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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 *elav*>*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

5.						
Catego	ço Term		PValue	Gene ID		
ry						
BP	GO:0009124~nucleoside	5	7 54E-04	FBGN0013972, FBGN0038172, FBGN0000053,		
	monophosphate biosynthetic process	5	7.542 04	FBGN0020513, FBGN0013973		
BP	GO:0009123~nucleoside	5	0.00100	FBGN0013972, FBGN0038172, FBGN0000053,		
	monophosphate metabolic process	9		FBGN0020513, FBGN0013973		
BP	GO:0034404-pucleobase_pucleoside		0.00192	FBGN0013972, FBGN0038172, FBGN0000053,		
	and nucleoside biosynthetic process	7		FBGN0028997, FBGN0020513, FBGN0026602,		
	and nucleonde biosynmetic process			FBGN0013973		
	GO:0034654~nucleobase, nucleoside,			FBGN0013972, FBGN0038172, FBGN0000053,		
BP	nucleotide and nucleic acid biosynthetic	e 7	0.00192	FBGN0028997, FBGN0020513, FBGN0026602,		
	process			FBGN0013973		
			0.00000	FBGN0013972, FBGN0038172, FBGN0031148,		
BP	GO:00442/1~nitrogen compound	8	0.00306	FBGN0000053, FBGN0028997, FBGN0020513,		
	biosynthetic process		4	FBGN0026602, FBGN0013973		
	GO:0006164~purine nucleotide		0.00371	FBGN0013972, FBGN0038172, FBGN0000053,		
BP	biosynthetic process	6	2	FBGN0028997, FBGN0020513, FBGN0013973		
	GO:0006163~purine nucleotide		0.00438	FBGN0013972, FBGN0038172, FBGN0000053,		
BP	metabolic process	6	8	FBGN0028997, FBGN0020513, FBGN0013973		
	GO:0009165~nucleotide biosynthetic		0.00821 1	FBGN0013972, FBGN0038172, FBGN0000053,		
BP	process	6		FBGN0028997, FBGN0020513, FBGN0013973		
	GO:0009168~purine ribonucleoside		0.00854			
BP	monophosphate biosynthetic process	3	6	FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0009127~purine nucleoside		0.00854			
BP	monophosphate biosynthetic process	3	6	FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0009126~purine nucleoside		0.00854			
BP	monophosphate metabolic process	3	6	FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0009167~purine ribonucleoside		0.00854 6			
BP	monophosphate metabolic process	3		FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0009161~ribonucleoside		0.01291			
BP	monophosphate metabolic process	3	7	FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0009156~ribonucleoside		0.01291			
BP	monophosphate biosynthetic process	3	7	FBGN0038172, FBGN0000053, FBGN0020513		
	GO:0051130~positive regulation of		0.01946			
BP	cellular component organization	3	6	FBGN0002948, FBGN0003687, FBGN0003317		
BP	GO:0009113~purine base biosynthetic		0.04090			
	process	2	2	FBGN0000053, FBGN0020513		
	GO:0051294~establishment of spindle		0.04888	FBGN0002948, FBGN0000147		
BP	orientation	2	2			
	GO:0006189~'de novo' IMP		0.04888	FBGN0000053, FBGN0020513		
BP	biosynthetic process	2	2			
BP	GO:0031334~nositive regulation of	2	0.04888	FBGN0002948, FBGN0003687		
	- stoss restriction of	4	0.01000			

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

	protein complex assembly		2	
CC GO:0019898~extr	CO 0010202	c	0.01669	FBGN0033697, FBGN0001253, FBGN0015035,
	GO.0019898~extrinsic to memorane	0	1	FBGN0000473, FBGN0003861, FBGN0020392
CC GO:0044427~chromoso		7	0.03015 6	FBGN0000588, FBGN0027259, FBGN0052438,
	GO:0044427~chromosomal part			FBGN0038979, FBGN0017414, FBGN0032105,
				FBGN0038612
CC	GO:0008074~guanylate cyclase	2	0.04816	ED (N0012072) ED (N0012072
	complex, soluble	2	6	FD0110013972, FD0110013973

