Supplemental Figure S1

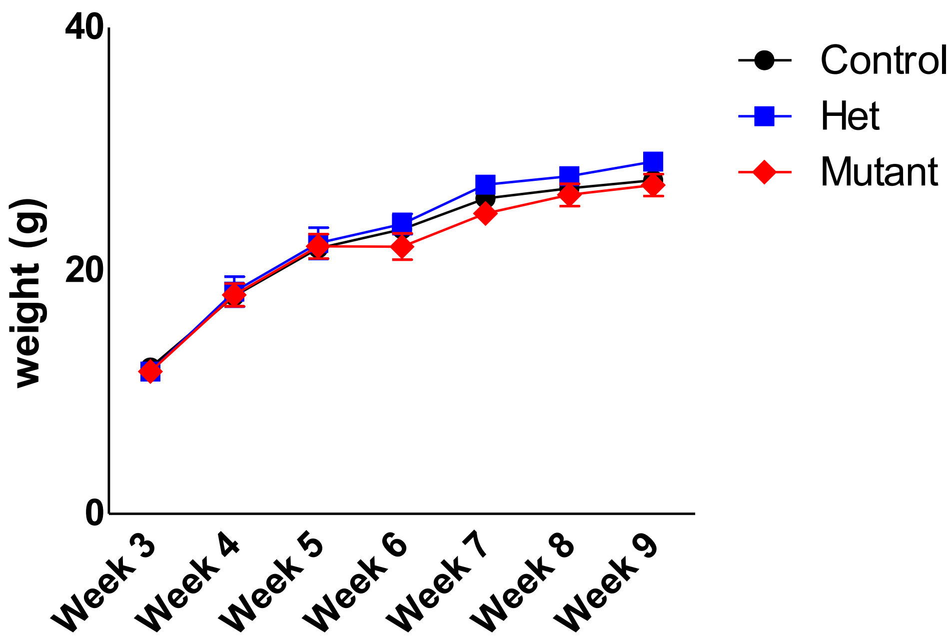

Figure S1. PC *Tsc1* hets and mutants displayed similar weights to control littermates ($p>0.05$ at all ages, two way ANOVA, Bonferroni's post hoc analysis). $n>5$ at each age. Mutants also only exhibited one handling related seizure, unlike the ubiquitous seizures found in previous neuronal or glial specific *Tsc* mutants.

Figure S2

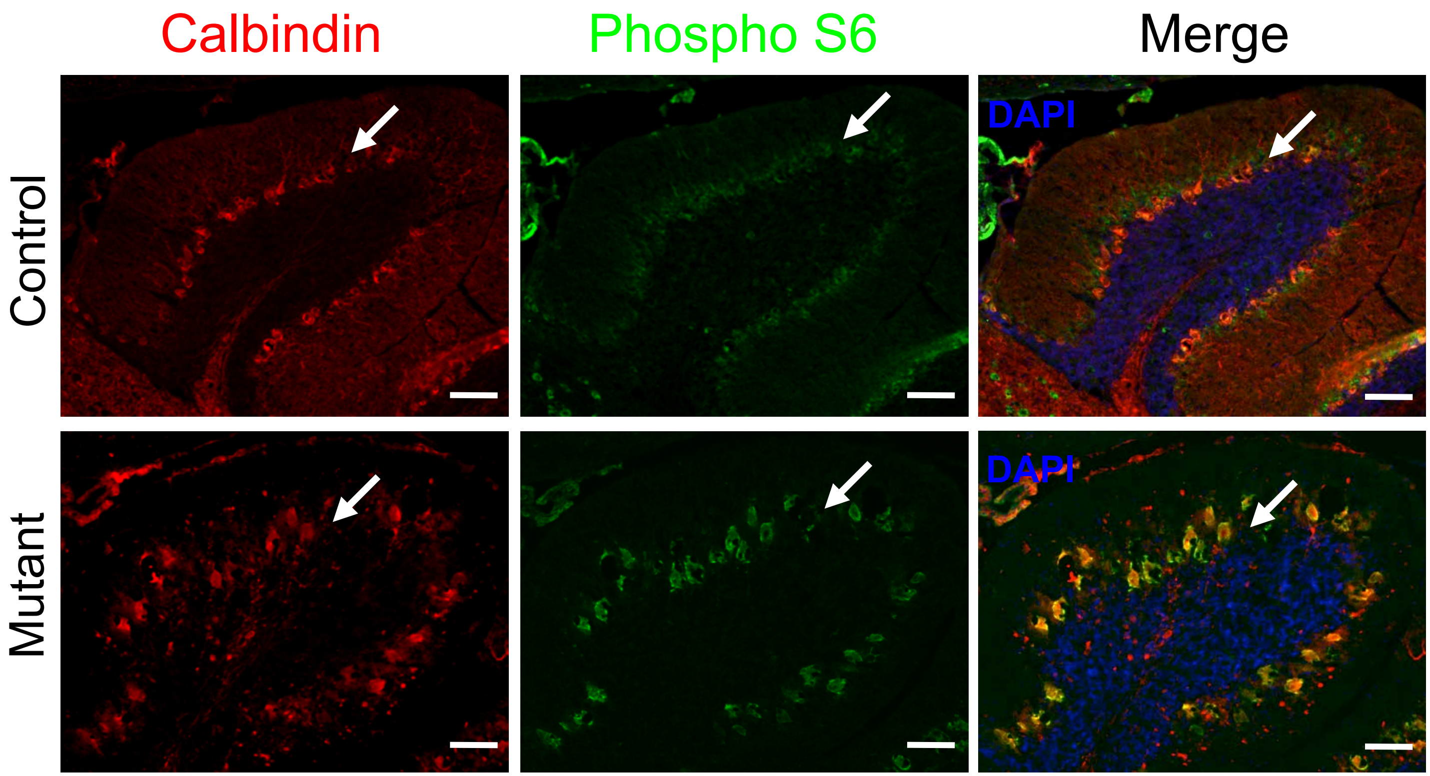

Figure S2. Mutants demonstrated increased phospho-S6 staining in cerebellar PCs, consistent with increased mTOR signaling from *Tsc1* deletion. Calbindin (red), phospho-S6, (green), DAPI (blue). Scale bars 100μm.

Figure S3

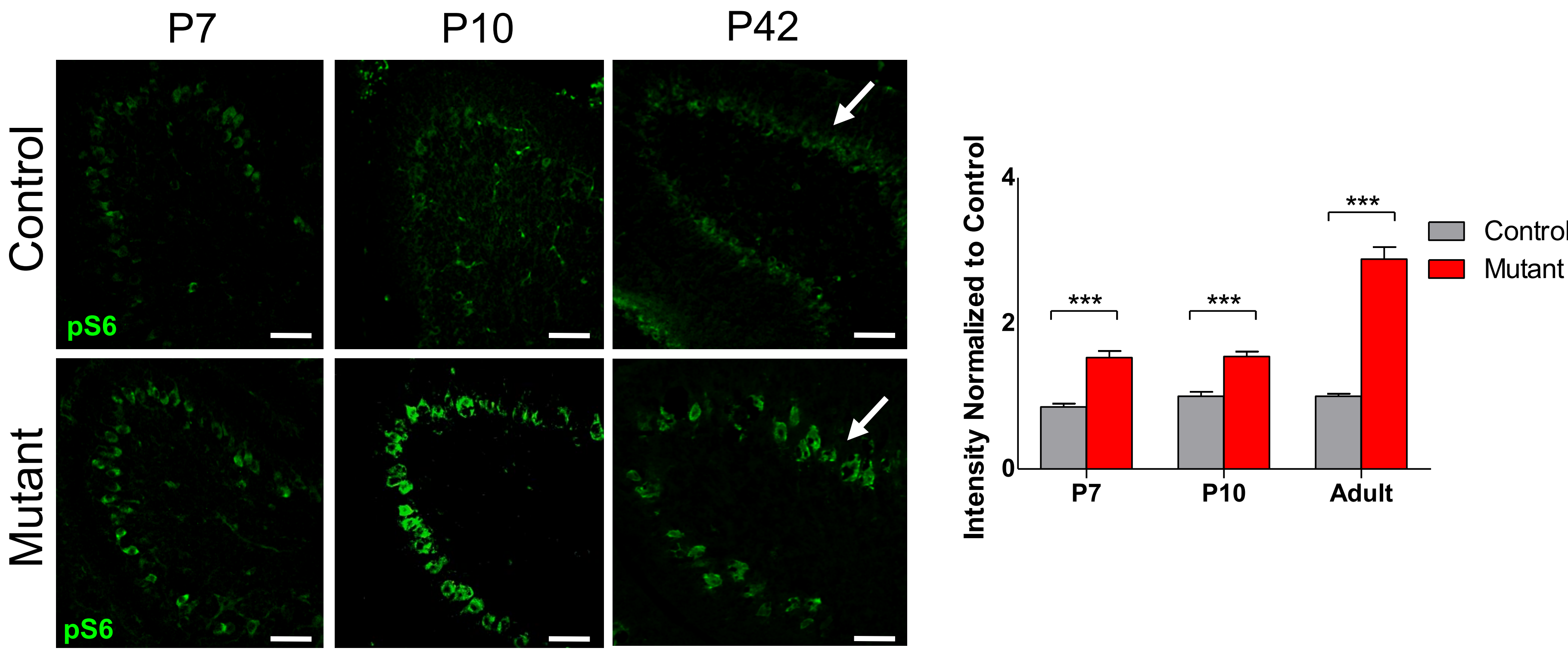

Figure S3. Phospho-S6 staining was increased in PC *Tsc1* mutants. PhosphoS6 (pS6, green) staining was increased in PC layers, consistent with increased mTOR signaling from *Tsc1* loss. Increase was detectable by P7. Arrows delineate the PC layer. (n > 30 cells, $\geq$2 mice per group). Scale bars 100μm. *** p <0.001, two way ANOVA, Bonferroni's post hoc analysis.

Figure S4

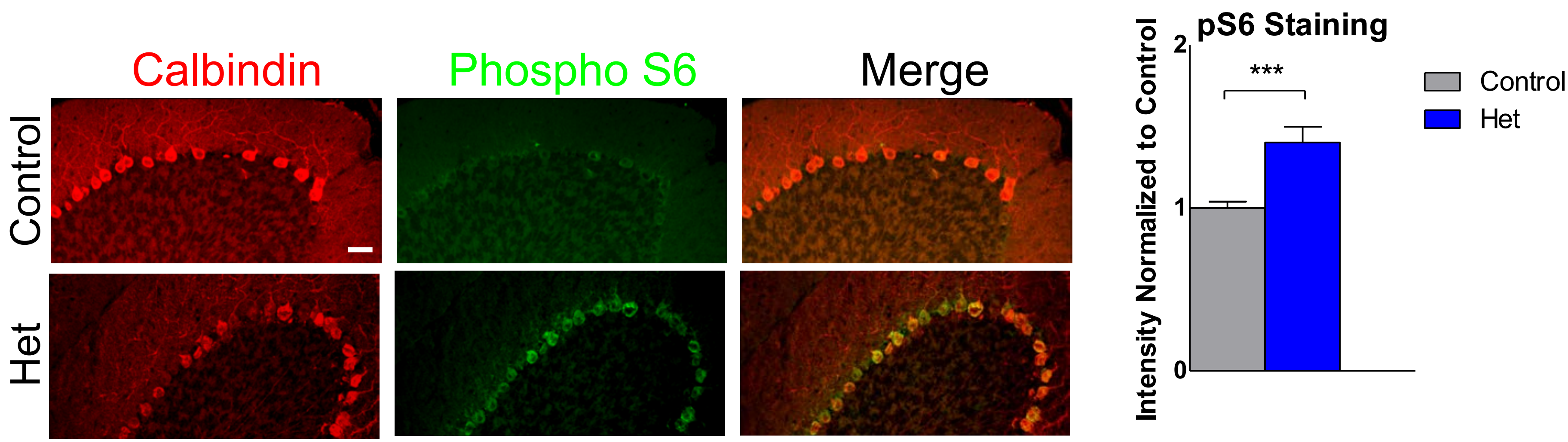

Figure S4. *Tsc1* hets (4 weeks) demonstrated increased PhosphoS6 (pS6) staining in cerebellar PCs, consistent with increased mTOR signaling. Calbindin (red), PhosphoS6 (green). Quantification on Left. (n > 25 cells, n = 2 mice). *** p <0.001, (t-test). Scale bars 100μm.

