

Figure 1	n
a total synapses/synapse density wild type 3D 37°C	2 mice, 192 images per mouse
a total synapses/synapse density w.t. 3D 18°C	4 mice, 192 images per mouse
a total synapses/synapse density 3D w.t. rewarmed	2 mice, 192 images per mouse
a synapse density 2D w.t. 37°C	93 images from 3 mice
a synapse density 2D w.t. 18°C	93 images from 3 mice
a synapse density 2D w.t. rewarmed	93 images from 3 mice
b synapse density prion 4 w.p.i. 37°C	93 images from 3 mice
b synapse density prion 4 w.p.i. 18°C	91 images from 3 mice
b synapse density prion 4 w.p.i. rewarmed	93 images from 3 mice
b synapse density prion 5 w.p.i. 37°C	92 images from 3 mice
b synapse density prion 5 w.p.i. 18°C	93 images from 3 mice
b synapse density prion 5 w.p.i. rewarmed	93 images from 3 mice
b synapse density prion 6 w.p.i. 37°C	93 images from 3 mice
b synapse density prion 6 w.p.i. 18°C	93 images from 3 mice
b synapse density prion 6 w.p.i. rewarmed	93 images from 3 mice

Figure	1	Statistical method
	P value	
a total synapses 3D	0.0096	Student's t-test
a total synapses 3D	0.0062	Student's t-test
a synapse density 3D	0.001	Student's t-test
a synapse density 3D	0.0069	Student's t-test
a synapse density 2D	<0.0001	Student's t-test
a synapse density 2D	<0.0001	Student's t-test
b prion synapse density 2D 4w.p.i.	<0.0001	Student's t-test
b prion synapse density 2D 5w.p.i.	<0.0001	Student's t-test
b prion synapse density 2D 6w.p.i.	n.s.	Student's t-test
c 5xFAD synapse density 2D 2 months	<0.0001	Student's t-test
c 5xFAD synapse density 2D 3 months	n.s.	Student's t-test

Figure 2	n
Wild type, W.B. 37°C	6 mice
Wild type, W.B. 18°C	6 mice
prion, 4 w.p.i., W.B. 37°C	11 mice
prion, 4 w.p.i., W.B. 18°C	10 mice
prion, 6 w.p.i., W.B. 37°C	8 mice
prion, 6 w.p.i., W.B. 18°C	6 mice
5xFAD, 2 months, W.B. 37°C	6 mice
5xFAD, 2 months, W.B. 18°C	6 mice
5xFAD, 3 months, W.B. 37°C	6 mice
5xFAD, 3 months, W.B. 18°C	6 mice

Figure	2	Statistical method
	P value	
a W.B. w.t.	0.0152	Mann Whitney test
b W.B. prion 4w.p.i.	0.0026	Student's t-test
b W.B. prion cooled 4w.p.i. v 6 w.p.i.	0.0119	Student's t-test
c W.B. 5xFAD 2 months	0.0087	Mann Whitney test
c W.B. 5xFAD cooled 2 months v. 3 months	0.0411	Mann Whitney test

Figure 3	n
a Control, W.B.	7 mice
a Prion, control 6 w.p.i., W.B.	9 mice
a Prion, early cooling 6 w.p.i., W.B.	9 mice
a Prion, control 7 w.p.i., W.B.	8 mice
a Prion, early cooling 7 w.p.i., W.B.	8 mice
a Prion, control 8 w.p.i., W.B.	8 mice
a Prion, early cooling 8 w.p.i., W.B.	9 mice
a Prion, control 9 w.p.i., W.B.	6 mice
a Prion, early cooling 9 w.p.i., W.B.	6 mice
a Prion, control 10 w.p.i., W.B.	3 mice
a Prion, early cooling 10 w.p.i., W.B.	3 mice
a Prion, control 10 w.p.i., W.B.	3 mice
a Prion, early cooling 10 w.p.i., W.B.	3 mice
a Prion, control 12 w.p.i., W.B.	3 mice
a Prion, early cooling 12 w.p.i., W.B.	3 mice
a Prion, control 12 w.p.i., W.B.	3 mice
a Prion, early cooling 12 w.p.i., W.B.	3 mice