Categor	Term	Coun t	PValue	Gene ID
<u>y</u>		ι		EBGN0013072 EBGN0003068 EBGN0004435
RP	GO:0009416~response to	7	6 33E-04	FBGN0014396 FBGN0019940 FBGN0003861
DI	light stimulus	,	0.552 01	FBGN0005614
				FBGN0013972, FBGN0003068, FBGN0004435,
ВР	GO:0009314~response to	7	0.001202	FBGN0014396, FBGN0019940, FBGN0003861,
	radiation			FBGN0005614
BP	GO:0009583~detection of	_		FBGN0013972, FBGN0004435, FBGN0019940,
	light stimulus	5	0.001999	FBGN0003861, FBGN0005614
	GO:0019731~antibacterial		0.000505	FBGN0010388, FBGN0041579, FBGN0004240,
BP	humoral response	4	0.002785	FBGN0010385
DD	GO:0009582~detection of	F	0.002822	FBGN0013972, FBGN0004435, FBGN0019940,
ВЬ	abiotic stimulus	5	0.002822	FBGN0003861, FBGN0005614
DD	GO:0009581~detection of	5	0.002852	FBGN0013972, FBGN0004435, FBGN0019940,
ВЬ	external stimulus	3	0.003833	FBGN0003861, FBGN0005614
RD	GO:0042742~defense	~	0.005088	FBGN0010388, FBGN0035806, FBGN0041579,
Dr	response to bacterium	5	0.003988	FBGN0004240, FBGN0010385
RD	GO:0007601~visual	5	0.006201	FBGN0013972, FBGN0004435, FBGN0019940,
DI	perception	5	0.000501	FBGN0003861, FBGN0005614
RD	GO:0050953~sensory	5	0.006624	FBGN0013972, FBGN0004435, FBGN0019940,
DI	perception of light stimulus	5	0.000024	FBGN0003861, FBGN0005614
RP	GO:0000096~sulfur amino	3	0.009274	FBGN0031148 FBGN0020385 FBGN0000565
Ы	acid metabolic process	5	0.009274	1 0010031140, 1 0010020303, 1 0010000303
	GO:0006952~defense		0.009833	FBGN0010388, FBGN0052282, FBGN0031970,
BP	response	7		FBGN0035806, FBGN0041579, FBGN0004240,
				FBGN0010385
BP	GO:0009617~response to	5	0.010038	FBGN0010388, FBGN0035806, FBGN0041579,
	bacterium			FBGN0004240, FBGN0010385
BP	GO:0007602~phototransdu	4	0.011786	FBGN0013972, FBGN0004435, FBGN0019940,
	ction			FBGN0003861
BP	GO:0045087~innate	5	0.016125	FBGN0010388, FBGN0035806, FBGN0041579,
	immune response			FBGN0004240, FBGN0010385
	GO:0050908~detection of			
BP	light stimulus involved in	3	0.020402	FBGN0013972, FBGN0003861, FBGN0005614
	visual perception			
BP	GO:0051606~detection of	5	0.021243	FBGN0013972, FBGN0004435, FBGN0019940,
	stimulus			FBGN0003861, FBGN0005614
BP	GO:0007616~long-term	3	0.02229	FBGN0023479, FBGN0003068, FBGN0010399
	memory			
BP	GO:0050962~detection of	3	0.02229	FBGN0013972, FBGN0003861, FBGN0005614
	light stimulus involved in			

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

sensory perception

BP	GO:0009628~response to		0.025496	FBGN0013972, FBGN0003068, FBGN0004435,
	GO:0009628~response to	7		FBGN0014396, FBGN0019940, FBGN0003861,
	abiotic stimulus			FBGN0005614
	GO:0050830~defense			
BP	response to Gram-positive	3	0.026273	FBGN0010388, FBGN0035806, FBGN0010385
	bacterium			
	CO:0015021 protein			FBGN0031298, FBGN0033460, FBGN0000003,
BP	transport	8	0.027386	FBGN0035947, FBGN0053180, FBGN0014396,
	transport			FBGN0035965, FBGN0035589
ВD	GO:0009584~detection of	3	0.028364	ERCN0013072 ERCN0003861 ERCN0005614
DI	visible light	5	0.028304	FBGN0013972, FBGN0003001, FBGN0003014
	GO:0045184~establishmen		0.030796	FBGN0031298, FBGN0033460, FBGN0000003,
BP	t of protein localization	8		FBGN0035947, FBGN0053180, FBGN0014396,
	t of protoin rocalization			FBGN0035965, FBGN0035589
RP	GO:0019730~antimicrobia	4	0.037693	FBGN0010388, FBGN0041579, FBGN0004240,
Di	l humoral response	·	0.037075	FBGN0010385
BP	GO:0007611~learning or	4	0.047813	FBGN0023479, FBGN0003068, FBGN0010399,
21	memory	·	01017012	FBGN0003861
CC	GO:0016028~rhabdomere	4	0.003215	FBGN0004435, FBGN0019940, FBGN0003861,
				FBGN0005614
CC	GO:0016027~inaD	3	0.00492	FBGN0004435, FBGN0003861, FBGN0005614
	signaling complex			
	GO:0005887~integral to		0.031467	FBGN0003317, FBGN0031970, FBGN0035806,
CC	plasma membrane	7		FBGN0010399, FBGN0003861, FBGN0003515,
				FBGN0005614
	GO:0031226~intrinsic to		0.033534	FBGN0003317, FBGN0031970, FBGN0035806,
CC	plasma membrane	7		FBGN0010399, FBGN0003861, FBGN0003515,
	60 0010000			FBGN0005614
CC	GO:0019898~extrinsic to	6	0.037689	FBGN0033979, FBGN0015037, FBGN0004435,
	memorane			FBGN0055790, FBGN0005801, FBGN0005014
	CO10005576 avtracellular			FBGN0010388, FBGN0052282, FBGN0029791,
CC	GO:0005576~extracentular	12	0.040842	FBGN0025479, FBGN0055800, FBGN0041579,
	region			FBG100080077, FBG100052048, FBG10004240,
	CO:0046082 mestoin			FBGN0031414, FBGN0010385, FBGN0055190
MF	betara dimenization activity	4	0.017524	FDGIN0005614
	CO:0008086 light activity			FDGIN0003014
ME	d voltage geted eslaium	2	0.022254	EDCN0002861 EDCN0005614
INIT	u vonage-gateu calcium	Z	0.025554	13GINUUU3001, 13GINUUU3014
	CO:0010461 light activate			
MF	d channel sofivity	2	0.023354	FBGN0003861, FBGN0005614
				EDCN0020051 EDCN0002060 EDCN0014206
MF	dimerization activity	5	0.034715	EBGN0003861 EBGN0005614
	dimenzation activity			LD010003901, LB010003014

and curve for an Alvin groups, Actuated to Figure of						
Category	Term	Count	PValue	Gene ID		
BP	GO:0022008~neurogenesis	5	0.079555	NELF-E, USE1, DCTN4-P62,		
		5		KMN1, INTS12		
CC	GO:0000795~synaptonemal complex	2	0.023697	CONA, MLH1		
MF	GO:0016887~ATPase activity	3	0.088953	CG1494, SMC5, MLH1		

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