Supplement

Supplemental Figure 1

Prolonged and more severe neurological deficits after SD in FHM1 mutant mice. Representative photographs demonstrating the wire grip and neurological deficits after a single SD in female wild type and homozygous R192Q and S218L mutant mice. In wire grip test, wild type mice showed minimal deficits soon after SD (a), while S218L mutant mice continued to fall off the wire for prolonged periods (b). Neurological examination showed leaning (c) and circling (d) in R129Q and S218L mutant mice. SD was evoked in the right hemisphere in all mice. (e) Graphs showing the time course of neurological deficits (only wire grip latency shown) from four representative FHM1 knockin mice. One or more episodes of transient neurological deterioration (red arrows) were observed after full or partial recovery in 7/7 homozygous female R192Q knockin, 4/6 homozygous male R192Q knockin, 3/3 homozygous female S218L knockin, and 4/5 heterozygous female S218L knockin. Vertical dashed line indicates a non-fatal generalized seizure that occurred shortly after the 40 min assessment time point.

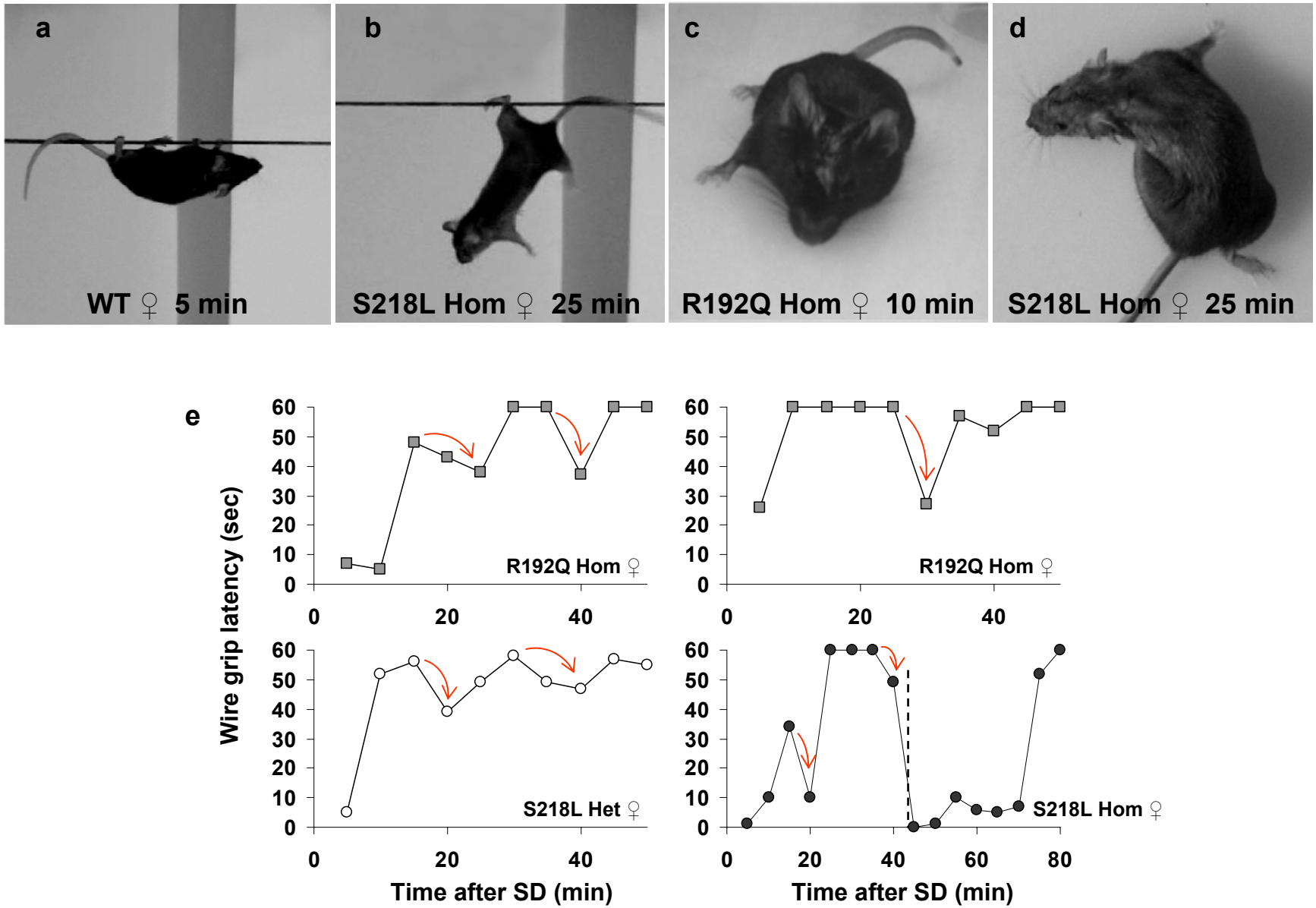
Supplemental Figure 2

Electrophysiological recording sites. Representative coronal gross brain sections showing the SD recording sites in cortex (C), striatum (S), thalamus (T), and hippocampus (H). The dark vertical stains (arrows) show the electrode tracks labeled using Coomassie Brilliant Blue.

