Supplementary Information:

Table S1: List of strains

Strain Name	Mutant	CGC Strain	Outcross Status	Figure No.
BAB6013	*flp-33 (gk1037)*	VC2422	Outcrossed 3X	1
BAB6014	*flp-8 (*pk360)	PT501	Outcrossed 3X	1
BAB6015	*flp-15 (*gk1186)	VC2504	Outcrossed 3X	1-6
BAB6016	*flp-17 (*ok3587)	RB2575	Outcrossed 3X	1
BAB6017	*nlp-49 (*gk546875*)*	From William Schafer Lab		1
BAB6018	*flp-2 (*ok3351*)*	VC2591	Outcrossed 3X	1
BAB6019	*flp-6 (*ok3056*)*	VC2324	Outcrossed 3X	1
BAB6020	*flp-20 (*pk1596*)*	PT505	Outcrossed 3X	1
BAB6021	*flp-9 (*ok2730*)*	RB2067	Outcrossed 3X	1
BAB6022	*ins-3 (*ok2488*)*	RB1915	Outcrossed 3X	1
BAB6023	*pdf-1 (*tm1996*)*	LSC27	Outcrossed 3X	1
BAB6024	*flp-5 (*gk3123*)*	Obtained from VC3280	Outcrossed 3X	1
BAB6025	*flp-3 (*ok3265*)*	VC2497	Outcrossed 3X	1
BAB6026	*nlp-11 (*syb530*)*	PHX530	Outcrossed 3X	1
BAB6027	*nlp-8 (*ok1799*)*	VC1309	Outcrossed 3X	1
BAB6028	*ins-4 (*ok3534*)*	RB2544	Outcrossed 3X	1
BAB6029	*nlp-3 (*ok2688*)*	RB2030	Outcrossed 3X	1
BAB6030	*nlp-14 (*ok1517*)*	VC1108	Outcrossed 3X	1
BAB6031	*nlp-15 (*ok1512*)*	VC1063	Outcrossed 3X	1
BAB6032	*flp-12 (*ok2409*)*	RB1863	Outcrossed 3X	1
BAB6033	*nlp-18 (*ok1557*)*	RB1372	Outcrossed 3X	1
BAB6034	*flp-7 (*ok2625*)*	RB1990	Outcrossed 3X	1
BAB6001	*npr-3 (*ind6001*)*	This study	Outcrossed 3X	4,5
BAB6037	*flp-15; npr-3*	This study		4
BAB6038	*cat-2* (e1112)	CB1112	Outcrossed 3X	6
BAB6039	*flp-15; cat-2*	This study		6

INF512	*flp-15*(gk1186) III; gnaIs1 IV	From Monika Scholz lab		3
BAB6002	IndEx6002 [*Pflp-15*::FLP-15cDNA :: T2A :: GFP ; *flp-15*]	This study		2, 3
BAB6003	IndEx6003 [*Pflp-15*::GFP]	This study		3
BAB6004	IndEx6004 [*Pflp-15*::GFP; *Pgur-3*::mCherry]	This study		3
BAB6005	IndEx6005 [P*npr-3*::NPR-3gDNA::GFP; *npr-3*]	This study		4
BAB6006	IndEx6006 [*Pnpr-3*::GFP]	This study		5
BAB6007	IndEx6007 [*Pnpr-3*::GFP; *Pdat-1*::mCherry]	This study		5
BAB6008	IndEx6008 [*Pnpr-3::GFP; Pnlp-12*::mCherry]	This study		5
BAB6009	IndEx6009 [*Pflp-15*::FLP-15cDNA::T2A::GFP; *npr-3*] *(*FLP-15 O/E in *npr-3* mutants)	This study		4
BAB6010	IndEx6010 [*Pdat-1*::NPR-3gDNA::mCherry; *npr-3*]	This study		5
BAB6011	IndEx6006 [*Pnlp-12*::NPR-3gDNA::mCherry; *npr-3*]	This study		5
BAB6012	IndEx6006 [*Pgur-3*::FLP-15cDNA :: T2A :: GFP ; *flp-15*]	This study		3
BAB6042	IndEx60042 [*Pflp-15*::HisCl1:: SL2 ::GFP]	This study		3

