

Supplementary Table S1: Cognitive impairment models of zebrafish and pharmacological studies for compounds with neuroprotective effects.

CI Model	Test Drug	Zebrafish (age, strain, sex)	Grouping	Administration Dosage, Route & Duration	Behavioral Findings (Drug Effects)	Other Findings (Drug Effects)	Reference
24h light exposure	Melatonin	Adult: 1y; WT SF; both sexes	(1) Normal light cycle (2) 24h light (3) Melatonin (4) Melatonin + 24h light	(1) melatonin: 0.232mg/L; AI for 24h (2) normal (14h light/10h dark) vs 24h light exposure	(1) IAT: ↑ latency to dark compartment with ES	(1) Body: ↓ cortisol	[79]
Aβ42	Li	Adult; WT	(1) Ctl (2) LiCl (3) Aβ42 (4) LiCl + Aβ42	(1) LiCl: 100μM; AI from 1hpf to 5dpf; EW daily (2) Aβ42: 10μM; CVI at 24hpf	(1) Bouncing-call avoidance test: ↑ escape response	(1) ↓ p-Tau protein	[56]
AlCl <sub>3</sub>	Nec-1	Adult: 6-8mo; TU	(1) Ctl (2) AlCl <sub>3</sub> (3) Nec-1 (4) AlCl <sub>3</sub> + Nec-1	(1) AlCl <sub>3</sub> : 200μg/L; AI for 30d (2) Nec-1: 15μmol/L; AI for 30d	(1) TM: ↑ latency to & accumulative time in target zone	(1) Brain: ↑ Ach; Neural cell no; mTOR & Caspase-8 mRNA (2) Telencephalon: ↓ RIP1, PARP2, Bmf1 & Rab25 mRNA; RIP1 staining; restored cellular & organelles changes	[78]
Alcohol	Taurine	Adult: 4-6mo; WT SF; both sexes	(1) Ctl (2) EtOH (3) Taurine (4) EtOH + Taurine	(1) EtOH: 1%; AI for 2min x 8d (2) Taurine: 42, 150, 400mg/L; AI after EtOH for 1h, 5 <sup>th</sup> -8 <sup>th</sup> d of EtOH	(1) Shoaling behavior test: ↑ inter-fish & farthest neighbor distances (2) IAT: ↑ latency to enter dark area with ES	-	[77]
Alcohol	Taurine	Adult: 3-5mo; WT; both sexes	(1) Ctl (2) Taurine (3) EtOH (4) Taurine + EtOH	(1) Taurine: 42, 150, 400mg/L; after training, AI for 1h AI (2) EtOH: 1%; after Taurine, AI for 1 h	(1) IAT: ↑ latency to enter dark side with ES & memory retention index	-	[76]
Alcohol	MA	Adult: 6-8mo, 4-5.5cm; WT Grey; both sexes	(1) Ctl (2) EtOH (3) EtOH + MA	(1) EtOH: dose escalation in 28d (a) D1-12: 0.125 to 0.375% (b) D13-28: 05% (2) MA: 100, 200μg/L for 28d	(1) LDPT: ↑ time spent in dark compartment (2) IAT: ↓ time spent in & no of entries into dark compartment with stirring	(1) Brain: ↓ AChE activity	[54]
HCD	LAB4 & LAB12	Adult: 2.5±0.5cm; male	(1) Ctl (2) HCD (3) HCD + LAB4 (4) HCD + LAB12	(1) HCD: hard-boiled egg yolk feed for 7w; 3% of total body weight (2) LAB: 10 <sup>9</sup> CFU/ g hard-boiled egg yolk for 7w	(1) spatial alternation task: ↑ correct response	(1) LAB4: ↓ body weight (2) LAB4 & 12: ↓ serum & liver cholesterol; intestinal <i>npc1117</i> & brain <i>appa</i> mRNA (2) LAB4 & 12: ↑ hepatic <i>abca1</i> mRNA	[75]
Hypoxia	MgT	Adult: 4-6mo, 2.5-3.5cm, 350±50mg; WT	(1) Ctl (2) Hypoxia (3) MgT (4) 10 uM MgT + Hypoxia	(1) MgT: 10μM; PO prior hypoxia (2) Hypoxia: hypoxic chamber for 1h & normoxic chamber for	(1) TM: ↑ time spent, distancemoved, entry frequency in target compartment	(1) ↓ cerebral infarction (2) Brain: ↑ EEAT4 protein	[64]

