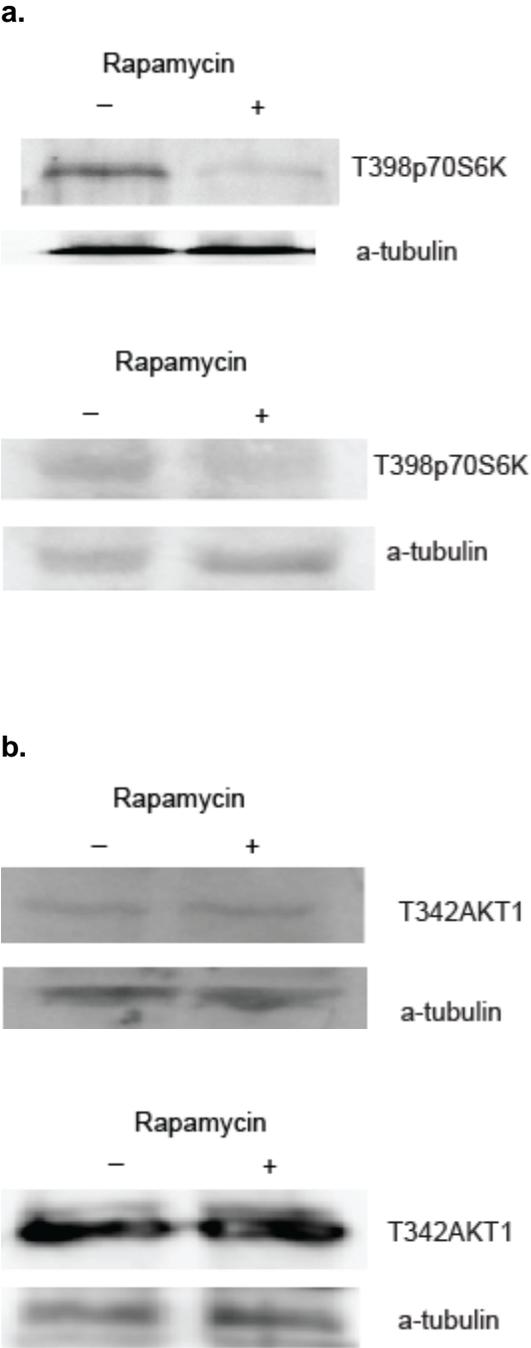


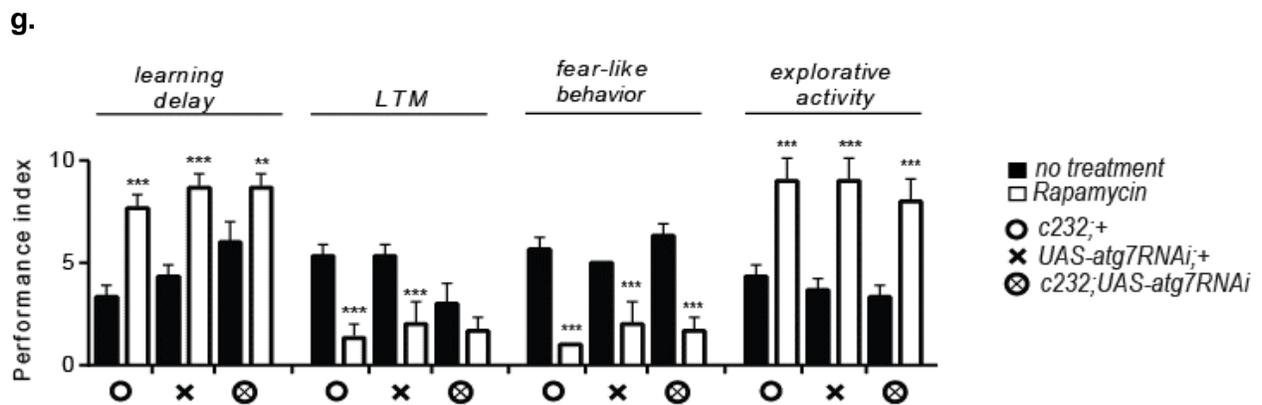
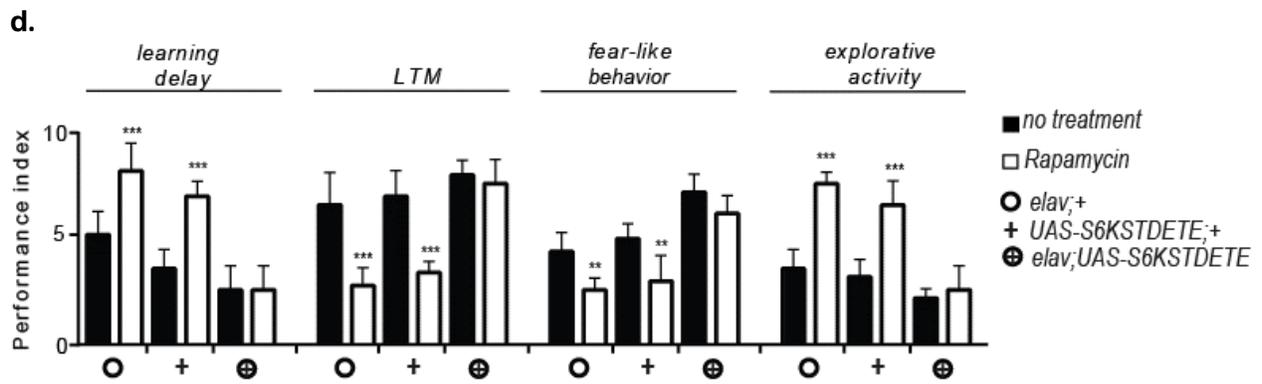