Figure S5

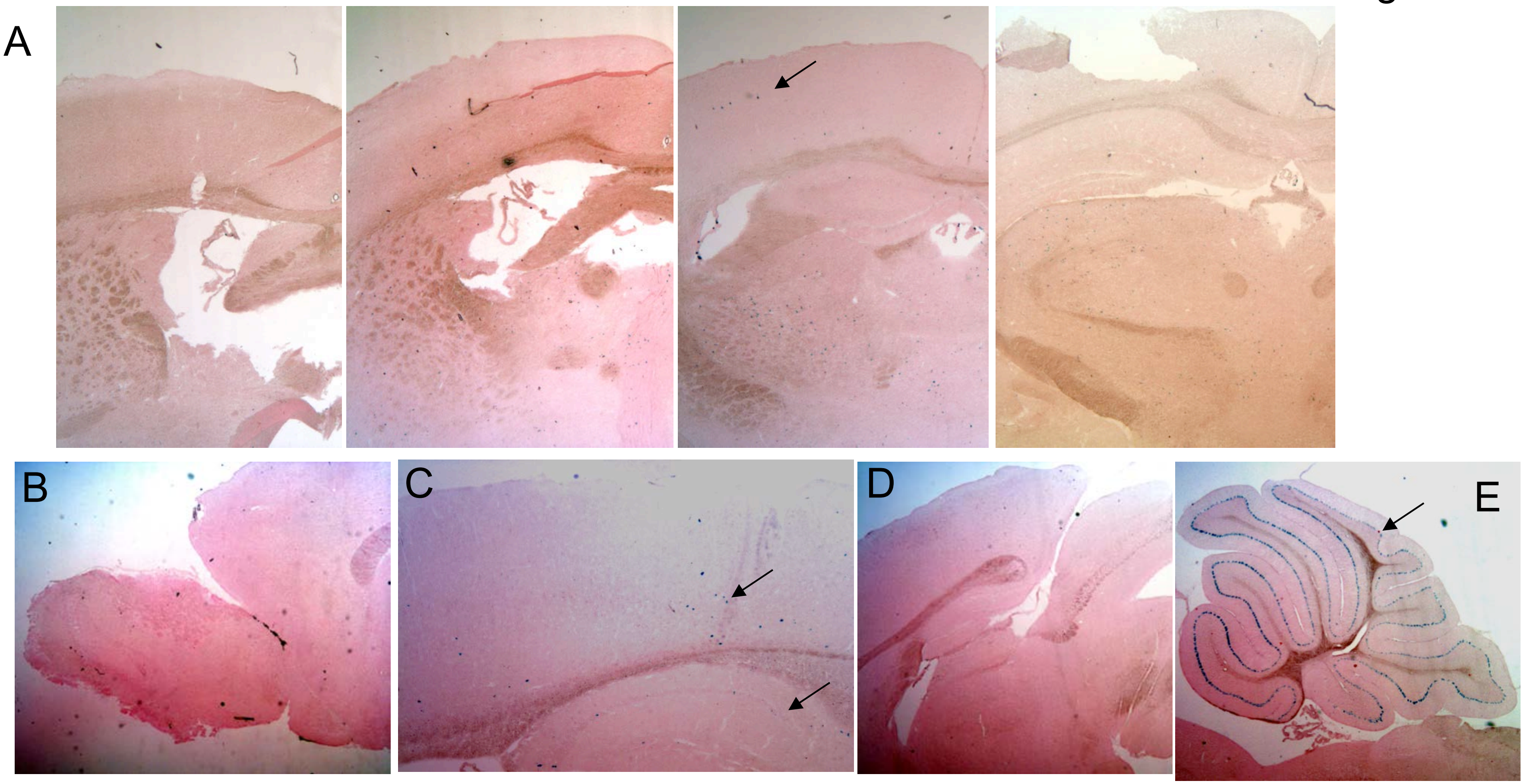

Figure S5. LacZ staining of PC *Tsc1* mutants. A. coronal sections from anterior to posterior from Left to Right and B-E. sagittal sections through B. olfactory bulb, C. cortex and hippocampus (2x view), D. posterior cortex and midbrain, and E. cerebellum reveal a few scattered, lacZ positive cells in various brain regions along with PC-specific expression in the cerebellum (arrows).

Figure S6

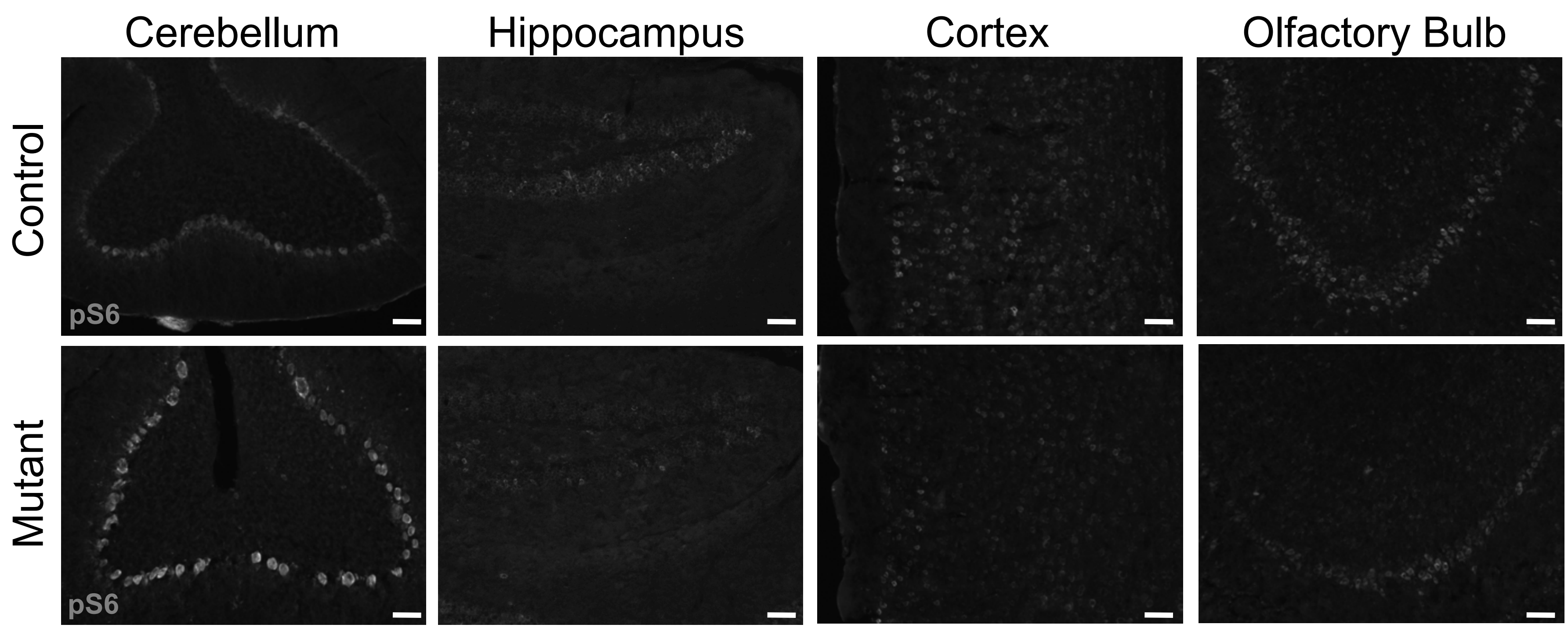

Figure S6. Mutants demonstrated increased phospho-S6 (pS6: grayscale) staining in cerebellar PCs but did not demonstrate additional areas of increased PhosphoS6 staining elsewhere in the central nervous system as compared to littermate controls. Scale bars 100mm.

Figure S7

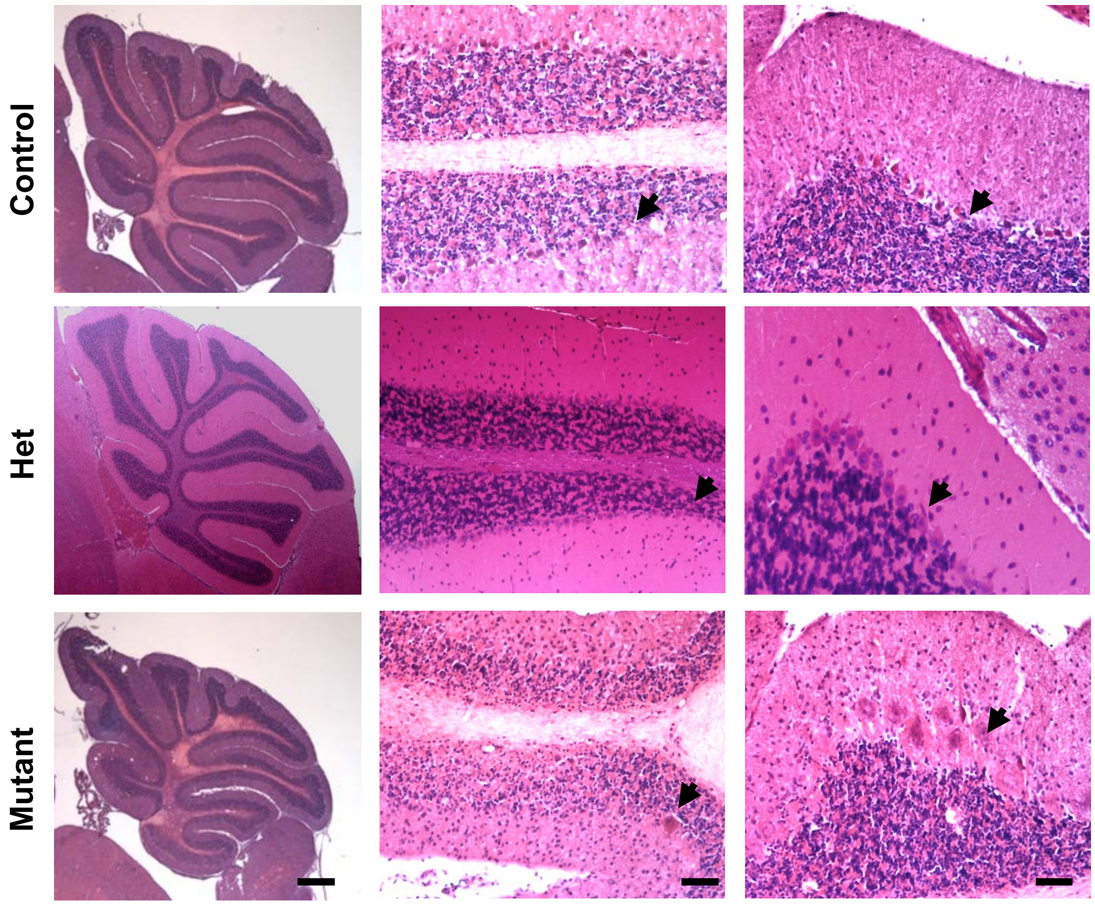

Figure S7. By hematoxylin and eosin staining, mutants displayed grossly normal cerebellar architecture but demonstrate reduced PC numbers. Scale bars: 20 μm (left), 50μm (middle), 100μm (right).