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5 **Table S2: List of plasmids**

Plasmid	Construct	Backbone
pBAB6001	*Pflp-15*::FLP-15cDNA::T2A::GFP	pPD95.75
pBAB6002	*Pgur-3*::FLP-15cDNA::T2A::GFP	pPD95.75
pBAB6003	*Pflp-15*::GFP	pPD95.75
pBAB6004	*Pgur-3*::mCherry	pPD49.26
pBAB6005	*Pnpr-3*::NPR-3gDNA::GFP	pPD95.75

pBAB6006	*Pnpr-3::GFP*	pPD95.75
pBAB6007	*Pdat-1*::mCherry	pPD49.26
pBAB6008	*pnlp-12*::mCherry	pPD49.26
pBAB6009	*Pdat-1*::NPR-3gDNA::mCherry	pPD49.26
pBAB6010	*Pnlp-12*::NPR-3gDNA::mCherry	pPD49.26
pBAB6042	*Pflp-15*::HisCl1:: SL2 ::GFP	Plasmid backbone gifted by Dr. Abhishek Bhattacharya

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8 **Table S3: List of primers**

Genotyping and cloning primers			
Gene	**Sequence (5'-3')**	**Primer Name**	**Comments**
flp-21	TCTGATGCGTTTACAGTCGG	USB01	External Forward
	GATAACAGAAATTTGTGCAGAGATCG	USB02	External Reverse
	GCAACCGTTTATCCAAATCGGAGAG	USB03	Internal Reverse
pdf-1	AATGTATTGACACTGCTGACTGC	USB04	External Forward
	CCTTGTGATTTTCCAGGTTATACAAACT	USB05	External Reverse
	CCTATTCCTGAGGTCGCAGTTGAT	USB06	Internal Reverse
flp-6	TGGCTTTTGACTCAGGTTAGGATC	USB07	External Forward
	GCACTTTTTCTCTTTTCCATTGGCA	USB08	External Reverse
	TCCGAAACGCATATACGCTGATTTAC	USB09	Internal Reverse

flp-12	GATCTTGAAAATAGTGTGCCTCGTTTTC	USB10	External Forward
	GTCCTCATCGAGCTCGATCTTTTTGA	USB11	External Reverse
	CTATCTGCTCTTTTCCTCGTCCTTCT	USB12	Internal Reverse
ins-1	TAGTTATATGGCGTGCGCTCATTTC	USB13	External Forward
	CAAACTTTAAAAGTGACAACATCCATTTGGT	USB14	External Reverse
	GCTAAAAGGGTTGTTGTGAGACGTGAT	USB15	Internal Reverse
flp-2	GATCTTGAAAATAGTGTGCCTCGTTTTC	USB16	External Forward
	GTCCTCATCGAGCTCGATCTTTTTGA	USB17	External Reverse
	CTATCTGCTCTTTTCCTCGTCCTTCT	USB18	Internal Reverse
flp-1	GTCCTCGTCAAGCACGTC	USB19	External Forward
	CTCGATGCTCTCCACCATGG	USB20	External Reverse
	AACCGGCTTTCTTTCCCAGCG	USB21	Internal Reverse
nlp-15	GGCAAAGACGGCAAAGTTTAGTTAACAA	USB24	External Forward
	GTCCAGCCAGTGAATCGAAAG	USB25	External Reverse
	CTGGACTTTGCTCAAAAACCGTTAG	USB26	Internal Reverse
flp-10	AACAATTCAATTTGCCACGTCATCAA	USB27	External Forward
	CAAACAAAAAAGCATTGGGATGTG	USB28	External Reverse
	TGACGCTTCTCCGATGCGACTT	USB29	Internal Reverse