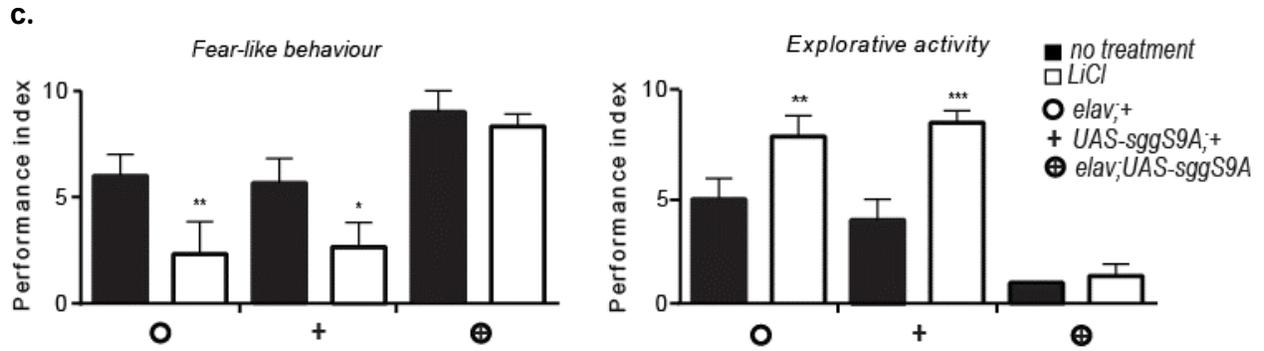
Table S1. List of transgenic flies used in the study.