Figure S8

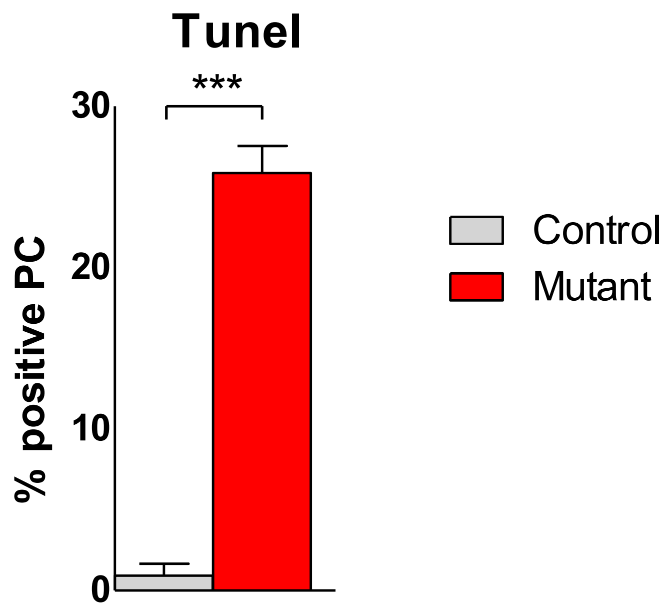

Figure S8. PC *Tsc1* mutants have increased Tunel staining compared to controls. (n > 500 cells, n=3 mice per group) ***, p<0.001 (t-test).

Figure S9

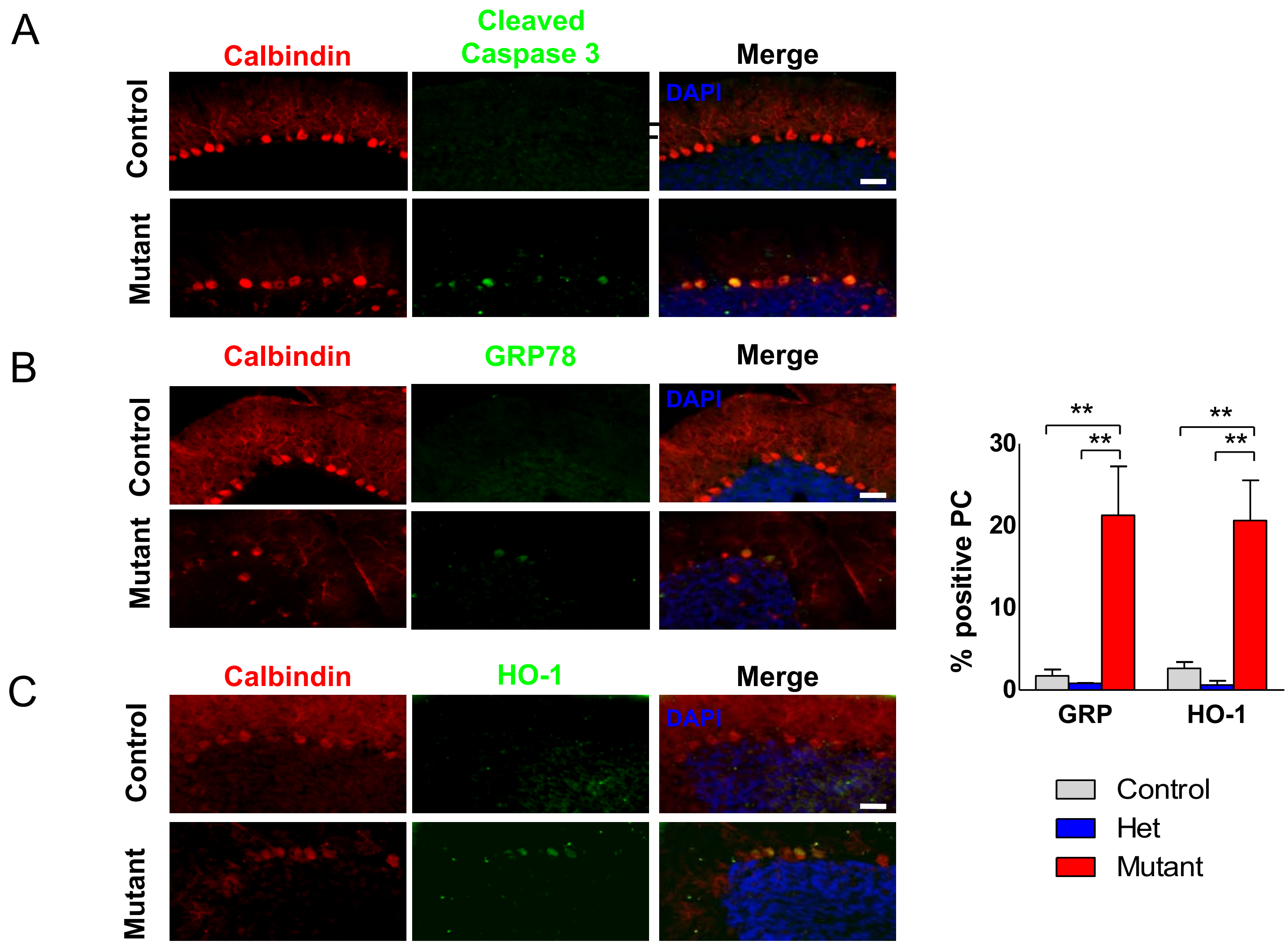

Figure S9. A. Mutant PCs (red, calbindin) showed increased apoptosis by cleaved caspase 3 staining (green). **B.** Mutant PCs also showed evidence of elevated neuronal stress with increased staining for GRP78 – an endoplasmic reticulum stress marker (green) – and **C.** HO-1 – a marker of oxidative stress (green). DAPI (blue). Quantification of GRP78 and HO-1 on right. controls/mutants: n=3 mice; hets, n=2 mice; >500 cells/group). ** $p<0.01$, two-way ANOVA, Bonferroni's post hoc analysis. Scale bars: 100μm.

Figure S10

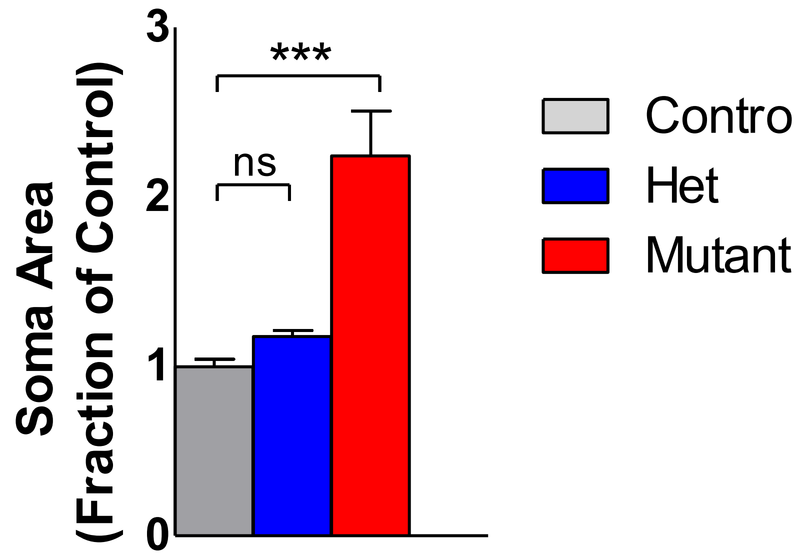

Figure S10. Mutant PCs display increased soma area compared with controls. (control: n=32cells, 3 mice; het: n=36 cells, 2 mice; mutant: n=15 cells, 3 mice). ns >0.05; *** p<0.001, two-way ANOVA, Bonferroni's post hoc analysis.

Figure S11

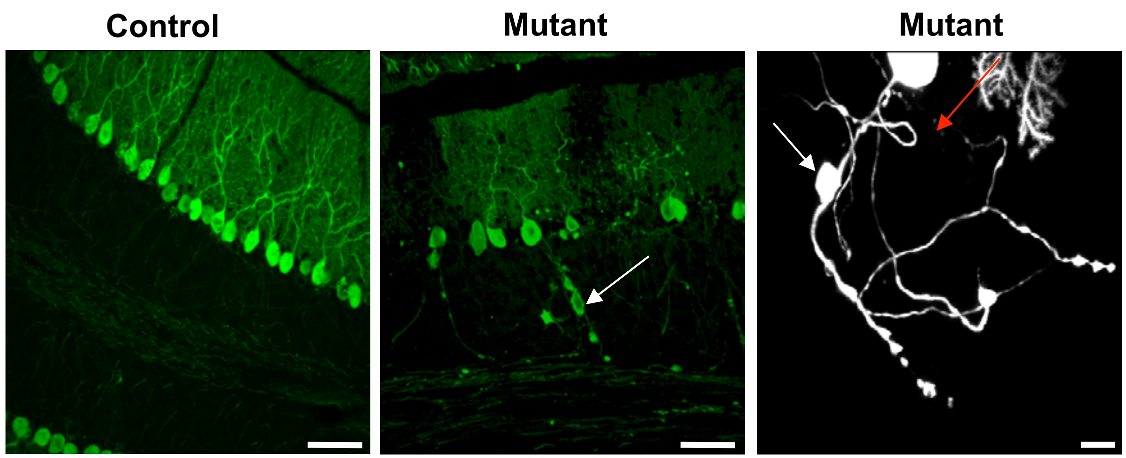

Figure S11. A. Mutant PCs displayed abnormal axonal projections (white arrows) with numerous protrusions and abnormal collateralization (red arrow). Scale bars – 100μm.

Figure S12

Reciprocal Social Interaction (Male-Female)

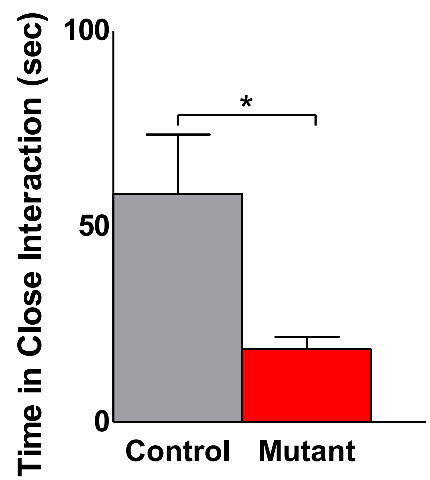

Figure S12. Mutants demonstrated impaired social interaction in open field, male-female interaction paradigm. n=10-11. * $p < 0.05$.

Figure S13

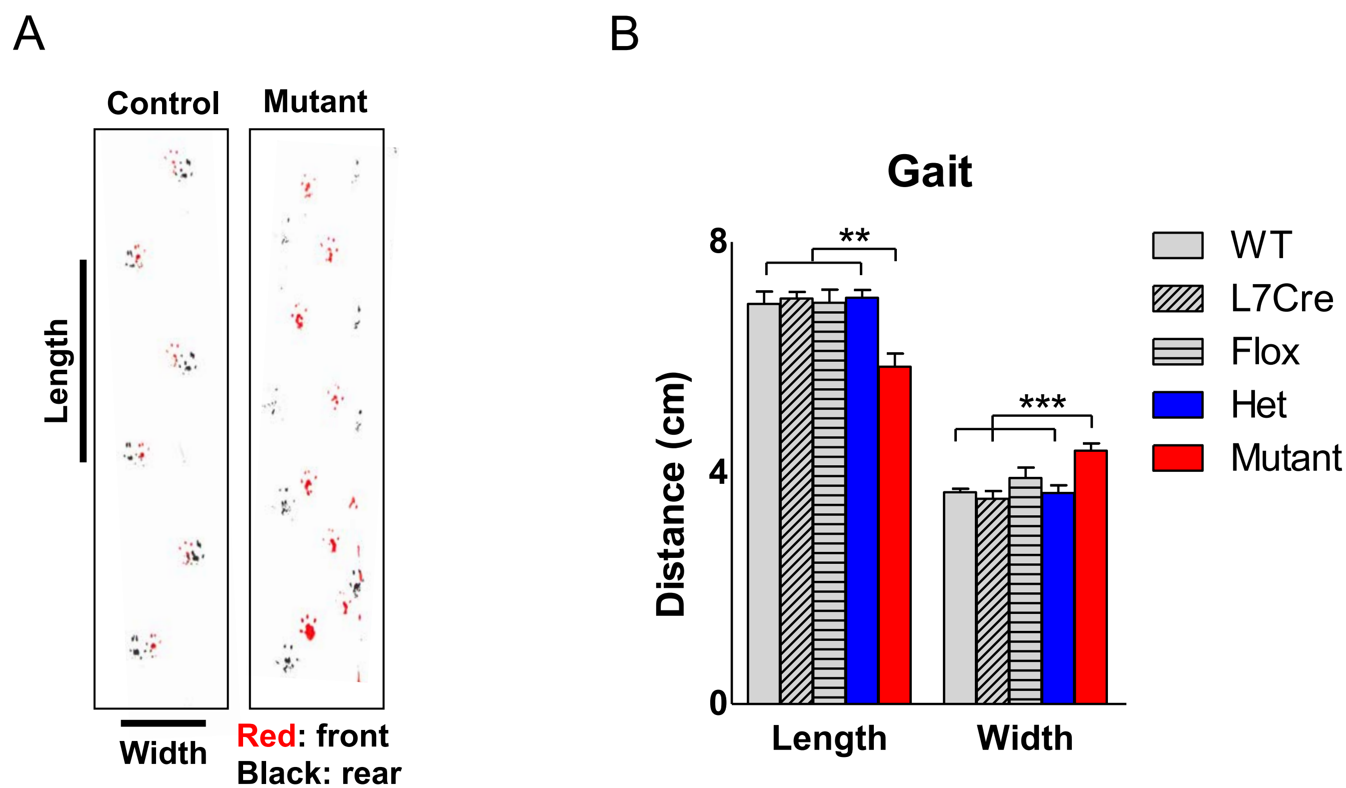

Figure S13. A. Mutant mice displayed ataxic gait with **B.** decreased stride length and increased stride width at 4 months. n≥6 per group. **, p <0.01; ***, p<0.001, two way ANOVA, Bonferroni's post hoc analysis.