ins-3	GCAGATTCATCAGAAGACCTTTCGCAT	USB30	External Forward
	GACCTAATTCTGTACTCTGCTGTGGTT	USB31	External Reverse
	GCTGCAAGTCTTATGCGTAACTGGAT	USB32	Internal Reverse
nlp-1	GCTCCACCCTTTGTTTACATATTC	USB39	External Forward
	ATTCAGAAGCGGAAAGAGCATG	USB40	External Reverse
	CAATTGTGTCCTCCCCCTAAAG	USB41	Internal Reverse
ins-22	CTTCAGGATCACGTGAAAAGTCTG	USB46	External Forward
	ACGACTTCCAATTTTGCGAGTATG	USB47	External Reverse
	TCGGTGATGCTTGGATACTCTG	USB48	Internal Reverse
nlp-3	GAATCGAAAGACCCTGGAAAACTTG	USB49	External Forward
	GCTAGCTTCATCATCAACTGACTG	USB50	External Reverse
	CCACGGATCAGTAAACCGGATAC	USB51	Internal Reverse
nlp-18	CTCCCCCAACAATCCATGATTTCC	USB52	External Forward
	GTGAAGTGGAATCGGATGATCGAC	USB53	External Reverse
	CTCAAACCTCCAATTTCCGAGTTC	USB54	Internal Reverse
ins-4	TGAAACCCCACCGAAAGAATTCTG	USB 58	External Forward
	GAGACGGCAAAAAATGGCAAAAAC	USB 59	External Reverse
	TTGATAAAAAAGACAACCGTCCCTC	USB 60	Internal Reverse

nlp-49	CAAGTCGCTAACATTCACATCATGT	USB61	External Forward
	TGGAGCTTCAATTTGTTGTGGAG	USB62	External Reverse
	CTTCCGGGAGAAAGTAAACTGACA	USB63	Internal Reverse
flp-33	CAATTTCCTCCCGCAAACAATAG	USB66	External Forward
	TAGTATAAAAGCTGTGCAGCCAG	USB67	External Reverse
	AGATTTAGGCTTAGGCTTAGGCTC	USB68	Internal Reverse
flp-15	CAGTGAGTCCGAAATTTTAAACCTGA	USB69	External Forward
	AGCATTCTAAAATTGCAGATTACGAC	USB70	External Reverse
	ACTGTGCTGCATGTGTTTCTATG	USB71	Internal Reverse
flp-17	ATGTGCCGACTGAAAGAAGAG	USB72	External Forward
	TGGGAATTTTAACAGGGGGTTG	USB73	External Reverse
	TTCATTTTTAGGGGTCTCACAGTC	USB74	Internal Reverse
flp-9	CTCTTGTCCATACGCATTTCCTC	USB75	External Forward
	TGATGACATCATTCAAAGTCACGAG	USB76	External Reverse
	GCACATTTTCGGAATTGGGGAG	USB77	Internal Reverse
flp-16	GAATTCAGGGCGATCCAGTGTC	USB99	External Forward
	CATATCTCATCGGTGTCGATTTAAGAG	USB100	External Reverse
	TCGATGACTTTTTCCTTCCATTTTTG	USB101	Internal Reverse

flp-7	CTGTTGCTTGGTCTTGTGCAATC	USB102	External Forward
	CGAGATCAGGCTTTTCTGTAGCTG	USB103	External Reverse
	CAAAACGGACCATCGATGATCTC	USB104	Internal Reverse
flp-33	CGAGCGAACCATGAAATTGTGTTC	USB105	External Forward
	CACACAGTATTTACGCATTCCTG	USB106	External Reverse
	GTAATGTGGAAGCGGTCTACTG	USB107	Internal Reverse
flp-5	CATCATCTCTAGTTCAGCTCCCAAC	USB108	External Forward
	TGTAATGCAGTGTGTACTCAGTCAC	USB109	External Reverse
	GGAAAGAATGGGTCAAAGTGCATC	USB110	Internal Reverse
flp-12	GTTAAGTAGCGATGTGTGAAGTTCTC	USB111	External Forward
	GAATTGGTGTCGTCGTGCTAAG	USB112	External Reverse
	GAGCAACTCGATCATTTCTCAATTG	USB113	Internal Reverse
npr-3	GAGAAGGCTCGCTGACATTAATG	USB114	External Forward
	CGATAGTCGTTTTCAGCAATTGTG	USB115	External Reverse
	GAAACGTGCCGATTCGAATGTTG	USB116	Internal Reverse
nlp-11	GTCCTCACCATTCCCCTAGG	USB120	External Forward
	GAATAGGAAGAGGGCGGAGG	USB121	External Reverse
	TCTGATCGACGCTGGAAAGA	USB122	Internal Reverse