Gal4 driver	Tissue specificity
<i>Elav^{c155}</i> (BDSC:458)	Nervous system
129Y (BDSC:30816)	Antennal nerves and subesophageal ganglia
GH146 (BDSC:3026)	Antennal lobes
OK107 (BDSC:854)	Mushroom bodies
C232 (BDSC:30828)	Ellipsoid bodies
C601 (BDSC:30844)	Protocerebrum
C205 (BDSC:30826)	Fan shaped body and subesophageal ganglia
<i>Nmdar2</i> (BDSC:46860)	NMDA receptor expressing cells
<i>Dilp2</i> (BDSC:37516)	Insulin-like peptide 2 expressing cells
R29H01 (BDSC:47343)	Prothoracic gland innervating cells
<i>Trh</i> (BDSC:38389)	Serotonergic cells
<i>ElavGS</i> (BDSC:43642)	Nervous system (mifepristone inducible)
<i>Sca</i> (BDSC:6479)	Epidermis
C929 (BDSC:25373)	Peptidergic cells
<i>5htr7</i> (by C. Nichols)	5HTR7 serotonin receptor expressing cells
UAS line	Effect on gene expression
UAS-SggS9A (BDSC:5255)	Constitutive expression
UAS-S6K ^{STDETE} (by L. Partridge)	Constitutive expression
UAS-5htr7 (by J. Dow)	Overexpression
UAS-atg1 (BDSC:51654)	Overexpression
UAS-gfpsert (BDSC:24463)	Overexpression
UAS-cd8rfp (BDSC:27392)	Overexpression
UAS-Epac1-camps (BDSC:25408)	Overexpression
UAS-sytegfp (BDSC:6925)	Overexpression
UAS-atg1RNAi (VDRC:16133)	Inhibition
UAS-sertRNAi (VDRC:100584)	Inhibition
UAS-5htr7RNAi (VDRC:104804)	Inhibition
UAS-atg7RNAi (VDRC:27432)	Inhibition
UAS-5htr1bRNAi (VDRC:110128)	Inhibition
UAS-nmdar2RNAi (VDRC:12187)	Inhibition
UAS-caspase3RNAi (VDRC:43028)	Inhibition
UAS-rutabagaRNAi (VDRC:5569)	Inhibition
UAS-pka ^{c1} RNAi (VDRC:31599)	Inhibition

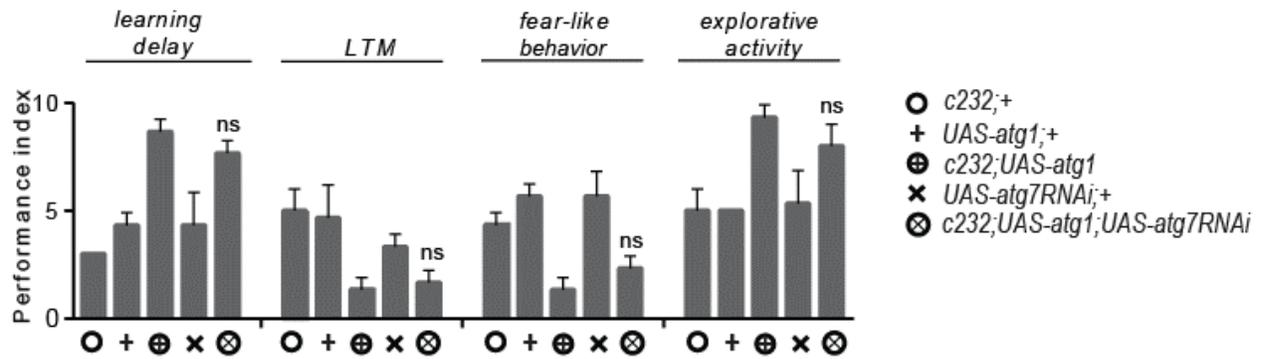
The *Gal4* and *UAS* transgenic *Drosophila* lines used in the study.

Figure S1. ATG7 is not required for rapamycin-induced behaviours.





h.



a) Acute rapamycin treatment (four days) of ten-day old female mated flies decreases phosphorylation of p70S6K at T398.

b) AKT1 phosphorylation at T342 in *Drosophila* heads is not affected by rapamycin feeding.

c) LiCl treatment (three-day feeding) induces similar to rapamycin treatment effects on behaviour, while constitutive GSK-3 β activation causes opposite to rapamycin treatment effects (n=3). Ten-day old mated female flies were used. For fear-like behaviour: $F(5, 12) = 18.87$, for explorative activity: $F(5, 12) = 51.27$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

d) Rapamycin treatment (four-days) affects cognition/behaviour via neuronal mTORC1 (n=5). Ten-day old mated female flies were used. For learning delay: $F(5, 24) = 24.40$, for LTM: $F(5, 24) = 22.60$, for fear-like behaviour: $F(5, 24) = 21.30$, for explorative activity: $F(5, 24) = 32.84$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

e) *elavGS;UAS-atg1RNAi* adults exhibited restricted loss of eyes' pigmentation in the absence of mifepristone.

