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Supplemental information

Genetic and functional analysis reveals *TENM4* contributes to schizophrenia

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Supplemental Figures

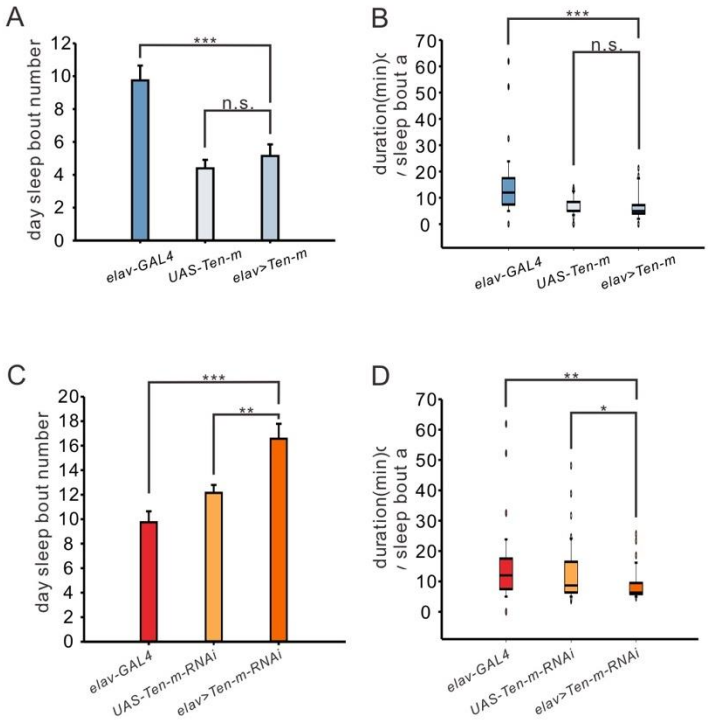

Figure S1. Day-sleep phenotypes in *Ten-m* overexpressed and down-expressed mutants, Related to Figure 2.

(A, B) Histograms of the number of day sleep bouts during day-time (A) and boxplots of the day sleep bout duration (B) for controls (*elav-GAL4* and *UAS-Ten-m*) and experimental flies (*elav>Ten-m*).

(C, D) Histograms of the number of day sleep bouts during day-time (C) and boxplots of the day sleep bout duration (D) for controls (*elav-GAL4* and *Ten-m-RNAi*) and experimental flies (*elav>Ten-m-RNAi)*.

Overexpression of *Ten-m* shows no difference with controls in day sleep time but shows difference in day sleep bout number and sleep bout duration. It suggested that over-expressing *Ten-m* would affect day-time sleep in *Drosophila* (Figure S1A, day sleep bout number: *elav-GAL4* vs *elav> Ten-m*, **p=0.004, *UAS-Ten-m* vs *elav>Ten-m*, p = 1.000; 1B, day sleep bout duration: *elav-GAL4* vs *elav> Ten-m*, ***p < 0.001, *UAS-Ten-m* vs *elav>Ten-m*, ***p < 0.001). Similarly, down-expression of *Ten-m*

performed decreased sleep bout number and decreased sleep bout duration, but no difference in day sleep time. We supposed that lack of *Ten-m* function would cause day sleep fragmentation in *Drosophila*. (Figure S1C, day sleep bout number: *elav-GAL4* vs *elav>Ten-m-RNAi*, ***p < 0.001, *UAS-Ten-m-RNAi* vs *elav>Ten-m-RNAi*, *p = 0.018; S1D, day sleep bout duration: *elav-GAL4* vs *elav>Ten-m-RNAi*, **p = 0.002, *UAS-Ten-m-RNAi* vs *elav>Ten-m-RNAi*, *p = 0.032).

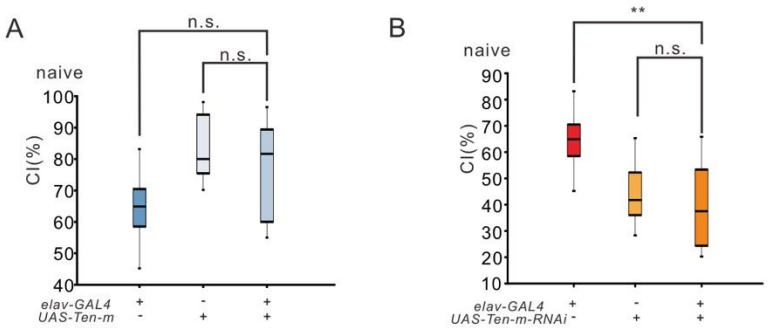

Figure S2. Aberrant expression of Ten-m has little effect on courtship behavior on naive files, Related to Figure 3.