				2h before probe test			
Hypoxia	UTI	Adult: 6-8mo, 2.5-3.5cm; WT AB & Tg (gad1b:gfp)	(1) Ctl (2) UTI (3) Hypoxia (4) UTI + Hypoxia	(1) UTI: 10k, 50k, 100kU/kg, IP before training (2) Hypoxia: hypoxic chamber for 10±0.5min & normoxic chamber for 2h before probe test	(1) TM: ↑ time spent in target compartment	(1) ↓ brain infarction, SA-β-galactosidase level (2) ↑ GABA <sub>A</sub> receptors	[65]
MK-801	PH	Adult: 2.5bm	(1) Ctl (2) PH (3) SCOP (4) PH + SCOP	(1) MK-801: 20μM; AI for 30min before test (2) PH: 20μM ; AI for 1h min before test	(1) IAT: ↑ crossing time to the compartment with dropping stone	-	[58]
MK-801	Taurine	Adult: 4mo; SF; both sexes	(1) Ctl (2) Taurine (3) MK-801 (4) Taurine + MK-801	(1) Taurine: 42, 150, 400mg/L; after training, AI for 1h (2) MK-801: 2mg/kg; after Taurine, AI for 1 h	(1) IAT: all doses ↑ latency to enter dark area with ES; 42 & 150mg/L ↑ memory retention index (2) NTT: 400mg/L ↓ distance traveled & time spent in top area	-	[59]
MK-801	SUL, OLA & KAL	Adult: <8mo; male	(1) Ctl (2) MK-801 (3) SUL, OLA or KAL only (4) MK-801 + SUL, OLA or KAL	(1) MK-801; 5μM; AI for 15min before drugs (2) Drugs: 9μM HAL, 50μM OLA or 250μM SUL; AI for 15min	(1) IAT: SUL & HAL ↑ latency to enter dark compartment with ES (2) SPT: SUL & HAL ↑ social interaction time	-	[66]
PTZ	EMB	Adult; WT	(1) Ctl (2) PTZ (3) EMB + PTZ	(1) PTZ: 170mg/kg, IP (2) EMB: 0.156, 0.312, 0.625, 1.25, 2.5, 5, 10mg/kg; IP	(1) TM: ↑ inflexion ratio; ↓ time spent in wrong arm and distance traveled (2) NTT: ↑ distance traveled, time spent in upper tank & distance traveled in upper tank	(1) ↓ seizure score & latency for seizure onset (2) Docking: ↑ affinity to GABA <sub>A</sub> receptor (3) Brain: ↑ GABA & ACh; ↓ Glu	[67]
PTZ	EMB	Adult; WT AB (SF)	(1) Ctl (2) PTZ (3) EMB + PTZ	(1) PTZ: 80mg/kg, IP for 10d (2) EMB: 0.156, 0.312, 0.62 mg/kg, IP before PTZ daily dose	(1) 3-axis maze test: ↑ maze navigation time; ↓ performance errors	(1) ↓ seizure score (2) Brain: ↑ GABA, ACh & Glu; ↓ CCL-2, TLR-4, TNF-α, IL-1 & IFN-γ mRNA	[68]
PTZ	SLN-Q	Adult: <8mo, 1-1.2g; WT; male	(1) Ctl (2) PTZ (3) Q + PTZ (3) SLN-Q + PTZ	(1) Q: 5, 10mg/kg; 30min prior PTZ (2) SLN-Q: 5, 10mg/kg; IP, 30min prior PTZ (3) PTZ: 7.5mM; AI for 3-4min	(1) LDPT: ↑ time spent in light (preferred) chamber; ↓ number of entry to dark chamber (2) Partition preference test: ↑ time spent in and entry to target chamber (3) 3 horizontal compartment test: ↑ time spent in upper (preferred) segment and ↓ time spent in lower segment (4) Others: GSH, TBARS, AChE in brain	(1) Brain: ↑GSH; ↓TBARS & AChE activity	[69]
SCOP	C1	Adult: 4-6mo	(1) Ctl (2) SCOP (3) C1 + SCOP (4) DPZ + SCOP	(1) C1: 15, 30μM; 1 h before SCOP (2) SCOP: 200μM; AI for 1 h before training	(1) TM: ↑ entries and time spent in correct arm	(1) In vitro: ↓ AChE activity (2) Larvae: ↓ acrylamide-induced neurotoxicity	[47]
SCOP	CAF, ZM 241385,	Adult: 0.3-0.5g; WT	(1) Ctl (2) CAF + SCOP	(1) CAF: 10mg/kg (2) ZM241385: 10μg/kg	(1) IAT: all drugs ↓ latency to enter dark compartment with ES	-	[70]

	DPCPX, DIPI, EHNA		(3) ZM241385 + SCOP (4) DPCPX + SCOP (5) DIPI + SCOP (6) EHNA + SCOP	(4) DPCPX: 0.5mg/kg (5) DIPI: 5mg/ (6) EHNA: 100µg/kg (7) All drugs: IP, 2h before exp (8) SCOP: AI for 1h before training			
SCOP	COT & 6HLN	Adult: 6-8mo; WT SF; both sexes	(1) Ctl (2) SCOP (3) COT + SCOP (4) 6HLN + SCOP	(1) SCOP: 100µM; AI for 30min before tests (2) COT or 6HLN: 1,2mg/L; AI for 3m; after SCOP	(1) NTT: (a) COT & 6HLN (both doses) ↑ distance traveled & time spent in top zone (b) COT & 6HLN (1mg/L) ↑ distance traveled & velocity (2) YM: (a) COT (1mg/L) & 6HLN (2mg/L) ↑ time in novel arm (b) COT & 6HLN (1mg/L) ↑ distance traveled (c) COT & 6HLN (both doses) ↑ turn angel (3) NORT: COT & 6HLN (both doses) ↑ % preference for novel object	(1) Brain: COT & 6HLN (both doses): ↓ AChE activity, MDA & carbonylated protein; ↑ SOD, CAT, GPx & GSH (2) Brain mRNA (a) <i>bdnf</i> : COT (both doses) & 6HLN (1mg/L) ↑ (b) <i>npv</i> : COT (1mg/L) & 6HLN (2mg/L) ↑ (c) <i>egr1</i> : COT (both doses) & 6HLN (2mg/L) ↑ (d) <i>nrf2a</i> : COT & 6HLN (both doses) ↑	[60]
SCOP	FAB	Adult: 3-4mo, 3-4cm; WT ST; both sexes	(1) Ctl (2) FAB (3) SCOP (4) FAB + SCOP	(1) FAB: 1, 3, 5µg/L; AI for 8d, EW at D3, 7 & 8 (2) SCOP: 100µM; AI for 30 min prior NTT (D7) & YM (D8)	(1) NTT: 3 & 5µg/L ↑ time spent in top; ↓ time spent in bottom (2) YM: 3 & 5µg/L ↑ spontaneous alternation %	(1) Brain: (a) all doses ↓ AChE activity & MDA; ↑ CAT & GPx (b) 1 & 3µg/L ↑ SOD	[61]
SCOP	Li	Adult: 6mo, WT SF; both sexes	(1) Ctl (2) Li <sub>2</sub> CO <sub>3</sub> (3) SCOP (4) Li <sub>2</sub> CO <sub>3</sub> + SCOP	(1) Li <sub>2</sub> CO <sub>3</sub> : 100 mg/L; AI for 7d, EW every 3d (2) SCOP: 100µM; AI for 1h before training	(1) NTT: ↓ total distance travelled, entries & time in upper zone (2) YM: ↑ time spent in novel arm	(1) Brain: ↑ AChE activity	[57]
SCOP	OEO	Adult: 3-4mo, 3-4cm; SF; both sex	(1) Ctl (2) SCOP (3) SCOP + OEO	(1) OEO: 25, 150, 300µL/L; AI once daily for 13d, 1h prior test (2) SCOP: 100µM; 30min before each test	(1) NTT: ↓ time spent in bottom zone & freezing duration, ↑ distance traveled & average velocity (2) YM: ↑ time spent in novel arm, spontaneous alternation behavior & distance traveled (3) NOR: ↑ exploratory time on & preference for novel object	(1) Brain: ↑ SOD, CAT, GPx & GSH; ↓ AChE activity, portein carbonyl & MDA	[55]
SCOP	PH	Adult: 2.5cm	(1) Ctl (2) PH (3) SCOP (4) PH + SCOP	(1) PH: 20µM, AI for 1h prior SCOP (2) SCOP: 200µM, AI for 1h prior training	(1) IAT: ↑ crossing time to the dark compartment with dropping weight	-	[53]
SCOP	Q & R	Adult: <8mo; both sexes	(1) Ctl (2) SCOP (3) Tween-20 (4) Tween-20 + SCOP (5) Q (6) Q + SCOP	(1) Q or R: 50mg/kg in 1% Tween-20 in saline; IP; 2 hr before training (2) SCOP: 200µM; AI for 1h before training	(1) IAT: ↑ latencies to enter dark compartment with ES	-	[71]