Figure S14

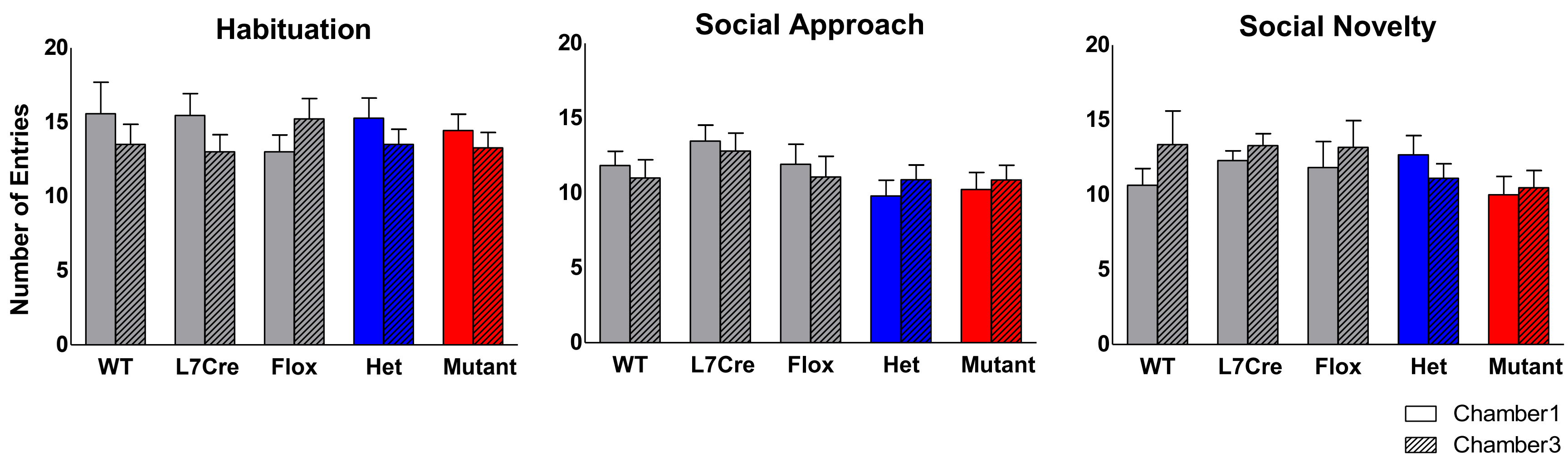

Figure S14. Locomotor activity within three-chambered social interaction apparatus was comparable between genotypes. Automated detection of crossing between chambers within the three chambered apparatus was recorded during habituation, social approach, and social novelty paradigms. n>11 per group. All values are not significant p>0.05, two way ANOVA, Bonferroni's post hoc analysis.

Figure S15

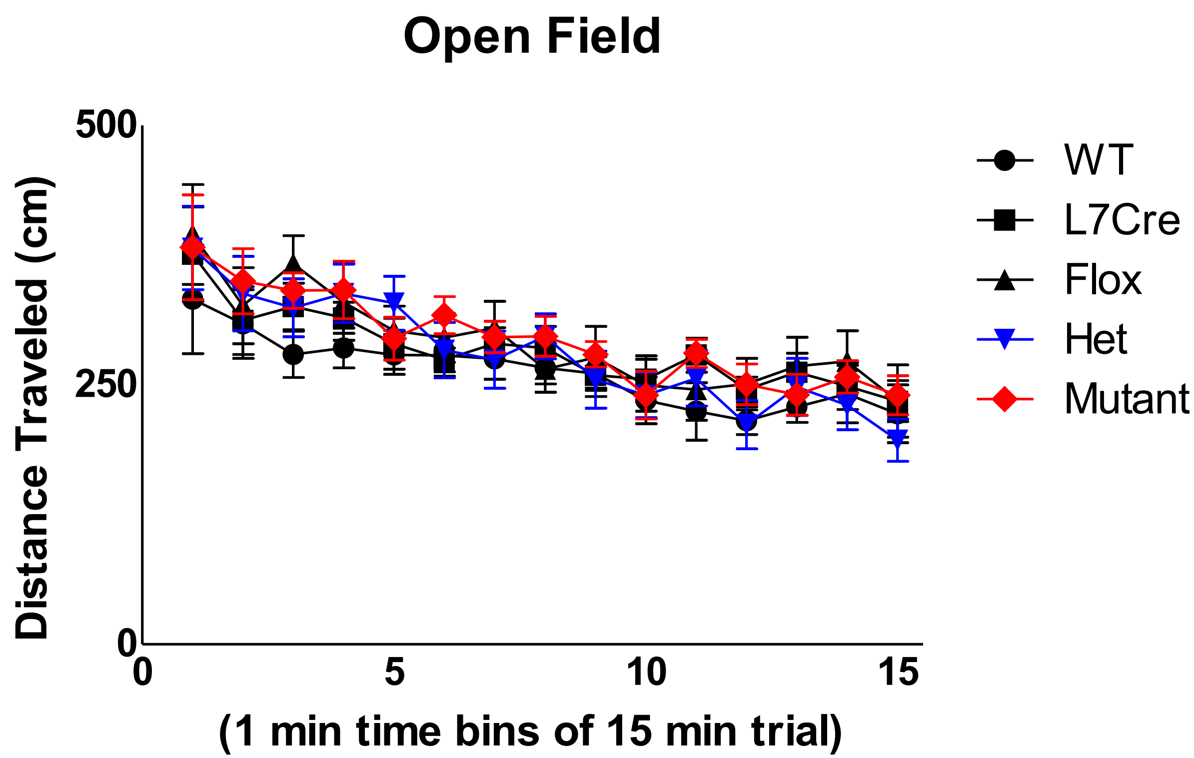

Figure S15. Locomotor activity in the open field was comparable between all genotypes. n≥8 per group. p >0.05, two way ANOVA Bonferroni's post hoc analysis.

Figure S16

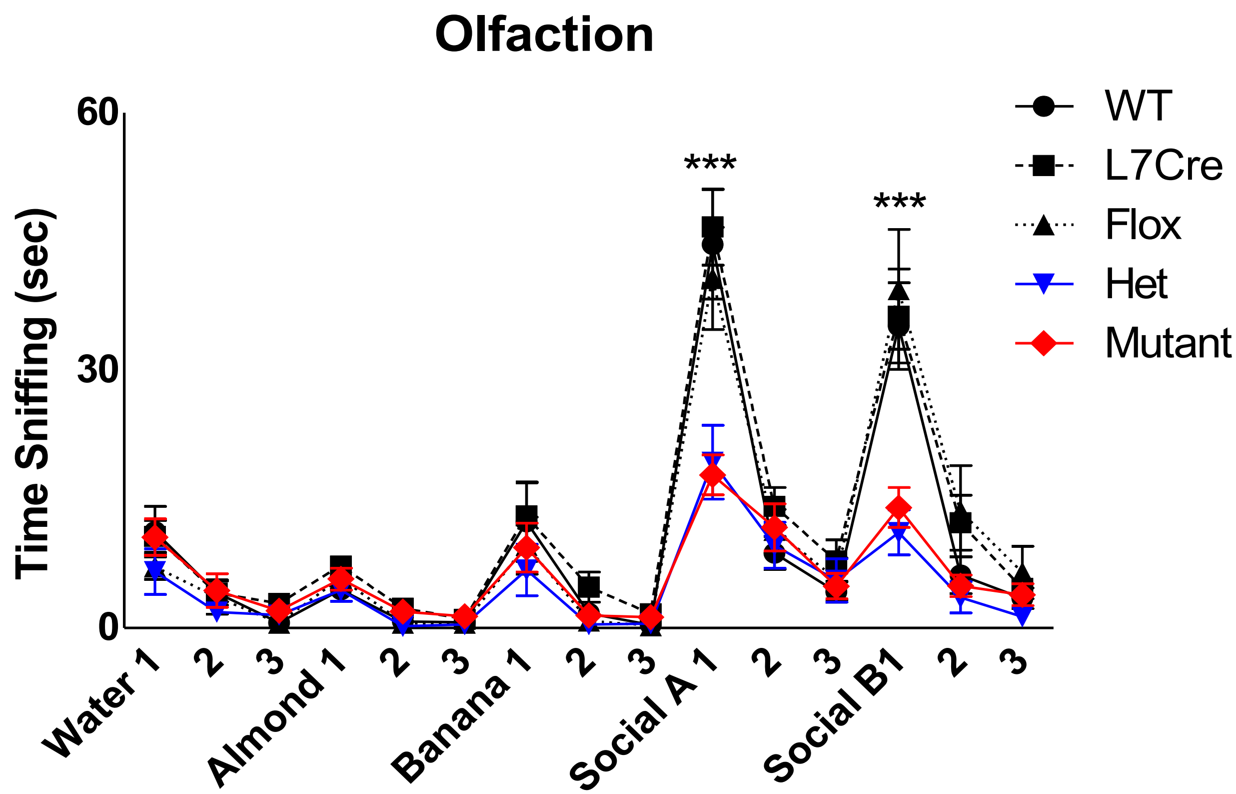

Figure S16. Mutants displayed comparable investigation of nonsocial, volatile olfactory cues ($p>0.05$, two way ANOVA, Bonferroni's post hoc analysis) but spent less time investigating social odors compared to controls. $n\geq8$ per group. ***, $p<0.001$, two way ANOVA, Bonferroni's post hoc analysis for both hets and mutants compared to all control genotypes.