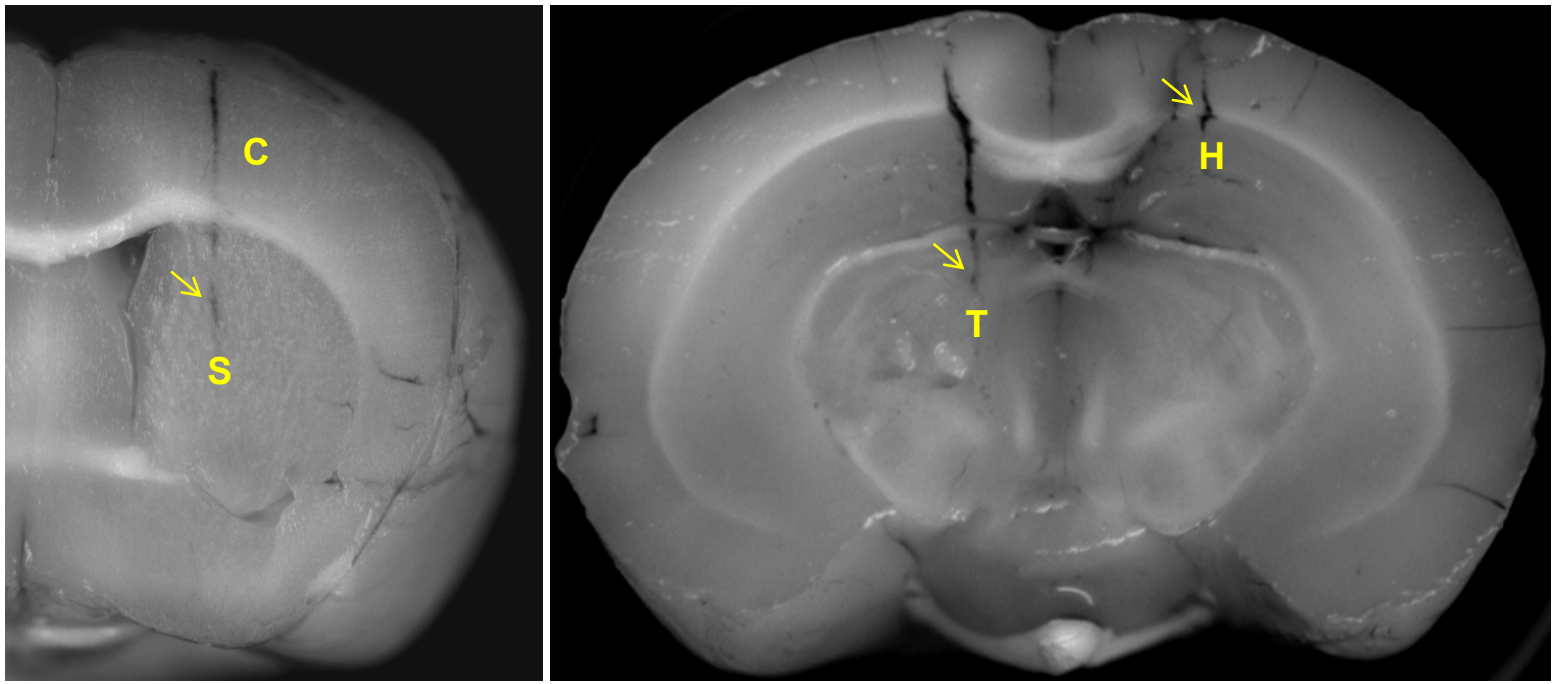
Supplemental Figure 3

Recurrent SD in FHM1 mutant mice. Representative tracings from S218L knockin mice (homozygous male and heterozygous female shown) showing spontaneous recurrent SDs (black dots) after an initial SD induced by brief topical KCl (red arrows, 300 mM) application immediately followed by extensive saline wash. (A) The initial KCl-induced cortical SD (upper tracing) propagates into striatum (lower tracing). Approximately 50 minutes after this initial SD, a recurrent SD spontaneously appeared in the cortical electrode followed by the striatal electrode. Extreme care was taken to avoid cortical drying, mechanical stimulation or trauma during these recordings. (B) In some experiments, the initial SD was followed in rapid succession by a striatal and a recurrent cortical SD, suggesting a cortico-striato-cortical reentrant SD. Vertical bars indicate 20 mV. Horizontal bars indicate 10 min (A) or 2 min (B).