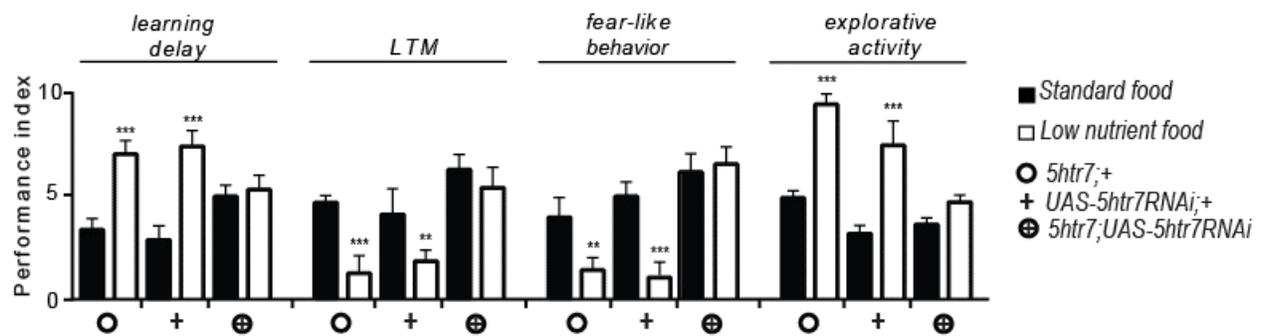
f) Mifepristone-induced neuronal *atg1* expression throughout development caused lethality. Very few death escapers had reduced size. Left side: *elavGS;UAS-atg1* male fed with normal food. Right side: *elavGS;UAS-atg1* male fed with mifepristone-enriched food.

g) RNAi of *atg7* does not blunt rapamycin effects on behaviour (n=3). Ten-day old flies were fed with rapamycin for four days. For learning delay: $F(5, 12) = 34.70$, for LTM: $F(5, 12) = 17.68$, for fear-like behaviour: $F(5, 12) = 48.17$, for explorative activity: $F(5, 12) = 33.33$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

h) Ellipsoid bodies-specific ATG7 is not required for *atg1*-induced behaviours (n=3). Three-day old flies were used. For learning delay: $F(4, 10) = 26.60$, for LTM: $F(4, 10) = 9.731$, for fear-like behaviour: $F(4, 10) = 21.75$, for explorative activity: $F(4, 10) = 12.96$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test, selected pairs: *c232;UAS-atg1* vs. *c232;UAS-atg1;UAS-atg7RNAi*.

*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$. Error bars represent s.e.m.

