786	56923404	24813547	0.053
SM 38:1	14.7	760	3447997	1201630	0.053
PC 33:1	13.4	804	7430263	1546312	0.056
PC 40:5	14	836	6939986	3795618	0.056
plasmenyl-PE 40:6	14.3	774	9495351	3883077	0.057
PE 39:7	14.3	774	9495351	3883077	0.057
PC 18:0	14.8	538	13346498	21399766	0.058
DG 33:3	16	594	9798888	15814772	0.058
PC 22:0	16	594	9798888	15814772	0.058
PC 35:2	13.5	772	5933618	1048544	0.061

PC 33:5	13.9	760	165858048	100220475	0.061
NAE 20:0	6.1	414	815115	2320952	0.072
PC 31:0	13.2	778	5486193	1041844	0.072
PC 32:1	12.1	790	9629590	3021733	0.072
PE 35:3	14.6	726	16335639	4985161	0.073
MGDG 25:0	4.7	655	15675998	30988373	0.074
PC 40:7	12.4	816	2816095	750348	0.076
PC 38:2	14.7	814	5370441	1620407	0.076
MGDG 21:0	3.6	599	4899817	14314581	0.077
PC 32:4	14.3	748	11762381	2936383	0.080
MGDG 19:0	15.5	566	19086022	25541805	0.086
PI 38:3	10	887	3156354	364885	0.087
Sphingosine	3.6	358	11783302	27976669	0.091
plasmenyl-PE 40:4	14.9	778	8104350	3775774	0.092
PE 39:6	14.6	776	7012146	4054184	0.094
N-(octadecanoyl)-sphing-4-enine	14.8	567	12268813	5823270	0.097
PC 38:6	12.6	790	5781723	1866995	0.100
PC 31:5	12.6	732	18406535	6122249	0.102
DG 38:3	15.8	664	2880749	665473	0.104
plasmenyl-PE 36:1	15.2	728	7831717	2207787	0.107
TG 54:6	18	896	1627518	3268849	0.107
PC 36:0	14.5	812	7444758	2275498	0.111
PC 34:2	12.9	816	3434267	873320	0.112
N-(hexadecanoyl)-sphing-4-enine	14	539	5692769	3126846	0.112
CL 72:5	14.4	726	4585510	1992032	0.114
PC 30:0	11.7	764	6180809	2020744	0.116
PC 36:5	11.7	764	6180809	2020744	0.116
N,N-Dimethylsphingosine	4.7	386	46863544	88150719	0.122
PE 40:5	14.5	794	11809395	5359529	0.130
PC 37:6	14.8	776	8219032	4242501	0.139
PC 32:2	9.9	730	3491337	746643	0.144
PE 40:3	15.2	798	3856415	1040698	0.152
plasmenyl-PE 36:3	14.4	724	7547618	2321413	0.164
PC 36:3	13.8	842	3407141	908160	0.170
PE 40:4	14.7	796	5169800	3171569	0.177
PC 34:3	11.4	756	2475957	374768	0.183
CL 68:3	14.3	700	114744	53518	0.186
PC 21:0	14.8	624	19935115	7711044	0.192
plasmenyl-PE 38:3	14.9	752	5867230	1783285	0.193
PE 37:4	14.9	752	5867230	1783285	0.193
PE 38:4	14.2	768	31148033	19739020	0.211
plasmenyl-PE 40:5	14.8	776	7605888	3685472	0.215
PC 34:0	14.6	820	10151492	5080510	0.220
PE 40:6	14	792	7653199	4558131	0.230
PE 38:3	14.7	770	10905128	2855981	0.235
PC 32:0	13.8	778	6274307	4434874	0.240
PC 38:4	14	868	3786977	2705120	0.268
PI 6:0	1.6	445	3811843	3237211	0.498
MGDG 15:0	14.1	515	2540384	1418963	0.505
lysoPA 14:1	1.5	381	1086724	2134695	0.591

MG 22:6	1.5	409	11941124	11403416	0.619
MGDG 28:1	14.9	671	5076155	5173572	0.903
CL 74:3	14.2	742	35939	ND	NA

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Three independent hippocampal primary neuronal cultures/genotype were performed using 10-12 embryos/culture and Mt isolated from each culture were processed independently. Unpaired two-tailed Student's t test was used for comparisons between genotypes.