			(7) R (8) R + SCOP				
SCOP	Rho	Adult; WT SF; both sexes	(1) Ctl (2) Rho (3) SCOP (4) Rho + SCOP	(1) Rho: 1, 3, 5µg/L; AI for 1h once daily for 9d (2) SCOP: 100µM; AI for 30 min prior tests	(1) NTT: all doses ↑ time spent in top, distance traveled, time spent in top/bottom ratio & distance top/bottom ratio (2) YM: all doses ↑ time spent in novel arm, distance traveled & turn angle (3) NORT: (a) all doses ↑ exploratory time on novel object (b) 3 & 5µg/L ↑ % preference for novel object	(1) Brain: (a) all doses ↓ AChE activity & MDA; ↑ SOD, CAT & GPx (b) 3 & 5µg/L ↓ protein carbonyl	[62]
SCOP	SFN	Adult: 6-8mo, 4-5.5cm; Grey strain; both sexes	(1) Ctl (2) IAT (3) IAT + SFN (4) IAT + SCOP (5) IAT + SFN + SCOP	(1) IAT daily for 10d (2) SFN: 25µM/L; AI for 1h before SCOP (3) SCOP: 400µM/L; AI for 1h before probe test	(1) IAT: ↓ time spent in & no of entries into dark compartment with stirring	-	[72]
SCOP	STF	Adult: 3-4mo, 3-4cm; WT ST; both sexes	(1) Ctl (2) STF (3) SCOP (4) STF + SCOP	(1) STF: 10, 25, 50µL/L; AI for 8d, EW at D3, 7 & 8 (2) SCOP: 100µM; AI for 30 min prior NTT (D7) & YM (D8)	(1) NTT: (a) 50µL/L ↑ total distance (b) all doses ↑ time spent & no of entries in top; ↓ latency to top (c) 20 & 50µL/L ↓ time spent & no of entries to bottom (2) YM: all doses ↑ no of arm entries & spontaneous alternation %	(1) Brain: ↓ AChE activity 7 MDA; ↑ SOD, CAT & GPx	[63]
SCOP	WPHs	Adult: 6mo; WT AB	(1) Ctl (2) SCOP (3) FY + SCOP (4) SGFDAE + SCOP	(1) WPHs: 20mg/L FY or 20mg/L SGFDAE; AI for 7d, EW every 2d (2) SCOP: 200µM; AI for 1h after training	(1) TM: WPHs ↑ time spent in target reservoir, latency to locate reservoir & total distance traveled	(1) Docking: WPHs ↑ binding affinity to AChE & Keap1	[73]
TCS	ST-III	Adult; WT AB	(1) Ctl (2) TCS (3) ST-III (4) TCS + ST-III	(1) TCS: 0.002% (v/v); A for 90dI, EW every 2d (2) ST-III: added into basal diet	(1) TM: ↓ distance traveled; ↑ transition no to targeted side (2) Bottom dwelling test: ↑ swim velocity & activity	(1) Restored intestinal flora structure & biodiversity. (2) ↓ intestinal lipid peroxidation & liver lipid accumulation (3) ↓ intestinal inflammation & immune response stimulation	[74]