Figure S17

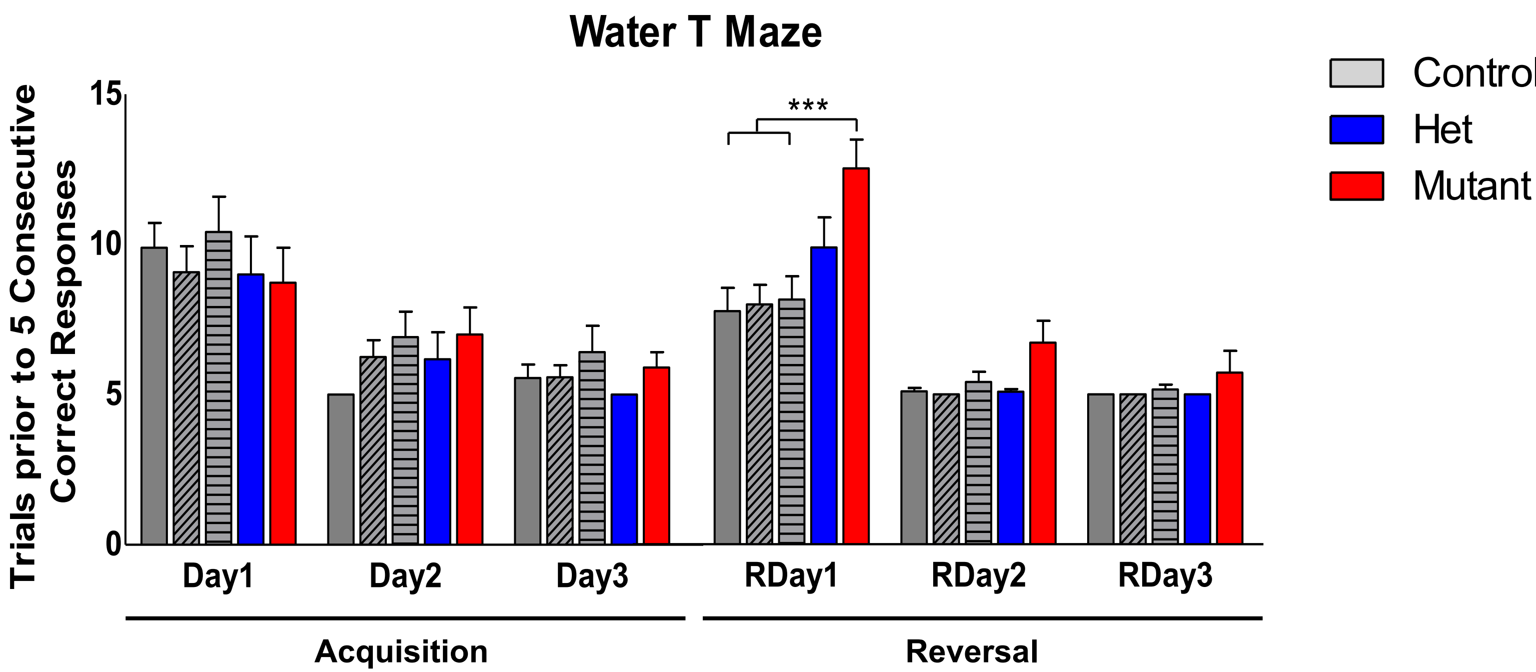

Figure S17. Mutants did not display impaired acquisition learning of the escape platform location in the water T maze by trials needed for 5 consecutive correct responses. Mutants, however, did demonstrate significantly impaired learning on reversal day (RDay) 1. n $\geq$ 13 for each group. *** $p < 0.001$, two way ANOVA, Bonferroni's post hoc analysis.

Figure S18

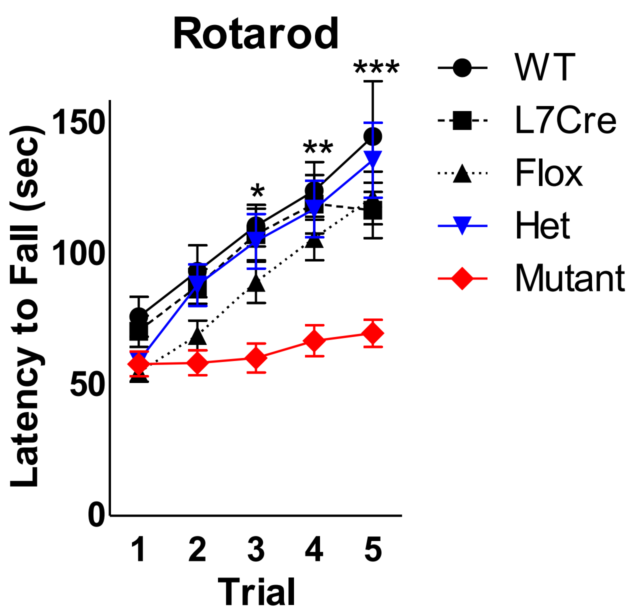

Figure S18. PC *Tsc1* mutants, but not hets, demonstrate impaired motor learning on the rotarod. n≥7 per group. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$; two way ANOVA, Bonferroni's post hoc analysis.

Figure S19

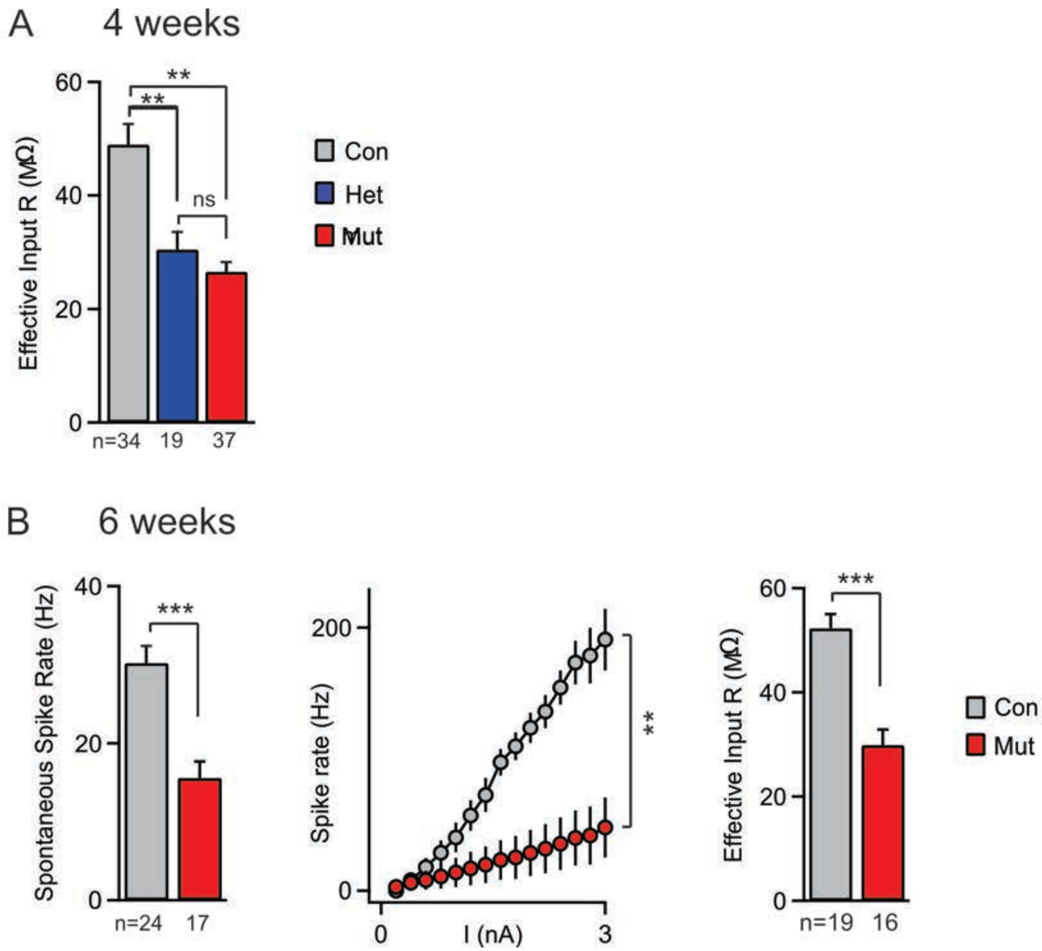

Figure S19. Excitability and resistance changes in mutant animals. (A) In whole cell recordings from PCs, small hyperpolarizing voltage steps (-5 mV) evoked small currents arising from the passive properties of PC, and small active currents consistent with IH, that were used to calculate the effective input resistance ($R=\Delta V/I$). (B) Experiments as In Figure 4 were performed on 6 week control and mutant mice. There were pronounced reductions in the spontaneous spiking, the excitability of PCs firing frequency evoked by current injection [reduced from 191 ± 23 Hz(n=9) in control animals to 48 ±23 Hz (n=9) in mutant animals ($p<0.01$)], and in the effective input resistance. ns, $p>0.05$; **, $p<0.01$; ***, $p<0.001$ two way ANOVA, Bonferroni's post hoc analysis.

Figure S20

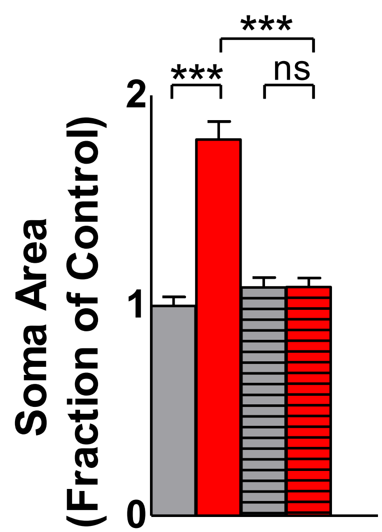

Figure S20. Increase in soma area seen in vehicle treated mutants is prevented with rapamycin treatment. (n ≥ 18cells; 2 mice per group). ns, p>0.05; ***, p<0.001. two way ANOVA, Bonferroni's post hoc analysis.

Figure S21

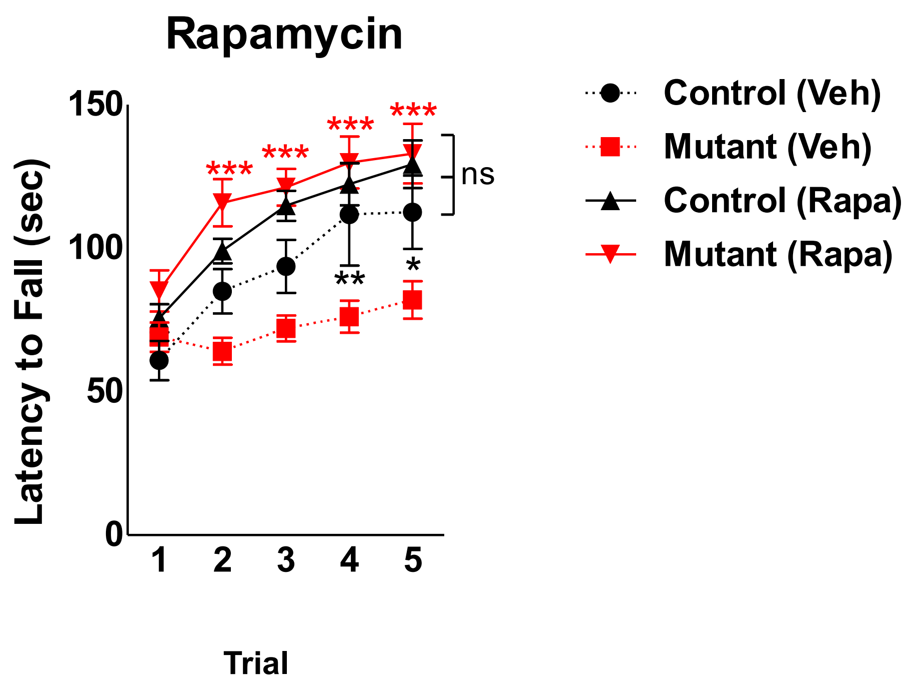

Figure S21. Motor learning impairment is prevented with rapamycin treatment. n≥8 per group. ns, $p>0.05$; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$; two way ANOVA, Bonferroni's post hoc analysis. (* comparison between vehicle treated controls and mutants; red * : comparison between vehicle and rapamycin treated mutants)