nlp-12	CATGCTCATCCTCGTATTCGTG	NLP-12_EF	External forward
	GTCTGCGTCTCTAACATGTTGAC	NLP-12_ER	External reverse
	CAAAGAACTCTGCGTCTCAACTC	NLP-12_IR	Internal reverse
P*flp-15*	CACAAGCTTCAATCAATATAGCCGGAAATGCCA	UB13	HindIII
	ACCAGGATCCGTATGTGGGAGACCTTCTTCCA	UB14	BamHI
flp-15 cDNA	ACCAGGATCCTGGAAGAAGGTCTCCCACATAC	UB15	BamHI
	CACAGGGCCCATTTCATAGAAACACATGCAGCAC	UB16	XmaI
P*gur-3*	ATATGCATGCACATCTCATTGGTTGATTTGATC	UB25	SphI
	CTATGGATCCGAAAACGTGACTGACTAACAC	UB26	BamHI
P*npr-3*	TGTGAAGCTTCTTAATACTGTCCGTCTGCAAG	UB33	HindIII
	CACACCCGGGTCAAAAATTCCAGAAGAGGAGAAC	UB34	XmaI
npr-3 gDNA	TCATCCCGGGATCCAAAATGGAGGGTGGTC	UB35	XmaI
	ACACGGTACCTCTAACAACCCGGTAGAATCATC	UB36	KpnI
P*dat-1*	ATCTGCATGCTGCCACCGATTTGTACAAATG	UB43	SphI
	CTATGGATCCGGCTAAAAATTGTTGAGATTCGAG	UB44	BamHI
flp-15	TGCTACACTTGCAGATTACGAC	IM05	qPCR
	TTACTGGTACCACGACGCGAC	IM06	
tba-1	CAGTGCGGATCTCATCAACAACAG	VB389	qPCR
	GAACTATGCCATCAGACCAACAAGC	VB389	

Supplementary figure legends

Figure S1: (A) Illustration of the protocol for screening the phenotype. A single young adult *C. elegans* was gently picked using an eyelash with halocarbon oil and placed on a plate without food to remove residual food by allowing it to crawl for 1 minute. The animals was then transferred to an assay plate and 2 minutes were allowed for the worm to adapt, this was followed by recording the locomotion for 5 minutes (local search). After remaining on the same plate for 25 minutes, a second 5-minute recording was taken (global search). (B) Violin plots showing quantification of number of body-bends/reversal during local search in neuropeptide mutants. In this plot, each dot corresponds to the number body-bends/reversal observed per 5 minutes from a single *C. elegans*. Statistical significance was determined using One-way ANOVA with Tukey test for multiple comparisons, "**"or "****" indicate p-values less than 0.01, or 0.0001, respectively. The absence of "*" indicates not significantly different from WT control animals.

Figure S2: (A) Illustration of the *flp-15* (*gk1186*) mutation which is a 708 base pair deletion that eliminates the entire third exon, which codes for all three isoforms of the FLP-15 neuropeptide. This likely results in a null mutation that eliminates *flp-15*. (B) Quantification of velocity in WT and *flp-15* mutants. In WT *C. elegans* the velocity increases significantly after the transition from local to global search. In *flp-15* mutants the velocity during local and global search is not significantly different**.** Each dot on the plots corresponds to the number of spontaneous reversals observed per 5 minutes from a single animal. Statistical significance was determined using Two- ANOVA with Tukey test for multiple comparisons, "**"or "****" indicate p-values less than 0.01, or 0.0001, respectively and "ns" stands for non-Significant.