6HLN: 6-hydroxy-L-nicotine; AB: AB strain; ACh: acetylcholine; AChE: acetylcholinesterase; AI: aqueous immersion; AlCl<sub>3</sub>: aluminium trichloride; C1: 1-Hydroxy-5,5-dimethyl-5,6,7,8-tetrahydro-9,10-anthraquinone (compound 1); CAF: caffeine; CAT: catalase; CI model: cognitive impairment model; COT: cotinine; Ctl: control; CVI: cerebroventricular injection; DIPI: dipyridamole; DPCPX: 8-cyclopentyl-1,3-dipropylxanthine; DPZ: donepezil; EAAT: Excitatory amino-acid transporter 4; EHNA: erythro-9-(2-hydroxy-3-nonyl)-adenine hydrochloride; EMB: Embelin; ES: electric shock; EtOH: ethanol; EW: exchange water/medium; FAB: agathisflavone; GABA: gamma-aminobutyric acid; GGRE: Glycyrrhiza glabra root extract; Glu: glutamate; GPx: glutathione peroxidase; GSH: reduced glutathione; HCD: high-cholesterol diet; IAT: inhibitory avoidance test IP: intraperitoneal injection; KAL: haloperidol; LAB12: Lactobacillus 1 plantarum LAB12; LAB4: Pediococcus acidilactici LAB4; LDPT: light-dark preference test; Li: lithium; Li<sub>2</sub>CO<sub>3</sub>: lithium carbonate; LiCl: lithium chloride; LPS: lipopolysaccharide; MA: mefenamic acid; MB: methylene blue; MB-005: 1,3-diaminopropane; MDA: malondialdehyde; MeHg: methylmercury; mgT: Magnesium L-threonate; MNE: Mediterranean natural extracts; mo: months; Nec-1: Necrostatin-1; NTT: novel tank test; OEO: Origanum vulgare ssp. hirtum (Lamiaceae) Essential Oil; OLA: olanzapine; PCM: piracetam; PH: physostigmine; PM: plus-maze test; PO: oral administration; PTZ: pentylenetetrazole; Q: quercetin; R: rutin; RE:

Rosemary extract ; Rho: rhoifolin; SCOP: scopolamine; SeMet: selenomethionine ; SF: Short-fin strain; SFN: sulforaphane; SLN-Q: solid lipid nanoparticle of quercetin ; SOD: superoxide dismutase; SPT: social preference test; ST: short-thin strain; STF:Schinus terebinthifolius essential oil; ST-II: probiotics Lactobacillus plantarum ST-III; SUL: sulpiride; TBARS: thiobarbituric acid reactive substances; TCS: triclosan; Tg: transgenic strain; TM: T-maze test; TU: Tuebingen strain; UTI: Ulinastatin; WPHs: peptides from walnut (*Juglans regia*) protein hydrolysates; WT: wild-type; YM: Y-maze test; ZM 241385: 4-(2-[7-amino-2-(2-furyl){1,2,4}triazolo-{2,3-a}{1,3,5}triazin-5-yl-amino]ethyl) phenol

Supplementary Table S2: Screening for nootropic agents with memory-enhancing properties using zebrafish as model.

Test Drug	Zebrafish (age, strain, sex)	Grouping & Dosage	Administration Route & Duration	Behavioral Findings	Other Findings	Reference
MB-005	Adult; WT SF; both sexes	(1) Acute: 0, 700mg/L (2) Chronic: 0, 200mg/L	(1) Acute: AI for 20 min (2) Chronic: AI for 14d	Acute treatments (1) IAT: ↓ incorrect entries; ↑ latency to incorrect compartment  Chronic treatment (1) IAT: ↓ latency to incorrect compartment; ↑ duration in and frequency to incorrect compartment (2) PM: ↑ freezing duration	-	[84]
MB	Adult: 3-6mo; WT	0, 0.1, 0.5, 5.0, 10μM	AI for 12h, immediately after last day of training; returned to home tank for 12h before probe test	(1) TM: 10μM ↓ performance (vs other doses)	-	[85]
MCL-11, MCL-28 & MCL-54	Adult: 6-12mo, 3- 4cm; WT SF; both sexes	(1) MCL-11: 0.00001-1 g/kg (2) MCL-28: 0.1-1000 g/kg (3) MCL-54: 0.5-20mg/kg	IP 20 min before TM & VORT first probe trial; immediately before CPP conditioning phase	(1) TM: MCL11 & MCL-28 ↓ latency to EC with an inverted U- shaped dose-response curve (2) VORT: MCL11 & MCL-28 ↑ DI (3) MCL-54 induced CPP	(1) Binding assay: MCL- 11most potent	[46]
MNE	Adult: 6-8mo, 3- 4cm, 0.4-1g; WT SF; both sexes	(1) GGRE: 0, 100, 250mg/L (2) RE: 0, 100, 250mg/L	AI for 30 min	(1) TM: ↓ latency to find target arm	-	[86]
NIC	Adult	0, 50, 100, 200mg/L,	AI for 3min, delay 0 -160min prior testing	(1) IAT: 100mg/L ↑ choice accuracy best at 20-40 min post administration; nicotinic antagonist (mecamylamine) reversed the effect when given before NIC	-	[87]
NIC	-	0, 50, 100, 150, 200, 400, 800mg/L	AL for 3min	(1) IAT: low dose (<100mg/L) ↑ choice accuracy; high dose ↓choice accuracy	-	[88]
PCM	Adult: 3-5mo; WT SF, both sexes	(1) Acute: 0, 100, 400, 700mg/L (2) Chronic: 0, 200mg/L	(1) Acute: AI for 20 or 90min (2) Chronic: AL for 7-8d, EW daily	(1) NTT: Acute PCM 700 mg/L ↓ time spent & entry duration in top (2) PM: Chronic PCM ↓latency to target arm; ↑ duration in target arm, entries to target arm, incorrect arm and total arm	-	[89]
UTI	Adult: 4-6mo, 2.5- 3.5cm; WT SF	0, 10k, 50k U/kg	IP daily for 2d before training	(1) TM: UTI 50k U/kg ↑ time, distance & frequency in target compartment (2) The same dose increased gene expressions of EAAT4 glutamate transporter, c-fos & BDNF	(1) Brain: UTI 50k U/kg UTI ↑ EAAT4 protein; c- fos & BDNF mRNA	[90]

AI: aqueous immersion; Ctl: control; EAAT: Excitatory amino-acid transporter 4; EW: exchange water; GGRE: Glycyrrhiza glabra root extract ; IAT: inhibitory avoidance test; IP: intraperitoneal injection; MB: methylene blue; MB-005: 1,3-diaminopropane; MNE: Mediterranean natural extracts; mo: months; NTT: novel tank test; PCM: piracetam; PM: plus-maze test; RE: Rosemary extract; SF: Short-fin strain; TM: T-maze test; UTI: Ulinastatin; WT: wild-type

Supplementary Table S3: Neurotoxicity studies for compounds that affect learning and memory in zebrafish.