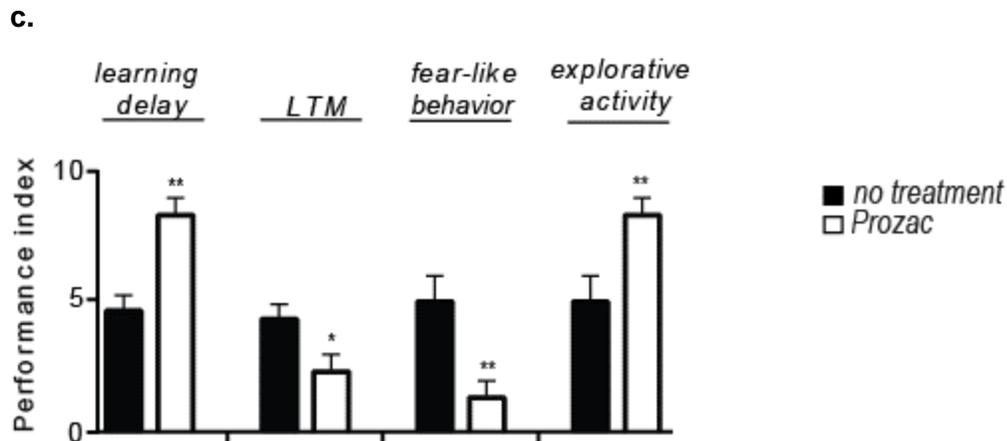
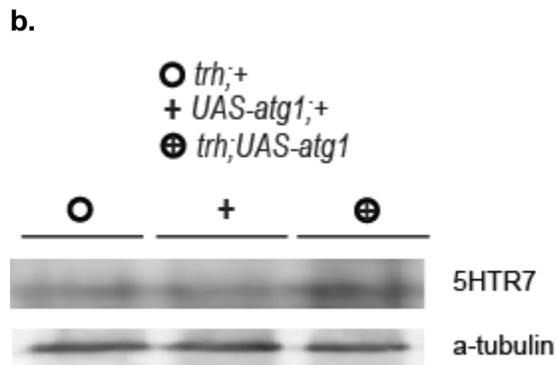
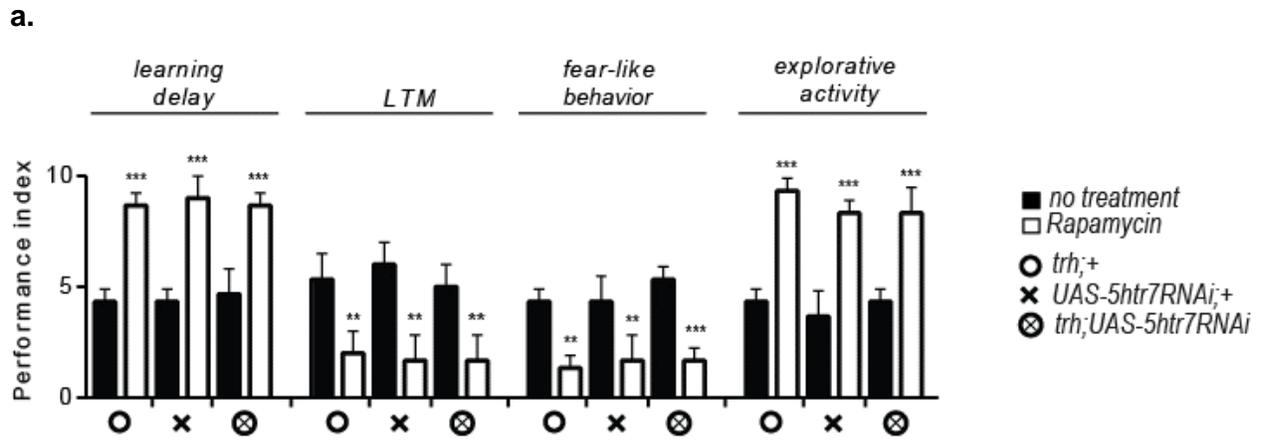
Figure S2. *5htr7* inhibition ameliorates low nutrient diet-evoked cognitive and behavioural effects.



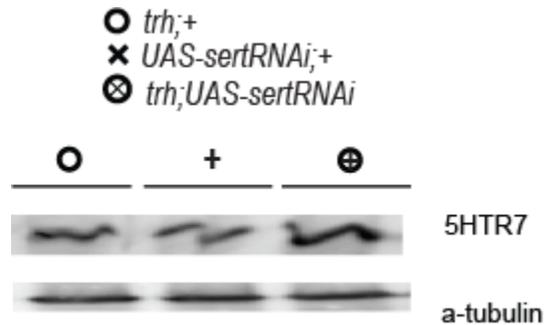
5htr7 inhibition ameliorates low nutrient diet-evoked cognitive and behavioural effects (n=5). Ten-day old flies were fed with low nutrient food for two days. For learning delay: $F(5, 24) = 21.19$, for LTM: $F(5, 24) = 8.02$, for fear-like behaviour: $F(5, 12) = 7.37$, for explorative activity: $F(5, 24) = 39.67$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$. Error bars represent s.e.m.