Figure S3: (A) FLP-15 gene is expressed in the tail neurons apart from the I2 neuron in the head. (B) Schematic of chemogenetic silencing using histamine-gated chloride channel. In the absence of histamine (left), neurons expressing HisCl1 remain active. Upon addition of histamine (right), the HisCl1 channel opens, allowing Cl^- influx, which hyperpolarizes and silences the neuron. Statistical significance was determined using Two- ANOVA with Tukey test for multiple comparisons, "**" indicates p-values less than 0.01.

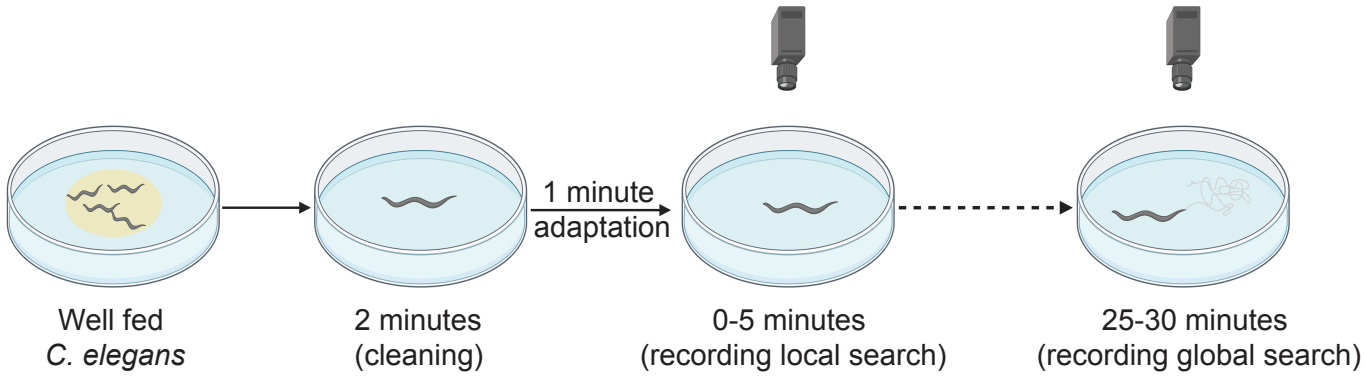
Figure S4: DNA gel image shows the *npr-3* deletion mutant generated by CRISPR Cas9. A 2816 bp region spanning exons 1 to 6 of the *npr-3* gene was deleted. The band corresponding to the mutant allele appears lower than the WT band confirming the deletion.

Figure S5: P*npr-3*::GFP shows expression in multiple head neurons and a tail neuron.

Figure S6: Quantification of reversals in *cat-2* mutants during local and global search indicating a temporal decay in reversal frequency in *cat-2* mutants during the transition from local to global search. Each dot on the plots corresponds to the number of spontaneous reversals observed per 5 minutes from a single animal. Statistical significance was determined using One-way ANOVA with Tukey test for multiple comparisons, "****" indicate p-values less than 0.0001.

Figure S1

A


1 minute
adaptation
Well fed
C. elegans
2 minutes
(cleaning)
0-5 minutes
(recording local search)
25-30 minutes
(recording global search)