(A) CIs of experimental naïve males (*elav>Ten-m*) compared with CIs of control naïve males (*elav-GAL4* and *UAS-Ten-m*), *elav-GAL4* vs e*lav>Ten-m*, p = 0.096, *UAS-Ten-m* vs *elav>Ten-m*, p = 0.649; It showed overexpressing Ten-m in all neurons would not affect courtship behavior.

(B) CIs of experimental naïve males (*elav>Ten-m-RNAi*) compared with CIs of control naïve males (*elav-GAL4* and *UAS-Ten-m-RNAi*, *elav-GAL4* vs *elav>Ten-m-RNAi*, **p = 0.002, *UAS-Ten-m-RNAi* vs *elav>Ten-m-RNAi*, p = 0.623); It suggested down-expressing *Ten-m* in all neurons had little effect on courtship behavior.

Supplemental Table S1 fly stocks, Related to Methods.

Fly Line	RRID	Collection
elav-GAL4	flybase_FBst0000458	Bloomington Stock Center
Mz19-GAL4	flybase_FBal0155865	Bloomington Stock Center
Mz699-GAL4	flybase_FBal0066073	Bloomington Stock Center
UAS-Ten-m	flybase_FBst0041569	Bloomington Stock Center
UAS-Ten-m-RNAi	flybase_FBtp0052660	Bloomington Stock Center
w;Cyo/sco;MKRS/Tb	flybase_FBst0305835	Kyoto Stock Center
LN1-GAL4	flybase_FBst0302813	Kyoto Stock Center

Supplemental Table S4 GO enrichment analysis of DEGs in *elav>Ten-m* group, Related to Figure 5.

Category	Term	Count	PValue	Gene ID
BP	GO:0009124~nucleoside monophosphate biosynthetic process	5	7.54E-04	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0020513, FBGN0013973
BP	GO:0009123~nucleoside monophosphate metabolic process	5	0.001009	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0020513, FBGN0013973
BP	GO:0034404~nucleobase, nucleoside and nucleotide biosynthetic process	7	0.00192	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0026602, FBGN0013973
BP	GO:0034654~nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process	7	0.00192	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0026602, FBGN0013973
BP	GO:0044271~nitrogen compound biosynthetic process	8	0.003064	FBGN0013972, FBGN0038172, FBGN0031148, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0026602, FBGN0013973
BP	GO:0006164~purine nucleotide biosynthetic process	6	0.003712	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0013973
BP	GO:0006163~purine nucleotide metabolic process	6	0.004388	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0013973
BP	GO:0009165~nucleotide biosynthetic process	6	0.008211	FBGN0013972, FBGN0038172, FBGN0000053, FBGN0028997, FBGN0020513, FBGN0013973
BP	GO:0009168~purine ribonucleoside monophosphate biosynthetic process	3	0.008546	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0009127~purine nucleoside monophosphate biosynthetic process	3	0.008546	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0009126~purine nucleoside monophosphate metabolic process	3	0.008546	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0009167~purine ribonucleoside monophosphate metabolic process	3	0.008546	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0009161~ribonucleoside monophosphate metabolic process	3	0.012917	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0009156~ribonucleoside monophosphate biosynthetic process	3	0.012917	FBGN0038172, FBGN0000053, FBGN0020513
BP	GO:0051130~positive regulation of cellular component organization	3	0.019466	FBGN0002948, FBGN0003687, FBGN0003317
BP	GO:0009113~purine base biosynthetic process	2	0.040902	FBGN0000053, FBGN0020513
BP	GO:0051294~establishment of spindle orientation	2	0.048882	FBGN0002948, FBGN0000147
BP	GO:0006189~'de novo' IMP biosynthetic process	2	0.048882	FBGN0000053, FBGN0020513
BP	GO:0031334~positive regulation of	2	0.04888	FBGN0002948, FBGN0003687

	protein complex assembly		2	
CC	GO:0019898~extrinsic to membrane	6	0.016691	FBGN0033697, FBGN0001253, FBGN0015035, FBGN0000473, FBGN0003861, FBGN0020392
CC	GO:0044427~chromosomal part	7	0.030156	FBGN0000588, FBGN0027259, FBGN0052438, FBGN0038979, FBGN0017414, FBGN0032105, FBGN0038612
CC	GO:0008074~guanylate cyclase complex, soluble	2	0.048166	FBGN0013972, FBGN0013973

Supplemental Table S5 GO enrichment analysis of DEGs in *elav>Ten-m-RNAi* group, Related to Figure 5.