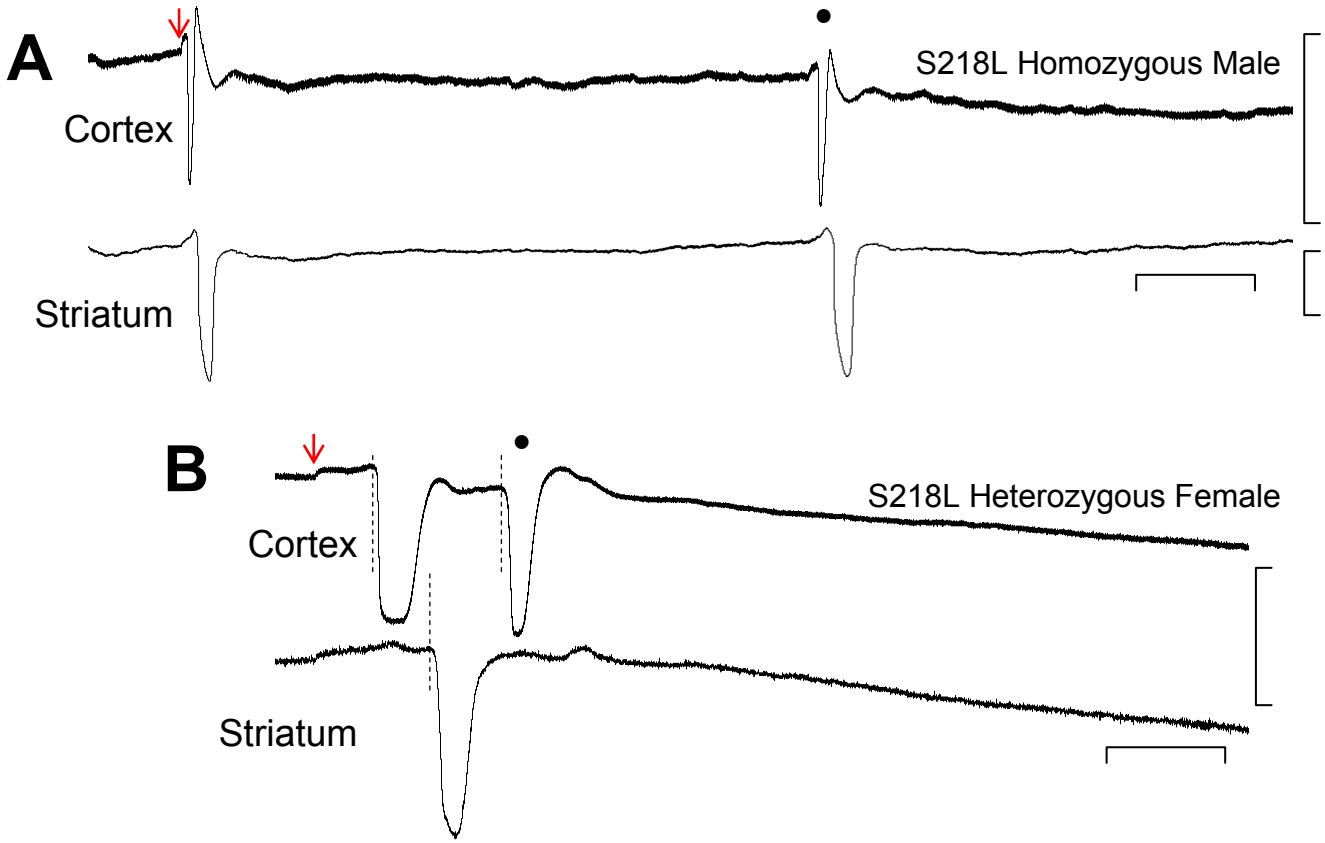
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Movie 1

Representative homozygous female R192Q mutant mouse with circling behavior 5 min after a single SD.

Supplemental Movie 2

Representative homozygous female R192Q mutant mouse from Supplemental Movie 1, with subsequent full recovery at 50 min.

Supplemental Movie 3

Representative wild type female mouse with normal gait 5 min after a single SD.

Supplemental Movie 4

Representative heterozygous female S218L mutant mouse with circling behavior 5 min after a single SD.

Supplemental Movie 5

Representative heterozygous female S218L mutant mouse from Supplemental Movie 5, with subsequent recovery at 70 min.

Supplemental Movie 6

Representative heterozygous female S218L mutant mouse with left hemiparesis 15 min after a single SD. Note the weakness of left forearm and paw grip. In wild type mice no weakness was demonstrated even at the earliest assessment point (5 min).

Supplemental Movie 7

Representative homozygous female R192Q mutant mouse with wire grip deficits 10 min after a single SD.

Supplemental Movie 8

Representative homozygous female R192Q mutant mouse from Supplemental Movie 7 with wire grip deficits 20 min after a single SD.

Supplemental Movie 9

Representative homozygous female S218L mutant mouse with wire grip deficits 35 min after a single SD.

Supplemental Movie 10

Representative homozygous female S218L mutant mouse from Supplemental Movie 9 with wire grip deficits 70 min after a single SD.

Supplemental Movie 11

Representative homozygous female S218L mutant mouse from Supplemental Movies 9 and 10 with recovery of wire grip deficits at 100 min.

Supplemental Movie 12

Representative wild type female mouse with normal wire grip performance 5 min after a single SD.

Supplemental Movie 13

Representative wild type female mouse with normal wire grip performance 5 min after a single SD.