Compound Category	Test Compound	Zebrafish (age, strain, sex)	Grouping & Dosage	Administration Route & Duration	Behavioral Findings	Other Findings	Reference
Alcohol	Ethanol	Embryo; WT AB	0, 20mM (0.12%)	AI from 2-9dpf; tested at mo	(1) YM: ↓ alternation	-	[42]
Alcohol	Ethanol	Adult	0, 0.1, 0.25, 1%	Set 1: CPP (1) Acute: single dose, test after 5d (2) Chronic: 7d, test after 5d  Set 2: Classical associative cognitive test (1) Chronic: 18d + 8d during test (2) Withdrawal: 15d + 3d no alcohol + 8d test without alcohol	Set 1: CPP (1) Acute & chronic (0.25 & 1%): ↑ time spent at less preferred place  Set 2: Cognitive test (1) Chronic: (0.25 & 1%): ↓ approaching index to feeding area	-	[113]
Alcohol	Ethanol	Embryo; AB	0, 0.25, 0.5, 0.75, 1%	AI for 2h, at 16hpf; tested at 6mo	(1) PM: all doses ↓ time spent in the target zone with food reward	-	[114]
Amino acid	Methionine	Adult: WT	0, 1.5 & 3mM	(1) Short-term: AI for 1h (2) Long-term: AI for 7d, EW daily	(1) LAT: long-term (3mM) ↓ latency to cross to dark compartment with ES	(1) Brain: long-term (3mM) ↑ AChE activity; long-term (both doses) ↓ AChE mRNA	[115]
Drug	DPZ	Adult: 5-6mo; WT AB	0, 1, 2.5ppm	AI for 21d, EW daily	(1) TM: 2.5ppm ↓ time spent in punish chamber with ES (2) NTT: 2.5ppm ↑ freezing time movement ratio; both doses ↑ time, entries to & distance traveled in top area (3) SPT: 1ppm ↑ interaction time (4) 2.5ppm ↓ shoaling formation	(1) Brain: (a) 2.5ppm: ↑ MDA; ↓ cortisol (b) 1ppm: ↓ oxytocin (2) Muscle: 2.5ppm ↑ MDA & ROS	[125]
Drug	MK-801	Adult: 3-6mo; AB	0, 20μM	AI for 1h for d	(1) IAT: ↓ latency to enter deep compartment with ES	(1) Brain: ↑ p-ERK	[82]
Drug	MK-801	Adult; 6-8mo; WT SF; both sexes	0, 20μM	AI for 30min before training, after training or before probe test	(1) PM: MK-801 administered after training or before probe test ↓ time spent in target compartment	-	[83]
Drug	MK-801	Adult: 6-8mo, WT SF, equal sexes	0, 2, 20, 100μM	AI for 30min before, during or after test	(1) NTT: 100μM before or during test ↑ clock-wise circling; 100μM during test ↑ time spent in bottle layer (2) Group preference test: 100μM during test ↓ time spent near stimulus fish	-	[116]
Drug	MK-801	Adult	0, 2, 20μM	AI for 37min or 1h	(1) LAT: ↑ circling behavior; ↓ swimming activity (2) TM: ↓ place preference	-	[81]
Drug-Anesthetic	Ketamine	Adult: 6mo; WT SF; both sexes	0, 2, 20, 40mg/L	AI for 20 min after training (1) Acute: 1d (2) Repeated: 7d, once daily	(1) IAT: Acute 40mg/L ↓ latency to enter dark area with ES (2) NTT: Repeated 40mg/L ↑ circling behavior	-	[117]