Category	Term	Count	PValue	Gene ID
BP	GO:0009416~response to light stimulus	7	6.33E-04	FBGN0013972, FBGN0003068, FBGN0004435, FBGN0014396, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0009314~response to radiation	7	0.001202	FBGN0013972, FBGN0003068, FBGN0004435, FBGN0014396, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0009583~detection of light stimulus	5	0.001999	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0019731~antibacterial humoral response	4	0.002785	FBGN0010388, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0009582~detection of abiotic stimulus	5	0.002822	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0009581~detection of external stimulus	5	0.003853	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0042742~defense response to bacterium	5	0.005988	FBGN0010388, FBGN0035806, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0007601~visual perception	5	0.006301	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0050953~sensory perception of light stimulus	5	0.006624	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0000096~sulfur amino acid metabolic process	3	0.009274	FBGN0031148, FBGN0020385, FBGN0000565
BP	GO:0006952~defense response	7	0.009833	FBGN0010388, FBGN0052282, FBGN0031970, FBGN0035806, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0009617~response to bacterium	5	0.010038	FBGN0010388, FBGN0035806, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0007602~phototransduction	4	0.011786	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861
BP	GO:0045087~innate immune response	5	0.016125	FBGN0010388, FBGN0035806, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0050908~detection of light stimulus involved in visual perception	3	0.020402	FBGN0013972, FBGN0003861, FBGN0005614
BP	GO:0051606~detection of stimulus	5	0.021243	FBGN0013972, FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0007616~long-term memory	3	0.02229	FBGN0023479, FBGN0003068, FBGN0010399
BP	GO:0050962~detection of light stimulus involved in	3	0.02229	FBGN0013972, FBGN0003861, FBGN0005614

	sensory perception			
BP	GO:0009628~response to abiotic stimulus	7	0.025496	FBGN0013972, FBGN0003068, FBGN0004435, FBGN0014396, FBGN0019940, FBGN0003861, FBGN0005614
BP	GO:0050830~defense response to Gram-positive bacterium	3	0.026273	FBGN0010388, FBGN0035806, FBGN0010385
BP	GO:0015031~protein transport	8	0.027386	FBGN0031298, FBGN0033460, FBGN0000003, FBGN0035947, FBGN0053180, FBGN0014396, FBGN0035965, FBGN0035589
BP	GO:0009584~detection of visible light	3	0.028364	FBGN0013972, FBGN0003861, FBGN0005614
BP	GO:0045184~establishment of protein localization	8	0.030796	FBGN0031298, FBGN0033460, FBGN0000003, FBGN0035947, FBGN0053180, FBGN0014396, FBGN0035965, FBGN0035589
BP	GO:0019730~antimicrobial humoral response	4	0.037693	FBGN0010388, FBGN0041579, FBGN0004240, FBGN0010385
BP	GO:0007611~learning or memory	4	0.047813	FBGN0023479, FBGN0003068, FBGN0010399, FBGN0003861
CC	GO:0016028~rhabdomere	4	0.003215	FBGN0004435, FBGN0019940, FBGN0003861, FBGN0005614
CC	GO:0016027~inaD signaling complex	3	0.00492	FBGN0004435, FBGN0003861, FBGN0005614
CC	GO:0005887~integral to plasma membrane	7	0.031467	FBGN0003317, FBGN0031970, FBGN0035806, FBGN0010399, FBGN0003861, FBGN0003515, FBGN0005614
CC	GO:0031226~intrinsic to plasma membrane	7	0.033534	FBGN0003317, FBGN0031970, FBGN0035806, FBGN0010399, FBGN0003861, FBGN0003515, FBGN0005614
CC	GO:0019898~extrinsic to membrane	6	0.037689	FBGN0033979, FBGN0015037, FBGN0004435, FBGN0035790, FBGN0003861, FBGN0005614
CC	GO:0005576~extracellular region	12	0.040842	FBGN0010388, FBGN0052282, FBGN0029791, FBGN0023479, FBGN0035806, FBGN0041579, FBGN0086677, FBGN0032048, FBGN0004240, FBGN0031414, FBGN0010385, FBGN0053196
MF	GO:0046982~protein heterodimerization activity	4	0.017524	FBGN0003068, FBGN0014396, FBGN0003861, FBGN0005614
MF	GO:0008086~light-activated voltage-gated calcium channel activity	2	0.023354	FBGN0003861, FBGN0005614
MF	GO:0010461~light-activated channel activity	2	0.023354	FBGN0003861, FBGN0005614
MF	GO:0046983~protein dimerization activity	5	0.034715	FBGN0039051, FBGN0003068, FBGN0014396, FBGN0003861, FBGN0005614

Supplemental Table S6 GO enrichment analysis of overlapped significant DEGs in *elav>Ten-m* and *elav>Ten-m-RNAi* groups, Related to Figure 5.

Category	Term	Count	PValue	Gene ID
BP	GO:0022008~neurogenesis	5	0.079555	*NELF-E, USE1, DCTN4-P62, KMN1, INTS12*
CC	GO:0000795~synaptonemal complex	2	0.023697	*CONA, MLH1*
MF	GO:0016887~ATPase activity	3	0.088953	*CG1494, SMC5, MLH1*