B

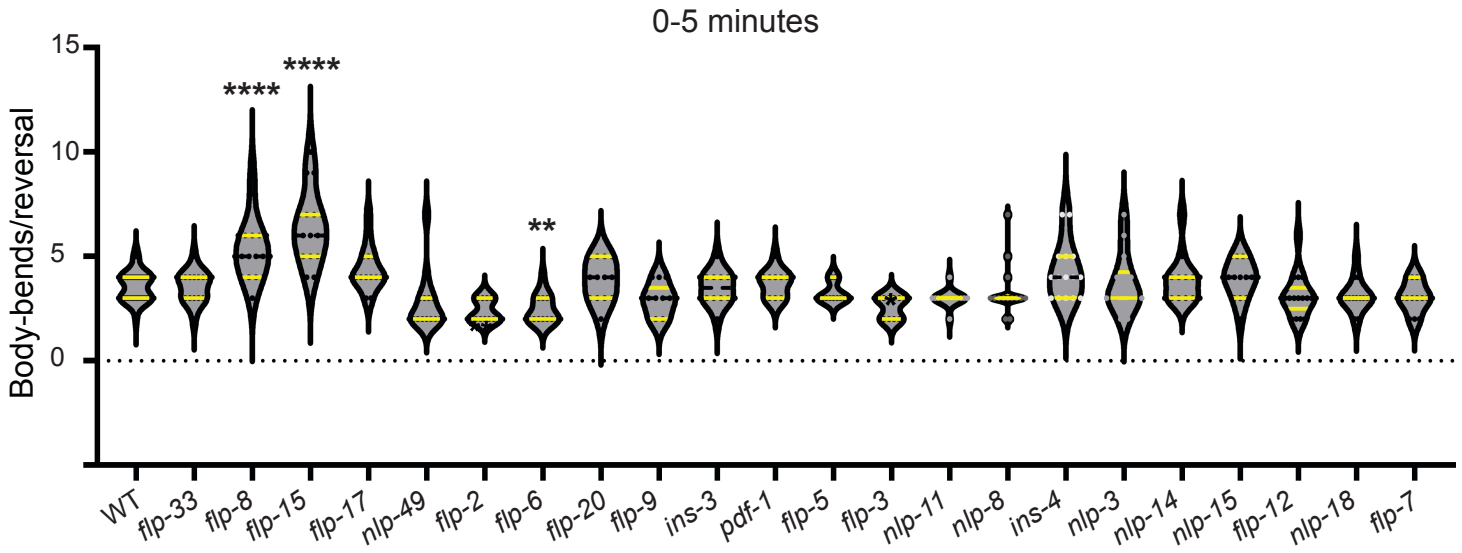
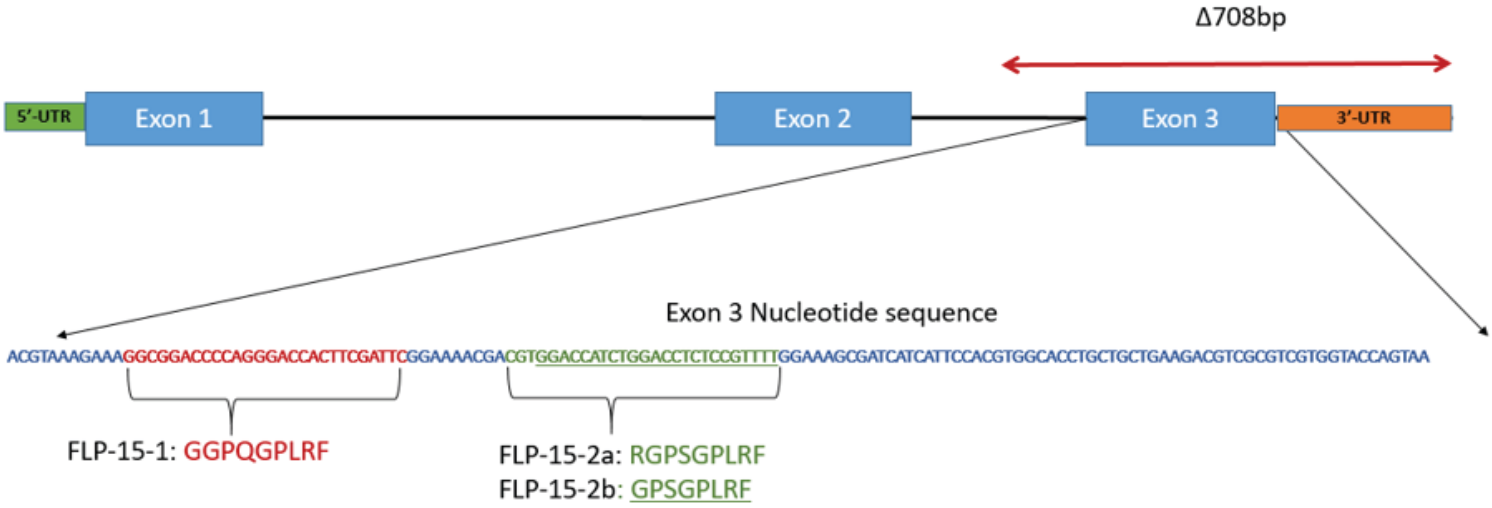