b control synapse density	60 images from 2 mice
b prion 6 w.p.i. synapse density	62 images from 2 mice
b prion 7 w.p.i. synapse density	62 images from 2 mice
b prion early cooling 7 w.p.i. synapse density	62 images from 2 mice
b prion 8 w.p.i. synapse density	62 images from 2 mice
b prion early cooling 8 w.p.i. synapse density	62 images from 2 mice
b prion 9 w.p.i. synapse density	62 images from 2 mice
c control, evoked EPSC amplitude	6 cells from 2 mice
c prion 7 w.p.i., evoked EPSC amplitude	6 cells from 2 mice
c prion 7 w.p.i. early cooled, evoked EPSC amplitude	8 cells from 2 mice
c prion 8 w.p.i., evoked EPSC amplitude	4 cells from 2 mice
c prion 8 w.p.i. early cooled, evoked EPSC amplitude	7 cells from 2 mice
c prion 9 w.p.i., evoked EPSC amplitude	6 cells from 2 mice
c prion 9 w.p.i. early cooled, evoked EPSC amplitude	7 cells from 2 mice
c control, mEPSC frequency	6 cells from 2 mice
c prion 7 w.p.i., mEPSC frequency	6 cells from 2 mice
c prion 7 w.p.i. early cooled, mEPSC frequency	8 cells from 2 mice
c prion 8 w.p.i., mEPSC frequency	4 cells from 2 mice
c prion 8 w.p.i. early cooled, mEPSC frequency	5 cells from 2 mice
c prion 9 w.p.i., mEPSC frequency	6 cells from 2 mice
c prion 9 w.p.i. early cooled, mEPSC frequency	6 cells from 2 mice
d burrowing control uninfected mice	20 mice
d burrowing prion 6 w.p.i.	12 mice
d burrowing prion, early cooled 6 w.p.i.	21 mice
d burrowing prion 7 w.p.i.	12 mice
d burrowing prion, early cooled 7 w.p.i.	21 mice
d burrowing prion 8 w.p.i.	17 mice
d burrowing prion, early cooled 8 w.p.i.	24 mice
d burrowing prion 9 w.p.i.	25 mice
d burrowing prion, early cooled 9 w.p.i.	23 mice
d burrowing prion 10 w.p.i.	25 mice
d burrowing prion, early cooled 10 w.p.i.	23 mice
d n.o.r. control uninfected mice	13 mice
d n.o.r. prion 8 w.p.i.	12 mice
d n.o.r. prion early cooled 8 w.p.i.	12 mice
d n.o.r. prion 8 w.p.i.	10 mice
d n.o.r. prion early cooled 8 w.p.i.	10 mice
e neuronal count, control uninfected mice	4 mice
e neuronal count, prion only	6 mice
e neuronal count, prion, early cooled	6 mice
e neuronal count, prion, early cooled + LV-shRNA-RBM3	2 mice
f Survival, prion early cooled	31 mice
f Survival, prion only	17 mice
f Survival, prion early cooled + LV-shRNA-RBM3	10 mice

Figure	3	Statistical method
	P value	
3a Early cooling, 6 w.p.i. W.B.	<0.0001	Student's t-test
3a Early cooling, 7 w.p.i. W.B.	0.003	Student's t-test
3a Early cooling, 8 w.p.i. W.B.	0.0022	Mann Whitney test
3a Early cooling, 9 w.p.i. W.B.	0.0043	Student's t-test
3b Early cooling, synapse density 2D 7 w.p.i.	<0.0001	Student's t-test
3b Early cooling, synapse density 2D 8 w.p.i.	<0.0001	Student's t-test
3b Early cooling, synapse density 2D 9 w.p.i.	<0.0001	Student's t-test
3c Evoked EPSC amplitude 8 w.p.i.	0.0424	Mann Whitney test
3c Evoked EPSC amplitude 9 w.p.i.	0.0005	Student's t-test
3c mEPSC frequency 9 w.p.i.	0.0049	Mann Whitney test
3d Early cooling prion, burrowing	<0.0001	One way ANOVA test
3d Early cooling prion, Novel Object Recognition	0.0003	One way ANOVA test
3e Early cooling, Neuronal count CA1 pyramidal layer	0.001	One way ANOVA test
3f Survival, prion only v. prion + early cooling	0.0003	Mann Whitney test
3f Survival, prion only v. prion + shRNA-RBM3 + early cooling	n.s.	Mann Whitney test