Figure S22

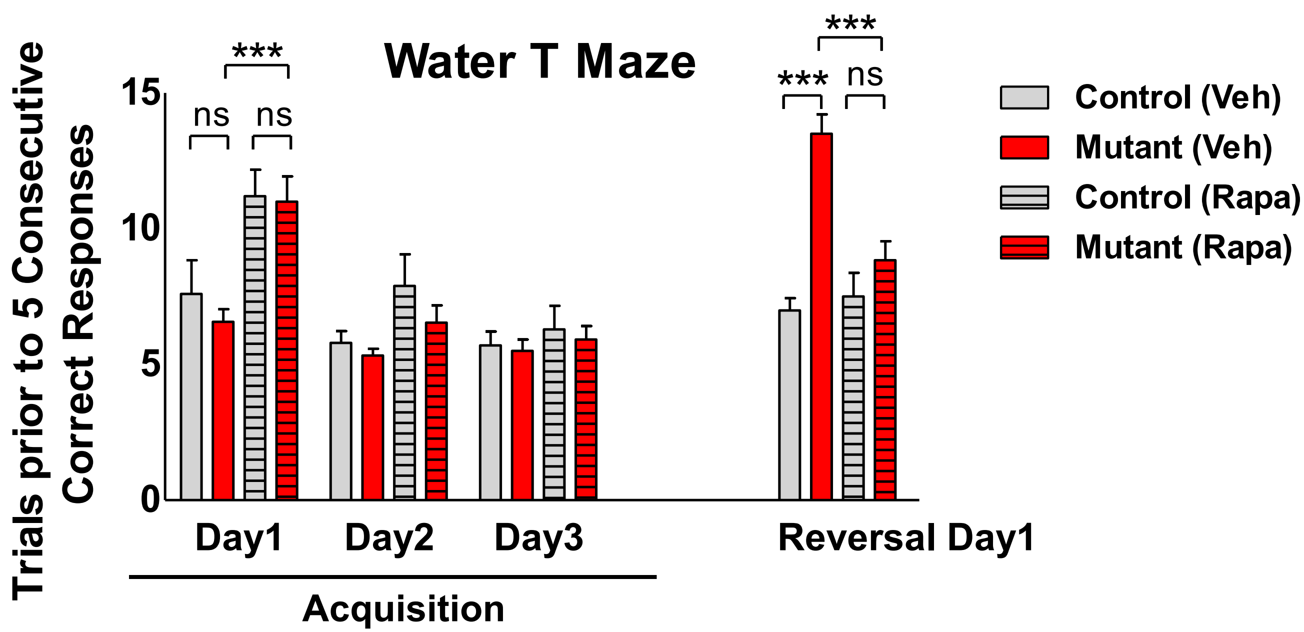

Figure S22. Rapamycin treatment prevents reversal learning impairment. Both controls and mutants treated with rapamycin display poorer performance on Day1 when compared to corresponding vehicle treated mice. n≥10 per group. ***, $p<0.001$, two way ANOVA, Bonferroni's post hoc analysis. However, no differences were noted on Day1 between controls and mutants within treatment groups. Upon reversal, whereas vehicle treated mutants perform significantly worse on the reversal trial (***, $p<0.001$, two way ANOVA), rapamycin treated control and mutant animals showed no significant differences during reversal trial (two way ANOVA, $p > 0.05$). Also, with reversal, unlike with acquisition learning, vehicle treated controls differed significantly from vehicle treated mutants, while displaying no significant differences with rapamycin treated cohorts.

Figure S23

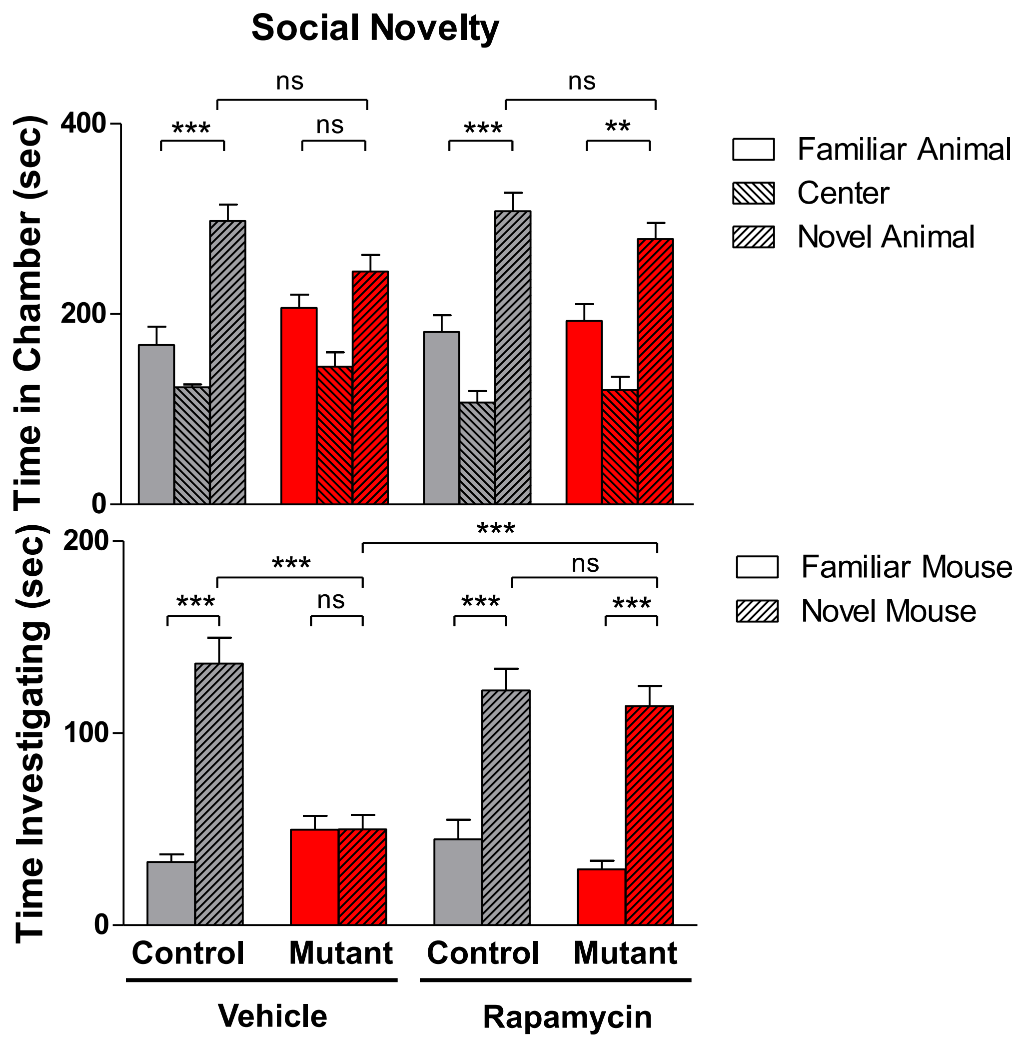

Figure S23. Social Novelty (rapa). A. Time in chamber and B. Time spent sniffing during social novelty assay. Vehicle treated mutants demonstrate impairments in social interaction in the social novelty assay while rapamycin treated mutants improved preference for social novelty. n≥10 per group. ns, p >0.05; **, p<0.01; ***, p<0.001; two way ANOVA, Bonferroni's post hoc analysis.

Figure S24

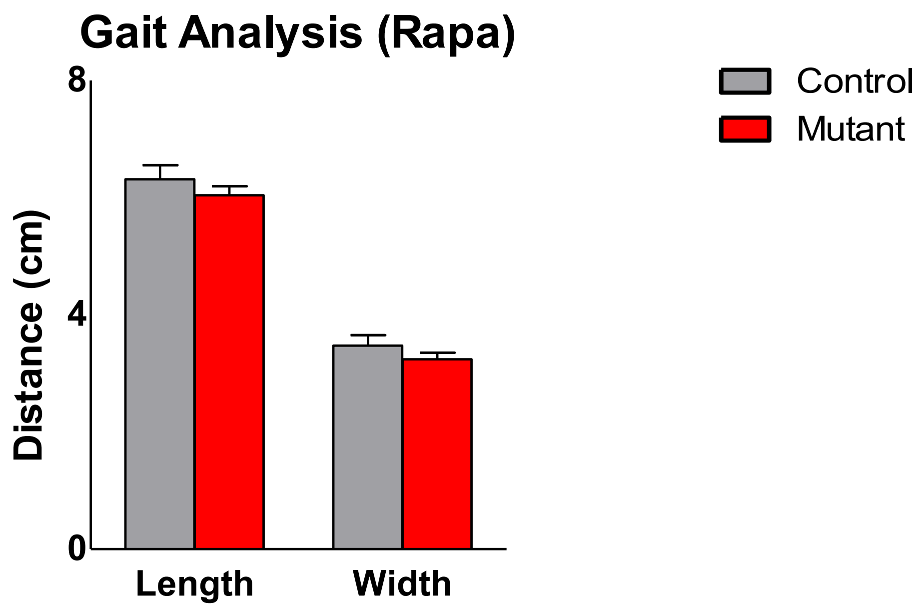

Figure S24. Rapamycin treated mutants did not demonstrate gait ataxia with comparable stride length and width when compared with controls. n≥7 per group. $p > 0.05$, two way ANOVA, Bonferroni's post hoc analysis.

Figure S25

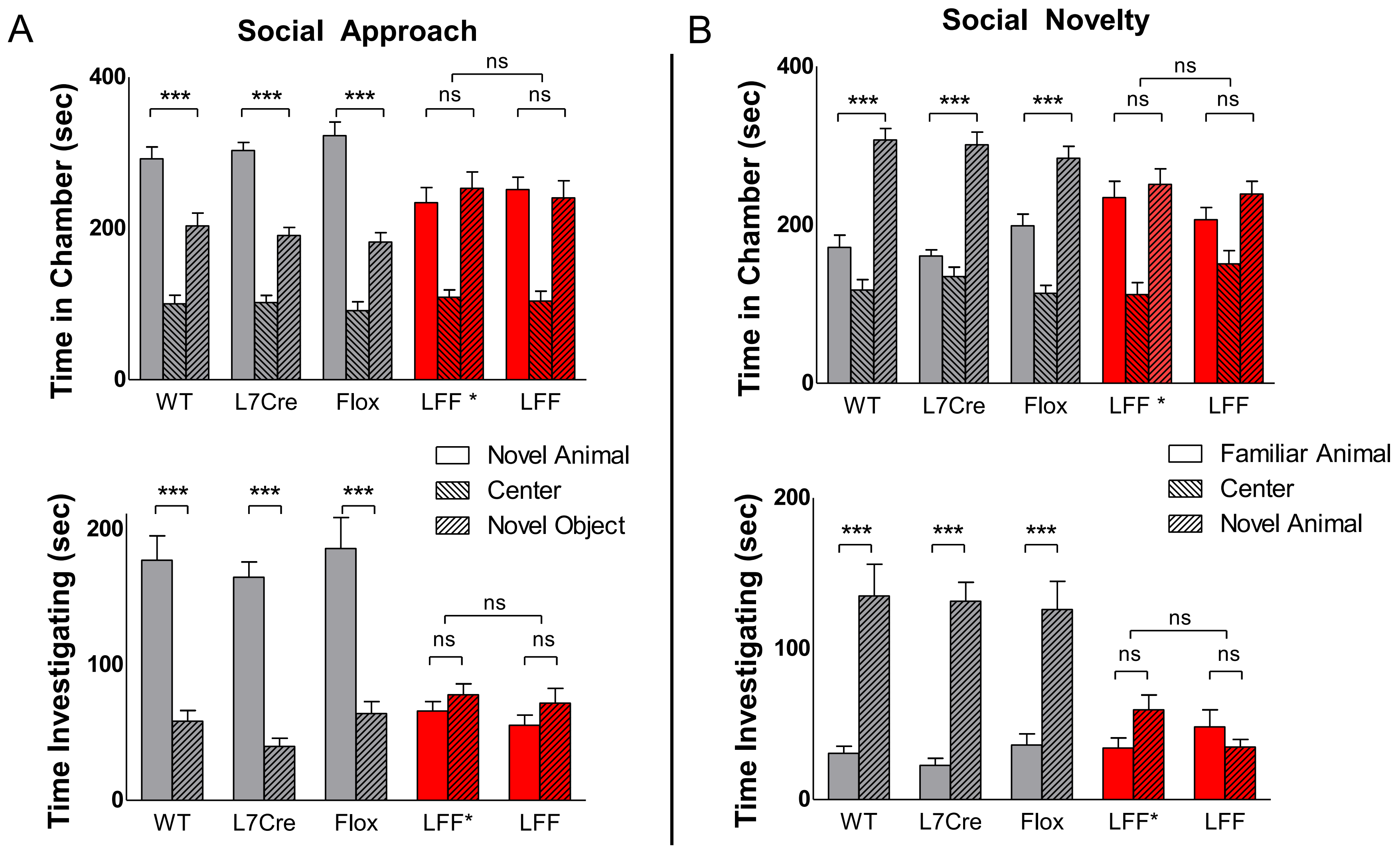

Figure S25. *L7^{Cre};Tsc1$^{flox/flox}$* (LFF) mutants did not differ significantly from a cohort of animals that included a small % of germline deletion (*L7Cre;Tsc1flox/-*) in one *Tsc1* allele (LFF*) in **A.** social approach or **B.** social novelty assays. n≥11 per group. ns, p>0.05; ***, p<0.001, two way ANOVA, Bonferroni's post hoc analysis.