0-5 minutes
Body-bends/reversal
15
10
5
0
****
****
**
WT
flp-33
flp-8
flp-15
flp-17
nlp-49
flp-2
flp-6
flp-20
flp-9
ins-3
pdf-1
flp-5
flp-3
nlp-11
nlp-8
ins-4
nlp-3
nlp-14
nlp-15
flp-12
nlp-18
flp-7

Figure S2

A


Δ708bp
5'-UTR
Exon 1
Exon 2
Exon 3
3'-UTR
Exon 3 Nucleotide sequence
ACGTAAAGAAAGGCGGACCCCAGGGACCACTTCGATTCGGAAAACGACGTGGACCATCTGGACCTCTCCGTTTTGGAAAGCGATCATCATTCCACGTGGCACCTGCTGCTGAAGACGTCGCGTCGTGGTACCAGTAA
FLP-15-1: GGPQGPLRF
FLP-15-2a: RGPSGPLRF
FLP-15-2b: GPSGPLRF

B

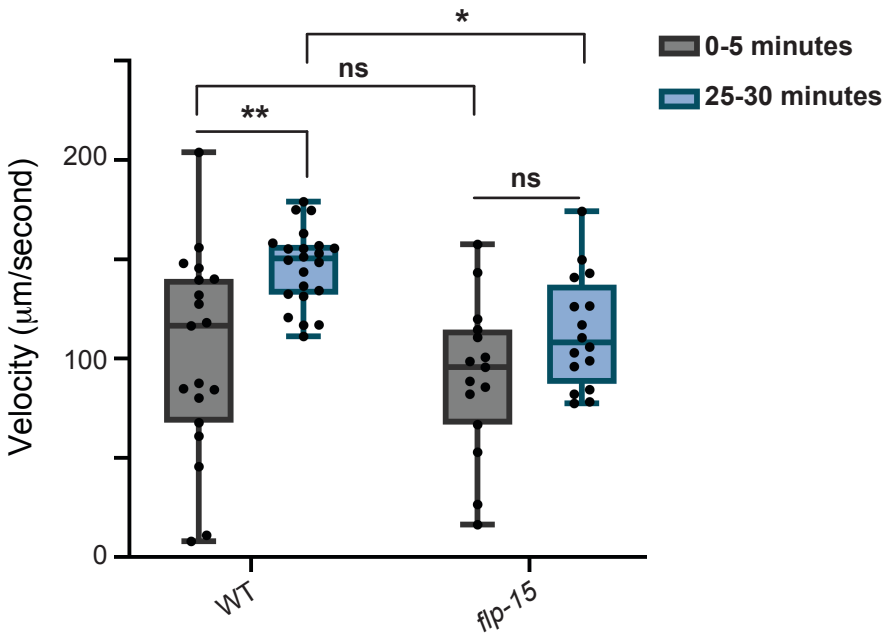

*
ns
**
ns
0-5 minutes
25-30 minutes
Velocity (µm/second)
200
100
0
WT
flp-15

Figure S3

A


Pflp-15::GFP
30 µm

B

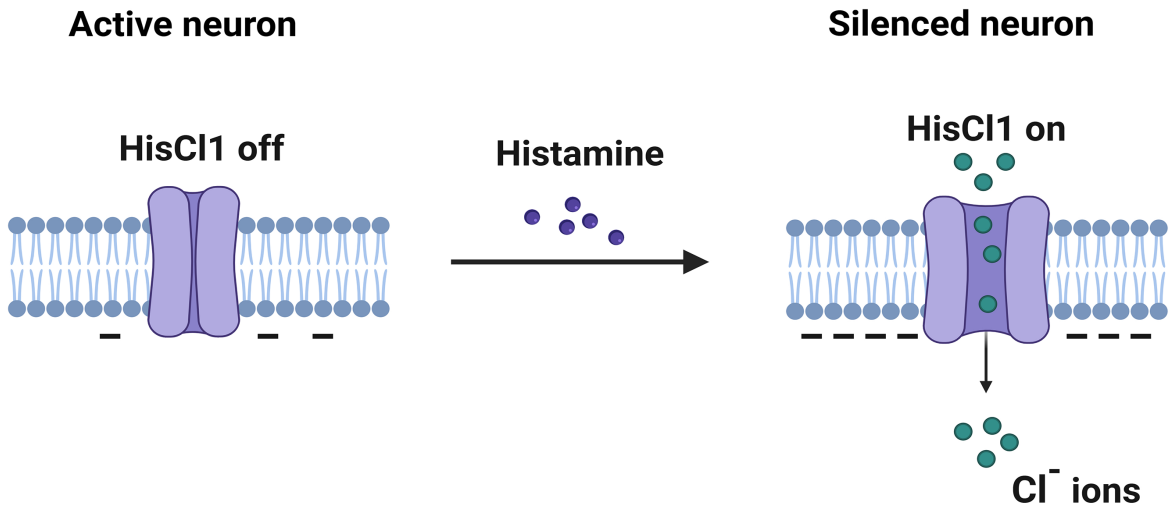

Active neuron
Silenced neuron
HisCl1 off
Histamine
HisCl1 on
Cl- ions

Figure S4

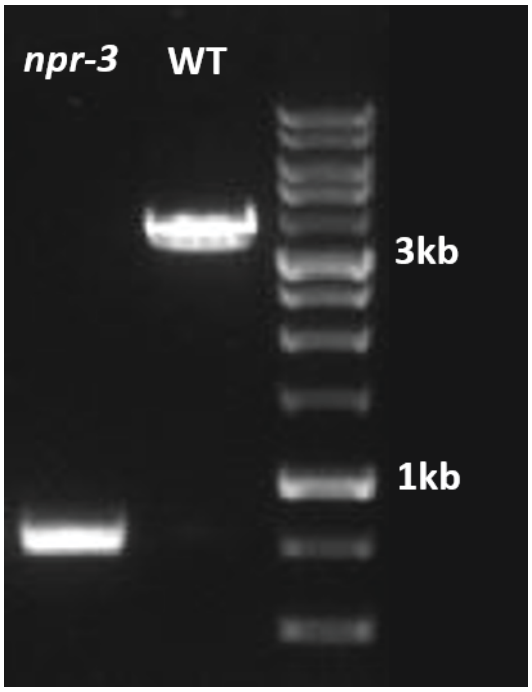


Figure S5

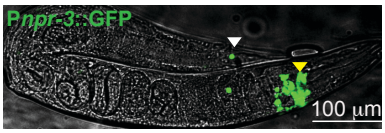
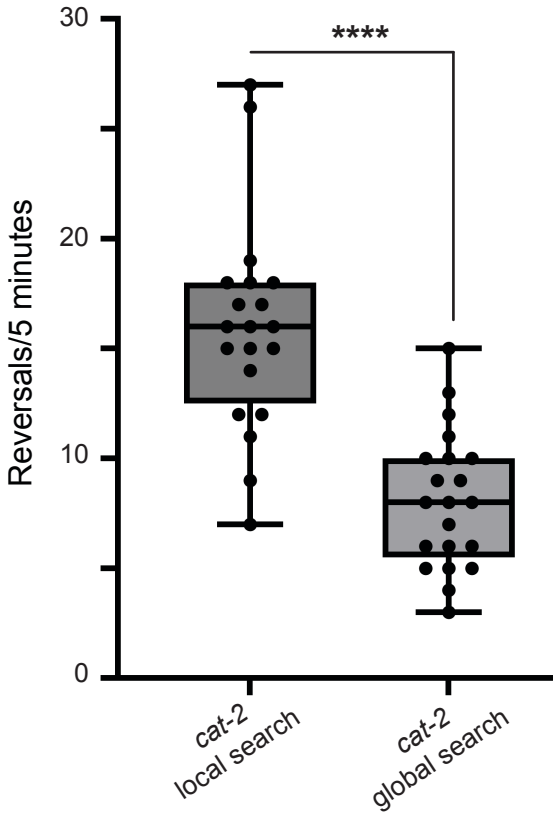


Figure S6


30
20
10
0
Reversals/5 minutes
****
cat-2
local search
cat-2
global search