Drug-Anesthetic	Propofol	Larvae: 6hpf; WT AB & NBT Tg [NBT:MAPT-GFP]zc1])	0, 1, 2, 4µg/mL	AI at 6 till 48hpf	(1) LDLAT: 4µg/mL ↓ activity response to LD cycle	(1) all doses ↓ axonal length of motor neurons	[118]
Drug-Antidepressant	Citalopram	Larvae & adult; WT AB	0, 0.1, 1, 10, 100µg/L	AI; 2 generations exposure: (1) F0 <sup>+</sup> larvae: 0-80hpf (2) F0 <sup>+</sup> adult: 0-150dpf (3) F1 <sup>+</sup> larvae: 0-80hpf (4) F1 <sup>+</sup> larvae: 0-80hpf without drug	(1) Swimming behavior test, F1 <sup>+</sup> larvae: 100µg/L ↓ no of touch response; max speed & acceleration (2) Open field test, F0 <sup>+</sup> adult male: 1, 10, 100µg/L ↓ max velocity  (3) Stimulus response test: (a) F0 <sup>+</sup> adult female: 1µg/L ↑ max velocity to dark stimulus (b) F0 <sup>+</sup> adult male: ↓ max velocity to dark (0.1, 10, 100µg/L), light (100µg/L), noise (10, 100µg/L) stimulus  (4) Modified TM: (a) F0 <sup>+</sup> adult female: 10µg/L ↑ latency to correct tunnel (b) F0 <sup>+</sup> adult male: 100µg/L ↑ latency to correct tunnel; 10, 100µg/L ↑ time spent in reward chamber	(1) spinal motor neurons: 100µg/L ↓ length axonal projections in F1 <sup>+</sup> larvae (2) spinal cord: 100µg/L ↓ no of Glu <sup>+</sup> /Hb9 <sup>+</sup> neurons in F0 <sup>+</sup> adult male (3) ventral telencephalon: 100µg/L ↓ no of TH-labeled dopaminergic neurons in F0 <sup>+</sup> adult male	[119]
Environmental Pollutant	ACE	Adult: 9mo; WT AB	0, 1, 10, 100mg/L	AI for 2mo, EW daily	(1) LDPT: ↑ time spent in dark chamber, distance traveled, & thigmotaxis (2) NTT: ↓ time & distance traveled in top segment (3) NORT: ↓ time spent & distance traveled in novel object zone (4) SPT: ↑ time spent & distance traveled in zone without conspecifics (5) CPP: ↓ time spent & distance traveled in preferred chamber	-	[102]
Environmental Pollutant	B[a]P	Larvae & Adult (15-18mo); WT 5D Tropical & AHR2-null (ahr2hu3335)	0, 1, 5, 10, 20, 25, 30, 40µM	AI from 6-120hpf	(1) Larval photomotor response test: hyperactive swimming in WT (2) AAT: ↓ time spent in non ES side	(1) LPR (120 hpf larvae): hyperactive swimming in WT, no change in mutant strain (2) AAT (15-18mo adults): dec time spent on non-shock side	[103]
Environmental Pollutant	BDE-47	Adult: 5-6mo; WT AB	0, 10, 50, 100, 500µg/L	AI for D15-35, 1/3 EW twice a day	(1) TM: ↑ latency in the start zone, latency to reach reward zone, freezing bouts; ↓ latency to stay in reward zone, reward arm ratio selection, instantaneous velocity	(1) Brain: ↑ <i>bcl-2</i> , <i>c-fos</i> , <i>grin1b</i> , <i>lingo 1b</i> mRNA	[104]
Environmental Pollutant	BP1	Larvae & adult (6mo; male); WT AB, Tg ( <i>vmat2:GFP</i> ) & Tg ( <i>elavl3:GFP</i> )	(1) Larvae: 0, 0.8, 1, 1.2, 1.6, 2.4µg/mL (2) Adult: 0, 1, 10, 100, 1000µg/L	(1) Larvae: AI at 4dpf for 148h (2) AI for 14d; EW daily	Larvae: (1) ↑ embryo mortality, deformity rate, CNS & dopaminergic neurons' developmental defects; ↓ hatching rate (2) LAT: ↓ distance traveled & average speed (3) LD challenge test: ↓ velocity & distance moved	Larvae: (1) mRNA: ↑ <i>mbpa</i> & <i>pmoc</i> ; ↓ <i>gfap</i> & <i>bdnf</i>  Adult: (1) TM: ↑ latency to deep-water zone; ↓ deep water area/total area duration ratio (2) NTT: ↓ total distance; ↑ bottom/total duration & distance (3) Brain: ↓ <i>bdnf</i> , <i>gfap</i> , <i>mbpa</i> & <i>pomc</i> (mixed result)	[105]



Environmental Pollutant	Bisphenol F	Adult: 9-11mo; WT AB; male	0, 0.001, 0.01, 0.1mg/L	AI for 28d connected to automated EW system	(1) NTT: ↑ cumulative time in immobile state; ↓ no of transition to top zone (2) TM: ↑ distance traveled & cumulative time in non-target arm	(1) ↑ in blood & brain (2) RNA-seq: affected various pathways in brain (3) Brain: ↑ choline, 17β-estradiol & cortisol; ↓ kynurenine, pregnenolone-sulfate & dehydroepiandrosterone-sulfate, indoleamine 2,3-dioxygenase & tryptophan-2,3-dioxygenase activity	[106]
Environmental Pollutant	Butyl-paraben	Adult: 10-12mo; WT AB; male	0, 0.01, 0.1, 1mg/L	AI for 28d connected to automated EW system	(1) Photomotor response test: 1mg/L ↓ photosensitivity (2) TM: 0.1 & 1mg/L ↑ distance moved & time spent in non-target arm	(1) ↑ in blood & brain (2) RNA-seq: affected various pathways in brain (3) Brain: ↑ cortisol & cortisone; ↓ allopregnanolone	[107]
Metal	Al	Adult: 3-4mo; both sexes	0, 50, 100, 200μg/L AlCl <sub>3</sub>	4d	(1) NTT: ↓ distance traveled, no of entries to top zone; ↑ time spent in bottom zone (2) TM: ↑ latency to favorable zone, time spent & no of entries to unfavorable zone (3) NORT: ↓ exploration time with novel object	(1) Brain: ↓ GSH, SOD, GABA, DA, noradrenaline & serotonin; ↑ MDA & glu (2) IHC: ↑ no of pyknotic neurons; ↓ Nrf2	[91]
Metal	Al	Adult: 6mo; WT TU	0, 20, 100, 500μg/L AlCl <sub>3</sub>	AI for 30d	(1) TM: ↑ latency to enter & ↓ cumulative time in EC	(1) Brain: ↓ <i>PI3K</i> , <i>Akt</i> & <i>mTOR</i> mRNA, neural cells; ↑ Al	[92]
Metal	Al <sub>2</sub> O <sub>3</sub> -NPs	WT TU	6.25, 12.5, 25, 50, 100mg/L	AI from 6 till 120hpf; tested at 6, 9, 12mo	(1) TM: ↑ latency to enter EC & ↓ cumulative time in EC at 6 & 12mo (2) LAT: ↓ speed & time spent in outer zone; ↑ freezing timemovement ratio at 6, 9 & 12mo (3) NTT: ↓ speed & time spent in outer zone; ↑ freezing time ratio at 6, 9 & 12mo	(1) ↑ Al in the brain at 6 & 12mo (2) Brain: ↓ ACh & DA; ↑ ROS & LDH at 6 & 12mo (3) Telencephalon region: ↑ neural cell death and autophagy at 6mo	[48]
Metal	Ag	Adult; AB	0, 10, 30, 50, 100, 1000ppb AgNO <sub>3</sub>	AI for 72h; EW daily	(1) NTT: 30ppb ↓ distance traveled (2) Swimming performance test: 30ppb ↓ swimming endurance (2) SPT: 10 ppb ↓ time spent in conspecific zone (3) SRT: 10 ppb ↓ time spent in familiar zone (4) AAT: 10 ppb ↓ leaner %; ↑ trial no, latency of avoidance	(1) 30 & ≥50ppb: ↑ mortality rate (2) 10 & 30 ppb: ↑ Ag in brain (3) ↓ c-fos mRNA in medial and dorsal zones of the dorsal telencephalic area	[93]
Metal	As	Embryo (24hpf), larvae (7dpf), juvenile (30 & 90dpf) & adult (150dpf); WT	0, 50, 500ppb	AI: 4 hpf to 5mo	(1) ↓ larval spontaneous tail coiling (2) Adultmotor activity: hyperactive (3) Juvenile & adult NTT: ↓ time spent in top zone (4) SRT: hyperactive (5) Adult IAT: ↓ latency to black compartment with ES	-	[94]
Metal	As	0.3 g; both sexes	0, 1, 10, 100μg/L	AI for 96h after training	(1) IAT: ↓ latency to enter dark compartment with ES	-	[95]
Metal	Cu	Adult; WT	0, 0.77, 1.52μM CuSO <sub>4</sub>	AI for 10d, EW every 2d	(1) NTT: 1.52μM ↓ velocity at D10; ↑ freezing bouts; increased latency to enter upper zone (2) TM: both doses ↑ time to complete trial; ↓ correct choice	(1) Body: ↑ Cu	[96]