Figure 4	n
a uninfected control samples, W.B.	3 mice
a LV-Control samples, W.B.	6 mice
a LV-RBM3 samples, W.B.	6 mice
a LV-shRNA-RBM3, W.B.	6 mice
b prion 6 w.p.i. 24h recovery, synapse density	93 images from 3 mice
b prion 6 w.p.i. 24h recovery+ LV-RBM3, synapse density	93 images from 3 mice
b 5xFAD 3 months 24h recovery, synapse density	93 images from 3 mice
b 5xFAD 3 months 24h recovery+ LV-RBM3, synapse density	93 images from 3 mice
c uninfected control, synapse density	60 images from 2 mice
c prion 6 w.p.i., synapse density	62 images from 2 mice
c prion 6 w.p.i.+ LV-shRNA-RBM3, synapse density	93 images from 3 mice
c prion 7 w.p.i., synapse density	62 images from 2 mice
c prion 7 w.p.i.+ LV-RBM3, synapse density	62 images from 2 mice
c prion 9 w.p.i., synapse density	62 images from 2 mice
c prion 9 w.p.i.+ LV-RBM3, synapse density	62 images from 2 mice
d uninfected control, Evoked EPSC amplitude	6 cells from 2 mice
d prion 7 w.p.i., Evoked EPSC amplitude	6 cells from 2 mice
d prion 9 w.p.i., Evoked EPSC amplitude	6 cells from 2 mice
d prion 9 w.p.i.+ LV-RBM3, Evoked EPSC amplitude	5 cells from 2 mice
d uninfected control, mEPSC frequency	6 cells from 2 mice
d prion 7 w.p.i., mEPSC frequency	6 cells from 2 mice
d prion 9 w.p.i., mEPSC frequency	6 cells from 2 mice
d prion 9 w.p.i.+ LV-RBM3, mEPSC frequency	5 cells from 2 mice
e uninfected control, burrowing	16 mice
e prion 6 w.p.i., burrowing	14 mice
e prion 6 w.p.i. + LV-RBM3, burrowing	16 mice
e prion 7 w.p.i., burrowing	15 mice
e prion 7 w.p.i. + LV-RBM3, burrowing	16 mice
e prion 7 w.p.i., burrowing	14 mice
e prion 8 w.p.i. + LV-RBM3, burrowing	16 mice
e prion 7 w.p.i., burrowing	12 mice
e prion 9 w.p.i. + LV-RBM3, burrowing	16 mice
e prion 7 w.p.i., burrowing	14 mice
e prion 10 w.p.i. + LV-RBM3, burrowing	16 mice
e uninfected control, n.o.r.	13 mice
e prion 7 w.p.i., n.o.r.	10 mice
e prion 7 w.p.i.+ LV-shRNA-RBM3, n.o.r.	11 mice
e prion 8 w.p.i., n.o.r.	11 mice
e prion 8 w.p.i.+ LV-RBM3, n.o.r.	11 mice
e prion 9 w.p.i., n.o.r.	11 mice
e prion 9 w.p.i.+ LV-RBM3, n.o.r.	10 mice
f uninfected control, 35S-Met labeling	6 mice
f prion 7 w.p.i., 35S-Met labeling	6 mice
f prion 9 w.p.i., 35S-Met labeling	6 mice
f prion 9 w.p.i.+ LV-RBM3, 35S-Met labeling	4 mice
f prion 9 w.p.i.+ LV-shRNA-RBM3, 35S-Met labeling	4 mice
g uninfected control, neuronal count	4 mice
g prion terminal+ LV-Control, neuronal count	9 mice
g prion terminal+ LV-RBM3, neuronal count	5 mice
g prion terminal+ LV-shRNA-RBM3, neuronal count	3 mice
h prion + LV-control, survival	31 mice
h prion + LV-RBM3, survival	20 mice
h prion + LV-shRNA-RBM3	14 mice