Figure S26

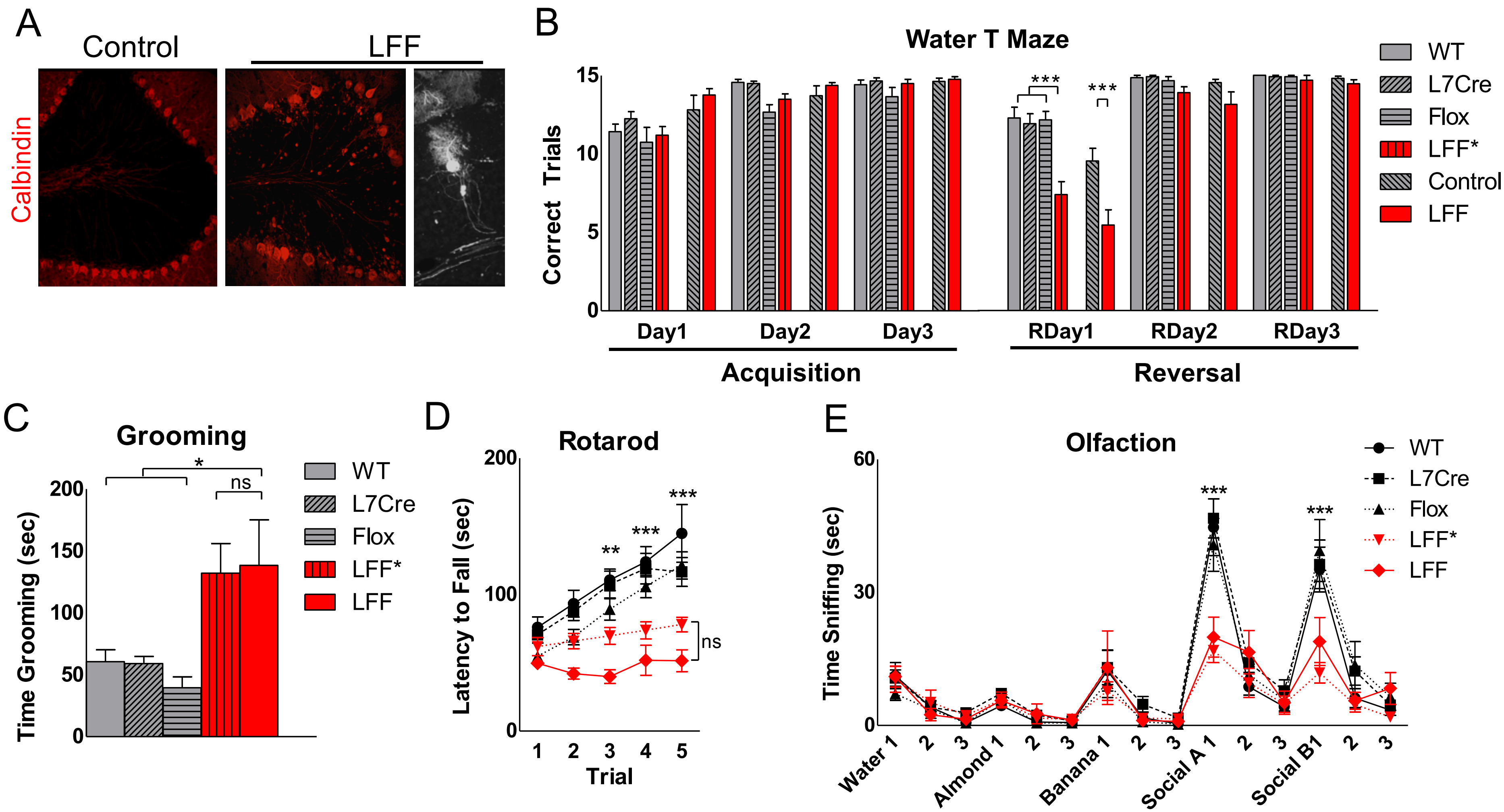

Figure S26. *$L7^{Cre}$;$Tsc1^{flox/flox}$* (LFF) mutants and a cohort of animals includng a small percentage of germline deletion in one allele (*$L7^{Cre}$;$Tsc1^{flox/-}$* (LFF*)) displayed similar **A.** pathology (Calbindin stain, gray scale on right) and abnormalities in **B.** reversal learning (RDay = Reversal Day, n≥8 per group), **C.** rotarod (n≥6 per group), **D.** grooming (n≥10 per group), and **E.** olfaction (n≥8 per group). No significant differences between LFF and LFF* cohorts are seen except with water T maze. Here, controls and LFF from new cohort *both* demonstrated worsened performance with reversal as compared to previous cohorts; however, LFF mutants demonstrate significantly worse performance than controls (ns, $p>0.05$; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$ two way ANOVA, Bonferroni's post hoc).

Supplemental Table S1

Behavioral Test	Compared Groups	n	p value	f	Statistical Test
Social Interaction					
Social Approach					
Time in Chamber	Novel Animal vs. Novel Object			f(2,200)=120.3	two way ANOVA, Bonferroni's post hoc
WT		13	**<0.001**		
L7Cre		19	**<0.001**		
Flox		17	**<0.001**		
Het		28	>0.05		
Mutant		29	>0.05		
Time spent in Chamber with Novel Animal *	Controls vs. Het/Mutant		Vs. Het/Mutant	f(4,200)=1.27	two way ANOVA, Bonferroni's post hoc
WT			**<0.05/<0.05**		
L7Cre			**<0.05/<0.05**		
Flox			**<0.001/<0.01**		
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,89) = 120.8	two way ANOVA, Bonferroni's post hoc
WT			**<0.001**		
L7Cre			**<0.001**		
Flox			**<0.001**		
Het			>0.05		
Mutant			>0.05		
Time interacting with novel animal *	Control vs. Het/Mutant		Vs. Het/Mutant	f(4,89) = 8.4	two way ANOVA, Bonferroni's post hoc
WT			**<0.001/<0.001**		
L7Cre			**<0.001/<0.001**		
Flox			**<0.001/<0.001**		
* Controls (WT, L7Cre, Flox)			>0.05		All comparisons between WT, L7Cre, and Flox were not significant
Social Novelty					
Time in Chamber	Familiar animal vs. Novel Animal			f(2,172) = 94.1	two way ANOVA, Bonferroni's post hoc
WT		11	**<0.001**		
L7Cre		16	**<0.001**		

Flox		15	**<0.001**		
Het		24	>0.05		
Mutant		26	>0.05		
Time spent in Chamber with Novel Animal *	Controls vs. Het/Mutant		Het/Mutant	f(4,172) = 0.54	two way ANOVA, Bonferroni's post hoc
WT			**<0.05/ <0.05**		
L7Cre			**<0.05**/ **<0.01**		
Flox			>0.05/ **<0.05**		
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,82) = 112.8	two way ANOVA, Bonferroni's post hoc
WT			**<0.001**		
L7Cre			**<0.001**		
Flox			**<0.001**		
Het			>0.05		
Mutant			>0.05		
Time interacting with novel animal *	Control vs. Het/Mutant		Het/Mutant	f(4,82) = 4.2	two way ANOVA, Bonferroni's post hoc
WT			**<0.001/<0.001**		
L7Cre			**<0.001/<0.001**		
Flox			**<0.001/<0.001**		
* Controls (WT, L7Cre, Flox)			>0.05		All comparisons between WT, L7Cre, and Flox were not significant
Locomotion between Chambers					
Habituation	Control vs. Het/Mutant	18/23	Het/Mutant	f(4,468) = 2	two way ANOVA, Bonferroni's post hoc
Chamber 1					
WT		12	>0.05/>0.05		
L7Cre		15	>0.05/>0.05		
Flox		13	>0.05/>0.05		
Chamber 3					
WT			>0.05/>0.05		
L7Cre			>0.05/>0.05		
Flox			>0.05/>0.05		
Social Approach	Control vs. Het/Mutant	25/23	Het/Mutant		
Chamber 1					
WT		13	>0.05/>0.05		
L7Cre		15	>0.05/>0.05		
Flox		13	>0.05/>0.05		
Chamber 3					
WT			>0.05/>0.05		

L7Cre			>0.05/>0.05		
Flox			>0.05/>0.05		
Social Novelty	Control v. Het/Mutant	18/18	Het/Mutant		
Chamber 1					
WT		11	>0.05/>0.05		
L7Cre		14	>0.05/>0.05		
Flox		11	>0.05/>0.05		
Chamber 3					
WT			>0.05/>0.05		
L7Cre			>0.05/>0.05		
Flox			>0.05/>0.05		
Male v. Female Interaction in Open Field	Control vs. Mutant		0.015		paired student's t-test, 2 tailed
	Control	10			
	Mutant	11			
Gait					
Length	Control vs. Het/Mutant		Het/Mutant	$F(4,44) = 8.7$	one way ANOVA, Bonferroni's post hoc
WT		7	>0.05/ **<0.01**		
L7Cre		9	>0.05/ **<0.001**		
Flox		6	>0.05/ **<0.001**		
Het		10			
Mutant		13			
Width	Control vs. Het/Mutant		Het/Mutant	$F(4,44) = 8.1$	
WT			>0.05/ **<0.01**		
L7Cre			>0.05/ **<0.001**		
Flox			>0.05/ >0.05		
Open Field					
Distance	Control vs. Het/Mutant		Het/Mutant	$f(4,672) = 0.45$	two way ANOVA, Bonferroni's post hoc
WT		10	>0.05/>0.05		
L7Cre		12	>0.05/>0.05		
Flox		8	>0.05/>0.05		
Het		13			
Mutant		10			
Controls (WT, L7Cre, Flox)			>0.05		All comparisons between WT, L7Cre, and Flox were not significant
Olfaction				$f(4,960) = 17.5$	two way ANOVA, Bonferroni's post hoc
Het		10			

Mutant		26			
Nonsocial Odors	Control vs. Het/Mutant		Het/Mutant		
WT		8	>0.05/>0.05		
L7Cre		14	>0.05/>0.05		
Flox		11	>0.05/>0.05		
Social Odors A, B	Control vs. Het/Mutant		Het/Mutant		
WT			**<0.001/<0.001**		
L7Cre			**<0.001/<0.001**		
Flox			**<0.001/<0.001**		
Grooming	Control vs. Het/Mutant		Het/Mutant	f(4,74) = 8.3	one way ANOVA, Bonferroni's post hoc
WT		13	**<0.05/<0.01**		
L7Cre		16	**<0.05/<0.01**		
Flox		13	**<0.01/<0.001**		
Het		14			
Mutant		25			
Water T Maze					
No. of Correct Responses				f(4,235) = 4	two way ANOVA, Bonferroni's post hoc
Het		11			
Mutant		23			
Day1-3	Control vs. Het		Day1/2/3		
WT		9	>0.05/>0.05/>0.05		
L7Cre		15	>0.05/>0.05/>0.05		
Flox		16	>0.05/>0.05/>0.05		
Reversal Day 1-3					
WT			>0.05/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			**<0.05**/>0.05/>0.05		
Day1-3	Control vs. Mutant		Day1/2/3		
WT			>0.05/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			>0.05/>0.05/>0.05		
Reversal Day 1-3					
WT			**<0.001**/>0.05/>0.05		
L7Cre			**<0.001**/>0.05/>0.05		
Flox			**<0.001**/>0.05/>0.05		
No. of Trials prior to 5 Consecutive				f(4,250) = 3.2	two way ANOVA, Bonferroni's post hoc