Metal	Cu	Larvae: 72hpf & adult; WT TU; both sexes	0, 5, 9, 20, 60µg/L CuCl <sub>2</sub>	AI for 96h, EW every 2d	Larva: (1) ↓ body length; ↑ distance traveled, velocity Adult: (1) YM: ↓ time spent in start & other arms (2) IAT: ↓ latency to enter dark compartment with ES	(1) Gills: ↓ GST & GPx	[97]
Metal	Hg	Adult: 6-8mo; LF; both sexes	0, 1, 5µg/L CH <sub>3</sub> HgCl	AI for 2, 16, 12, 24, 32h	(1) Swimming performance test: ↓ distance traveled, speed, max acceleration, full clockwise rotation numbers, alter activity/inactivity period (2) MBT: ↓ distancemoved (3) TM: ↓ associative learning	(1) Body: ↑ SDO & MDA	[98]
Metal	Mn	Larvae: dpf & adult: 6-8mo, 0.2-0.4g; WT TU	MnCl <sub>2</sub> : (1) Larva: 0, 0.1, 0.25, 0.5, 1, 1.5mM (2) Adult: 0, 0.1, 0.25, 0.5, 1, 1.5mM	(1) Larvae: AI at 1hpf to 5dpf (2) Adult: AI for 62h, EW daily	(1) Larval exploratory behavior test: ↓ distance traveled, absolute body turn angle, movement time, immobile episodes (2) Adult exploratory behavior test: ↓ line crossing, absolute turn angle, time spent in the upper tank (2) Adult IAT: ↓ latency to enter dark compartment with ES	(1) Brain: ↑ TH, DOPAC, apoptosis; ↓ TH enzyme	[99]
Metal	Pb	Adult: 5-6mo; WT AB	0, 50, 100, 1000ppb (µg/L) PbCl <sub>2</sub>	AI for 24 & 96h, 7, 10 14 & 30d, EW every 2d	50ppb: (1) 3D LAT: ↓ speed, angular velocity, total distance traveled, increased freezing timemovement ratio at D7 (2) NTT: ↓ entries to top compartment, ↑ freezing timemovement ratio at D30 (3) MBT: ↓ speed, mirror biting time at D7 & duration in mirror side at D4 (4) circadian rhythm LAT: altered at D30 (5) IAT: ↓ latency to enter dark compartment with ES at D30	(1) Brain: 50 ppb PbCl <sub>2</sub> ↑ SOD, cortisol & MDA; ↓ AChE activity, melatonin & serotonin	[101]
Metal	Pb	Larva & Adult; WT AB	0, 0.025, 0.05mg/L PbAc	AI at 6 to 120hpf, tested at 150dpf	(1) TM: ↓ accuracy rate; ↑ time to find food reward	(1) Developmental test: Induced malformation (2) Spontaneous movement test: ↓ tail bend frequency (3) larval LD stimulation test: ↑ hyperactivity	[100]
Metal	Zn	Adult: 6-7mo; WT AB	ZnCl <sub>2</sub> : (1) Acute: 0, 2, 4, 6, 8, 10, 12, 15mg/L (ppm) (2) Chronic: 0, 0.1, 0.5, 1, 1.5mg/L	(1) Acute: AI for 24, 48, 72, 96h (2) Chronic AI for 21d; EW daily	(1) 3D LAT: ↓ speed, distance traveled, time spent in top tank; ↑ angular velocity, meandering, fast latent time (2) MBT: ↓ mirror biting time % (3) IAT: ↓ latency to dark chamber with ES (4) Circadian rhythm test: ↓ circadian rhythm	(1) Brain: ↑ MDA, TBARS, 4-HNE, catecholamine, cortisol, AChE, DA, Glu, GABA, Aβ <sub>42</sub> , p-Tau; ↓ GSH, GPx, SOD, Gly, His	[52]
Peptide	Aβ <sub>42</sub>	Adult: 6mo (0.4-0.6g) & 36mo (0.8-1.2g); WT AB; both sexes	Aβ <sub>42</sub> M, O, P: 0, 10µM	CVI: (1) Young (6mo) (2) Old (36mo)	(1) Open tank test (7dpi): Aβ <sub>42</sub> O ↓ distance traveled in young fish (2) IAT (21dpi): Aβ <sub>42</sub> O & P ↓ latency to enter dark compartment with ES in young & old fish	-	[120]
Poison-neurotoxin	BMAA	Adult	0, 16.3µg/fish	IP on D0 & 7	(1) TM: ↑ latency to enter EC	-	[121]
Poison-Herbicide	Pq	Adult: 0.4-0.6g; WT; male	0, 10, 2 mg/kg,	6xIP, every 3d	(1) LAT: ↓ distance traveled, altered locomotion (2) YM: ↓ time spent in novel arm	(1) Brain: ↑ DA, DAT mRNA; ↓ DOPAC	[122]