Figure S3. Serotonergic cells-specific and SERT inhibition increases 5HTR7 levels in *Drosophila* heads.



d.



a) Serotonin-producing cells-specific *5htr7RNAi* expression did not block rapamycin effects (n=3). Ten-day old flies were fed with rapamycin for four days. For learning delay: $F(5, 12) = 27.80$, for LTM: $F(5, 12) = 10.68$, for fear-like behaviour: $F(5, 12) = 13.73$, for explorative activity: $F(5, 12) = 28.88$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

b) *Trh;UAS-atg1* flies have increased expression of 5HTR7 in the heads. 3-day old flies were used.

c) Acute (two days) Prozac treatment (100 μ M) of ten-day old *W^{Dah}* flies induces similar to rapamycin treatment effects on behaviour and cognition (n=3). Individual comparisons by two-tailed Mann Whitney test.

d) Inhibition of serotonin transporter via RNAi increases 5HTR7 levels in *Drosophila* heads. 3-day old flies were used.

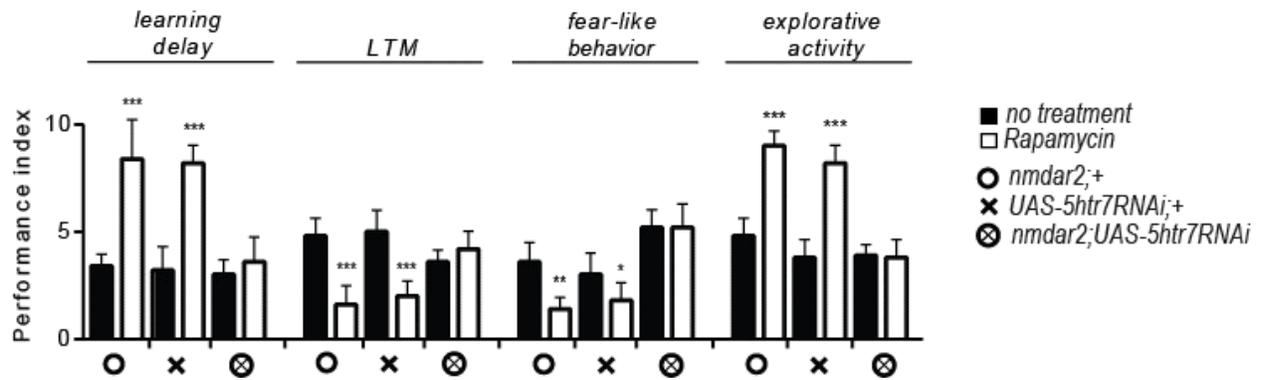
*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$. Error bars represent s.e.m.

Figure S4. RNAi inhibition of *5htr7* at NMDAR2-expressing cells ameliorates rapamycin effects on behaviour/cognition.

a.



b.