Correct Responses					
Day1-3	Control vs. Het		Day1/2/3		
WT			>0.05/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			>0.05/>0.05/>0.05		
Reversal Day 1-3					
WT			>0.05/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			>0.05/>0.05/>0.05		
Day1-3	Control vs. Mutant		Day1/2/3		
WT			>0.05/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			>0.05/>0.05/>0.05		
Reversal Day 1-3					
WT			**<0.001**/>0.05/>0.05		
L7Cre			**<0.001**/>0.05/>0.05		
Flox			**<0.001**/>0.05/>0.05		
Controls (WT, L7Cre, Flox)			>0.05		All comparisons between WT, L7Cre, and Flox were not significant for all days
Vocalizations	Vs. Het	P5:48 P7:52 P10:49 P12:38	P5/P7/P10/P12	f(4, 484) = 7	two way ANOVA, Bonferroni's post hoc
WT		P5:13 P7:21 P10:28 P12:14	>0.05/>0.05/**<0.001**/>0.05		
L7Cre		P5:21 P7:26 P10:11 P12:9	>0.05/>0.05/>0.05/>0.05		
Flox		P5:8 P7:15 P10:14 P12:11	>0.05/>0.05/**<0.05**/>0.05		
	Vs. Mutant	P5:35 P7:43 P10:32 P12:18	P5/P7/P10/P12		
WT			>0.05/**<0.05**/**<0.001**/>0.05		
L7Cre			>0.05/**<0.01**/**<0.05**/>0.05		
Flox			>0.05/**<0.05**/**<0.01**/>0.05		
Rotarod				f(4, 244) =	two way ANOVA, Bonferroni's

				72.3	post hoc
Het		16			
Mutant		19			
	WT vs.				
Trial 1	Het/Mutant	7	>0.05/ >0.05		
2			>0.05/ **<0.05**		
3			>0.05/ **<0.001**		
4			>0.05/ **<0.001**		
5			>0.05/ **<0.001**		
	L7Cre vs.	17			
Trial 1	Het/Mutant		>0.05/ >0.05		
2			>0.05/ **<0.05**		
3			>0.05/ **<0.001**		
4			>0.05/ **<0.001**		
5			>0.05/ **<0.001**		
	Flox vs.	15			
Trial 1	Het/Mutant		>0.05/ >0.05		
2			>0.05/ >0.05		
3			>0.05/ **<0.05**		
4			>0.05/ **<0.01**		
5			>0.05/ **<0.001**		

Supplemental Table S2

Behavioral Test	Compared Groups	n	p value	f	Statistical Test
Gait (Rapa)				f(1,28) = 1	two way ANOVA, Bonferroni's post hoc
Control		7			
Mutant		9			
Length	Control vs. Mutant		>0.05		
Width	Control vs. Mutant		>0.05		
Social Interaction					
Social Approach					
Time in Chamber	Novel animal vs. novel object			f(2,86) = 94.8	two way ANOVA, Bonferroni's post hoc
Control (Veh)		10	**<0.001**		
Mutant (Veh)		14	**>0.05**		
Control (Rapa)		13	*<0.001*		
Mutant (Rapa)		14	**<0.001**		
Time spent in Chamber with Novel Animal				f(3,86) = 0.26	
Control (Veh) vs. Mutant (Veh)			**<0.01**		
Control (Rapa) vs. Mutant (Rapa)			**>0.05**		
Control (Veh) vs. Control (Rapa)			>0.05		
Mutant (Veh) vs. Mutant (Rapa)			**<0.05**		
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,41) = 105.9	
Control (Veh)			**<0.001**		
Mutant (Veh)			>0.05		
Control (Rapa)			**<0.001**		
Mutant (Rapa)			**<0.001**		
Time interacting with novel animal				f(3,41) = 5.8	

Control (Veh) vs. Mutant (Veh)			**<0.001**		
Control (Rapa) vs. Mutant (Rapa)			**>0.05**		
Control (Veh) vs. Control (Rapa)			>0.05		
Mutant (Veh) vs. Mutant (Rapa)			**<0.001**		
Social Novelty					
Time in Chamber	Novel animal vs. novel object			f(2,129) = 96	two way ANOVA, Bonferroni's post hoc
Control (Veh)		10	**<0.001**		
Mutant (Veh)		14	>0.05		
Control (Rapa)		13	**<0.001**		
Mutant (Rapa)		14	**<0.01**		
Time spent in Chamber with Novel Animal				f(3,129) = 0.02	
Control (Veh) vs. Mutant (Veh)			>0.05		
Control (Rapa) vs. Mutant (Rapa)			>0.05		
Control (Veh) vs. Control (Rapa)			>0.05		
Mutant (Veh) vs. Mutant (Rapa)			>0.05		
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,41) = 70.8	
Control (Veh)			**<0.001**		
Mutant (Veh)			>0.05		
Control (Rapa)			**<0.001**		
Mutant (Rapa)			**<0.001**		
Time interacting with novel animal				f(3,41) = 1.2	
Control (Veh) vs. Mutant (Veh)			**<0.001**		
Control (Rapa) vs. Mutant (Rapa)			**>0.05**		
Control (Veh) vs. Control (Rapa)			>0.05		
Mutant (Veh) vs. Mutant (Rapa)			**<0.001**		

Water T Maze				
Control (Veh)	9			
Mutant (Veh)	12			
Control (Rapa)	10			
Mutant (Rapa)	13			
No. of Correct Responses			f(3,120) = 3.6	two way ANOVA, Bonferroni's post hoc
Day1-3		Day1/2/3		
Control (Veh) vs. Mutant (Veh)		**>0.05/>0.05/>0.05**		
Control (Rapa) vs. Mutant (Rapa)		**>0.05/>0.05/>0.05**		
Control (Veh) vs. Control (Rapa)		>0.05/>0.05/>0.05		
Mutant (Veh) vs. Mutant (Rapa)		*<0.05*/>0.05/>0.05		
Reversal Day1				
Control (Veh) vs. Mutant (Veh)		**<0.001**		
Control (Rapa) vs. Mutant (Rapa)		**>0.05**		
Control (Veh) vs. Control (Rapa)		>0.05		
Mutant (Veh) vs. Mutant (Rapa)		*<0.001*		
No. of Trials prior to 5 Consecutive Correct Responses			f(3,123) = 3.3	two way ANOVA, Bonferroni's post hoc
Day1-3				
Control (Veh) vs. Mutant (Veh)		**>0.05/>0.05/>0.05**		
Control (Rapa) vs. Mutant (Rapa)		**>0.05/>0.05/>0.05**		
Control (Veh) vs. Control (Rapa)		*<0.01*/>0.05/>0.05		
Mutant (Veh) vs. Mutant (Rapa)		*<0.001*/>0.05/>0.05		
Reversal Day1				
Control (Veh) vs. Mutant (Veh)		**<0.001**		
Control (Rapa) vs. Mutant (Rapa)		**>0.05**		
Control (Veh) vs. Control (Rapa)		>0.05		
Mutant (Veh) vs. Mutant (Rapa)		*<0.001*		

Rotarod				f(3,156)=10.8	two way ANOVA, Bonferroni's post hoc
Control (Veh)			9		
Mutant (Veh)			17		
Control (Rapa)			8		
Mutant (Rapa)			9		
	VEH				
	Trial 1	Control vs. Mutant	>0.05		
	2		>0.05		
	3		>0.05		
	4		**<0.01**		
	5		**<0.05**		
	Rapa				
	Trial 1	Control vs. Mutant	>0.05		
	2		>0.05		
	3		>0.05		
	4		>0.05		
	5		>0.05		
	Trial 1	Mutant (Veh) vs. Mutant (Rapa)	>0.05		
	2		**<0.001**		
	3		**<0.001**		
	4		**<0.001**		
	5		**<0.001**		

Supplemental Table S3

Behavioral Test	Compared Groups	n	p value	f	Statistical Test
Social Interaction					
Social Approach					
Time in Chamber	Novel Animal vs. Novel Object			f(2,144)=133.8	two way ANOVA, Bonferroni's post hoc
WT		13	**<0.001**		
L7Cre		19	**<0.001**		
Flox		17	**<0.001**		
LFF*		16	>0.05		
LFF		13	>0.05		
Time spent in Chamber with Novel Animal *	LFF* vs. LFF		>0.05	f(4,144)=1.27	
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,64) = 98.6	two way ANOVA, Bonferroni's post hoc
WT			**<0.001**		
L7Cre			**<0.001**		
Flox			**<0.001**		
LFF*			>0.05		
LFF			>0.05		
Time interacting with novel animal *	LFF* vs. LFF		>0.05	f(4,64) = 7.8	
Social Novelty					
Time in Chamber	Familiar Animal vs. Novel Animal			f(2,126) = 88.3	two way ANOVA, Bonferroni's post hoc
WT		11	**<0.001**		
L7Cre		16	**<0.001**		
Flox		15	**<0.001**		
LFF*		13	>0.05		
LFF		13	>0.05		
Time spent in Chamber with Novel Animal *	LFF* vs. LFF		>0.05	f(4,126) = 1.23	
Time in Close Interaction	Novel Animal vs. Novel Object			f(1,59) = 85.5	two way ANOVA, Bonferroni's post hoc
WT			**<0.001**		
L7Cre			**<0.001**		
Flox			**<0.001**		

LFF*			>0.05		
LFF			>0.05		
Time interacting with novel animal *	LFF* vs. LFF		>0.05	f(4,59) = 4.9	
Olfaction				f(4,756) = 3.2	two way ANOVA, Bonferroni's post hoc
LFF		8			
Nonsocial Odors	Vs. LFF				
WT		8	>0.05		
L7Cre		14	>0.05		
Flox		11	>0.05		
LFF*		18	>0.05		
Social Odors	Vs. LFF		Odor A, B		
WT			**<0.001/<0.01**		
L7Cre			**<0.001/<0.001**		
Flox			**<0.001/<0.001**		
LFF*			**>0.05**		
		10			one way ANOVA,
Grooming	Vs. LFF			F(4,74)=6.6	Bonferroni's post hoc
WT		13	**<0.05**		
L7Cre		16	**<0.05**		
Flox		13	**<0.01**		
LFF*		15	**>0.05**		
Water T Maze					
No. of Correct Responses				F(5,295) = 4.9	Two way ANOVA, Bonferroni's post hoc
LFF		13			
Day1-3	Vs. Control	11	Day1/2/3		
WT		8	>0.05/ >0.05/>0.05		
L7Cre		12	>0.05/>0.05/>0.05		
Flox		12	*<0.05*/>0.05/>0.05		
LFF*		10	>0.05/>0.05/>0.05		
Reversal Day 1-3					
WT			*<0.01*/>0.05/>0.05		
L7Cre			*<0.01*/>0.05/>0.05		
Flox			*<0.01*/>0.05/>0.05		
LFF*			*<0.05*/>0.05/>0.05		
Day1-3	Vs. LFF		Day1/2/3		
WT			*<0.05*/>0.05/>0.05		
L7Cre			>0.05/>0.05/>0.05		
Flox			*<0.001*/>0.05/>0.05		
LFF*			*<0.01*/>0.05/>0.05		
Control			**>0.05**/>0.05/>0.05		

Reversal Day 1-3					
WT			*<0.001*/>0.05/>0.05		
L7Cre			*<0.001*/>0.05/>0.05		
Flox			*<0.001*/>0.05/>0.05		
LFF*			*<0.05*/>0.05/>0.05		
Control			**<0.001**/>0.05/>0.05		
Rotarod				F(4, 196) = 9.3	Two way ANOVA, Bonferroni's post hoc
LFF		6			
Trial 1	WT vs. LFF	7	>0.05		
2			*<0.01*		
3			*<0.001*		
4			*<0.001*		
5			*<0.001*		
Trial 1	L7Cre vs. LFF	17	>0.05		
2			*<0.01*		
3			*<0.001*		
4			*<0.001*		
5			*<0.001*		
Trial 1	Flox vs. LFF	15	>0.05		
2			>0.05		
3			*<0.01*		
4			*<0.001*		
5			*<0.001*		
Trial 1	LFF* vs. LFF	13	**>0.05**		
2			**>0.05**		
3			**>0.05**		
4			**>0.05**		
5			**>0.05**		