Figure	4	Statistical Method
	P value	
4a W.B., LV-Control v. LV-RBM3	< 0.0001	Student's t-test
4a W.B., LV-Control v. LV-shRNA-RBM3	0.0132	Student's t-test
4b prion synapse density	<0.0001	Student's t-test
4b 5xFAD synapse density	<0.0001	Student's t-test
4c synapse density, 6w.p.i., LV-Control v. LV-shRNA-RBM3	<0.0001	Mann Whitney test
4c synapse density, 7w.p.i., LV-Control v. LV-RBM3	<0.0001	Mann Whitney test
4c synapse density, 9w.p.i. LV-Control v. LV-RBM3	<0.0001	Mann Whitney test
4d Evoked EPSC amplitude, prion 9 w.p.i. LV-RBM3	0.0109	Student's t-test
4d mEPSC frequency, prion 9 w.p.i. LV-RBM3	0.0127	Mann Whitney test
4e prion + LV-RBM3, burrowing	<0.0001	One way ANOVA test
4e prion + LV-shRNA-RBM3, prion + LV-RBM3	<0.0001	One way ANOVA test
4f 35S-Met labeling	<0.0001	One way ANOVA test
4g Neuronal count	0.0005	One way ANOVA test
4h Survival, LV-Control v LV-RBM3	0.0008	Mann Whitney test
4h Survival, LV-Control v. LV-shRNA-RBM3	0.0082	Mann Whitney test

Extended Figure 2	<i>n</i>
a prion disease, SNAP25 W.B.	6 mice per time point
a prion disease, VAMP2 W.B.	3 mice per time point
a prion disease, PSD95 W.B.	6 mice per 4 w.p.i. and 9 mice per 6 w.p.i. time points
a prion disease, NR1 W.B.	3 mice per time point
b 5xFAD, SNAP25 W.B.	6 mice per time point, 5 mice per control 3 months, time point
b 5xFAD, VAMP2 W.B.	6 mice per time point
b 5xFAD, PSD95 W.B.	6 mice per time point
b 5xFAD, NR1 W.B.	6 mice per time point

Extended Figure 3	<i>n</i>
3a prion 6 w.p.i., W.B., prot. K digestion	6 mice per time point
3b 5xFAD 3 months, W.B.	6 mice per time point

Extended Figure 4	<i>n</i>
a prion disease, CIRP W.B.	6 mice per time point
b 5xFAD, CIRP W.B.	9 mice per time point, 7 mice per cool 3 months, time point
c wild type, RBM3 W.B.	6 mice per 37°C, cooled and 12h recovery time point
c wild type, RBM3 W.B.	3 mice per 48h recovery time point
c wild type, RBM3 W.B.	4 mice per 72h recovery time point

Extended Figure	4	Statistic Method
	P value	
ED4c, W.B. w.t. 37°C v cooled	0.0152	Mann Whitney test
ED4c, W.B. w.t. 37°C v 24hrs recovery	0.0087	Mann Whitney test
ED4c, W.B. w.t. 37°C v 48hrs recovery	0.0476	Mann Whitney test
ED4c, W.B. w.t. 37°C v 72hrs recovery	0.0381	Mann Whitney test

Extended Figure 6	<i>n</i>
ED6b and c uninfected control, n.o.r.	13 mice
ED6b and c prion 9 w.p.i., n.o.r.	15 mice
ED6b and c prion early cooling + LV-shRNA-Control 9 w.p.i., n.o.r.	11 mice
ED6b and c prion early cooling + LV-shRNA-RBM3 w.p.i., n.o.r.	16 mice

Extended Figure	6	Statistic Method
	P value	
ED6a	n.s.	One way ANOVA test
ED6b	0.0001	One way ANOVA test
ED6c	n.s.	One way ANOVA test

Extended Figure	7	Statistic Method
	P value	
ED7	n.s.	Student's t-test

Extended Figure	9	Statistic Method
	P value	
Survival, prion mild early cooling	0.0039	Student's t-test

Extended Figure 10	<i>n</i>
a 5xFAD 3 months LV-Control, 24h recovery, synapse density	93 images from 3 mice
a 5xFAD 3 months LV-shRNA-RBM3, 24h recovery, synapse density	82 images from 3 mice
b wild type, LV-Control and LV-shRNA-RBM3, synapse density	93 images from 3 mice per condition
b wild type, LV-Control, n.o.r.	11 mice
b wild type, LV-shRNA-RBM3, n.o.r.	10 mice

Extended Figure	10	Statistic Method
	P value	
ED10a, 5xFAD synapse density after rewarmed	<0.0001	Student's t-test
ED10b, w.t. synapse density	<0.0001	Student's t-test
ED10c, w.t. Novel Object Recognition	0.0186	Mann Whitney test