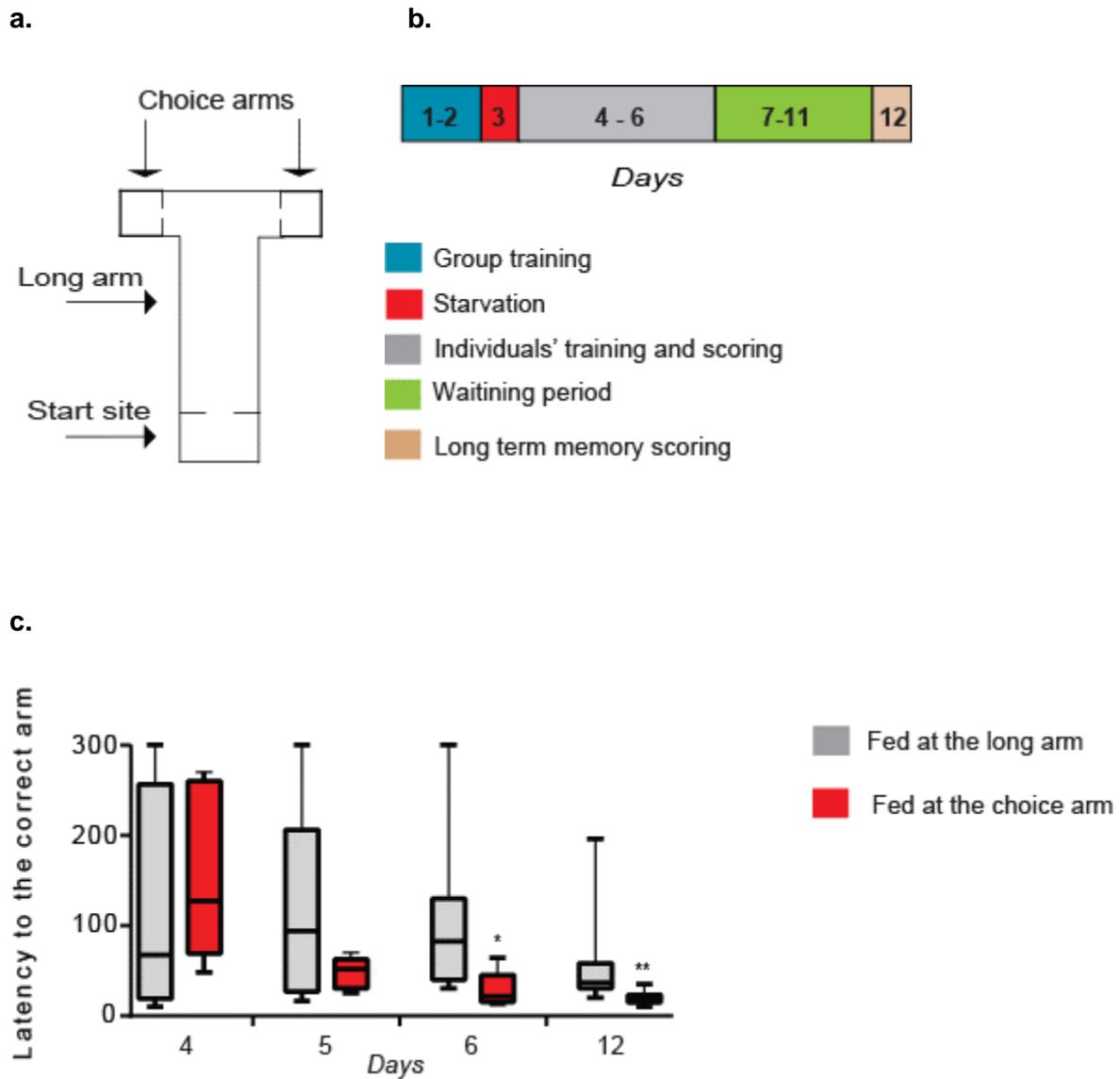
a) *Nmdar2* is mainly expressed the ellipsoid bodies and fan-shaped body in *Drosophila* brain (dissected brain of *nmdar2:UAS-sytagfp* flies, posterior view).

b) Behaviour and cognitive performance of flies with RNAi inhibition of *5htr7* at NMDAR2-expressing cells are not affected by rapamycin (n=5). Ten-day old flies were treated for four days with rapamycin. For learning delay: $F(5, 24) = 27.58$, for LTM: $F(5, 24) = 15.44$, for fear-like behaviour: $F(5, 24) = 16.89$, for explorative activity: $F(5, 24) = 44.22$. One-way ANOVA, individual comparisons by Sidak's multiple comparisons test.

*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$. Error bars represent s.e.m.

c) Paneuronal RNAi inhibition of *5htr1b* increased Tyr1472 phosphorylation of NMDAR2 receptor, while it did not inhibit rapamycin-induced de-phosphorylation of NMDAR2 in *Drosophila* heads. Ten-day old flies were rapamycin-treated for four days.

Figure S5. T-maze and learning protocol for zebrafish analysis.



a-b) T-maze and learning protocol.

c) Zebrafish learns to locate food sources after training and retain relative memory for at least six days after the end of training. Two-tailed Mann Whitney test (n=8).

** $p < 0.01$, and * $p < 0.05$. Error bars represent s.e.m.