Poison-pesticide	CPF + DM	Embryo: 2 hpf; WT SB	Co-exposure of low medium, high doses: (1) CPF: 4.8, 39.06, 78.13µg/L (2) DM: 0.06, 1.6, 3.19µg/L	AI from 2 to 144hpf, EW daily	(1) CPF + DM ↑mortality and malformation rate; ↓ hatching rate. (2) Dark-to-light stimulation test: high dose of CPF + DM ↓ swimming speed and adaptability to repeated stimulation	(1) Metabolomics: altered metabolisms of glycerophospholipids & amino acids	[123]
Sugar	Sucrose	Adult: 6-10mo; WT SF; both sexes	0, 83.25mM	AI for 14d	(1) T-plus maze test: ↓ time in and visit frequency to target arm with food reward, total no of arm visits; ↑ time showing immobility (2) Spatial learning test: ↓ time in, preference toward & time spent in target zone with stimulus fish; ↑ immobile time	(1) ↑ blood glucose	[124]
Stimulant	Ayahuasca	Adult: 2.5±0.2g; WT; both sexes	0, 0.1 or 0.5ml/L	(1) Acute: AI for 1h at D14 (2) Chronic: AI for 1h daily for 13d	(1) One-Trial discrimination test: ↓ DI; ↑ speed & distance traveled	-	[108]
Stimulant	CAF & CBD	Larvae & Adult; WT TU; both sexes	Set 1 (CBD dose response) CBD: 0, 0.1, 0.5, 5, 10mg/kg  Set 2 (CAF long-term pre-treatment): 20mg/kg CAF + 5mg/kg CBD  Set 3 (adenosine receptor antagonists): (1) Ctl (2) 6mg/L Agonist (DCPX or ZM241385) + 5mg/kg CBD	Set 1: CAF, IP, 1h before or after training  Set 2: CBD, AI at 3dpf for 4mo, EW every 3 d; CAF same as set 1  Set 3: Agonist, AI for 1h; CBD same as set2	Set 1: CDB (1) NTT: 0.5mg/kg ↑ time on upper zone (inverted U-shaped dose response curve) (2a) IAT (CBD before training): ↓ latency to cross dark compartment with ES (2b) IAT (CBD after training): 0.1, 5, 10mg/kg ↓ latency to cross dark compartment with ES; 0.5mg/kg ↑ latency to cross dark compartment with ES (U-shaped dose response curve)  Set 2: CAF pre-treatment (1) IAT (CBD after training): CAF ↑ latency to cross dark compartment with ES for CBD pre-treated group given after training  Set 3: Agonist: (1) IAT (CBD after training): ZM ↑ latency to cross dark compartment with ES	-	[109]
Stimulant	MPH + CAF	Adult: 3-6mo; WT; both sexes	Co-exposure: MPH: 80mg/L + CAF: 150mg/L	AI for 30min	(1) NTT: MPH + CAF ↓ traveled distance, crossing between zones (2) SPT: MPH + CAF ↓ time in conspecific segment (3) YM: MPH + CAF ↓ time in new arm	(1) Body: MPH + CAF ↑ protein carbonylation, Complexes II-III & IV activities	[110]
Stimulant	MPH	Larvae: 6dpf) AB	0, 12.5, 25, 50mg/L	AI from 0 to 5 dpf	(1) NTT: ↓ time spent in bottom 3rd of tank (2) IAT: ↓ correct choice	(1) Larvae: ↑ norepinephrine, DA, serotonin	[111]
Stimulant	THC	1y age, 3-4mo; both sexes	0.1, 0.3, 3µM	AI for 1 h before test	(1) Open field maze: ↓ spatial memory	(1) Telencephalon: ↑ p-Erk	[112]

4-HNE: 4-hydroxynonenal; AAT: Active avoidance test; AB: AB strain; ACE: acesulfame; ACh: acetylcholine; AChE: acetylcholinesterase; Ag: silver; AgNO<sub>3</sub>: silver nitrate; Al<sub>2</sub>O<sub>3</sub>-NPs: Al<sub>2</sub>O<sub>3</sub> nanoparticles; AlCl<sub>3</sub>: aluminium chloride; As: arsenic ; Aβ<sub>42</sub>: Amyloid-β<sub>42</sub>; Aβ<sub>42</sub>M: monomeric Aβ<sub>42</sub>; Aβ<sub>42</sub>O: oligomeric Aβ<sub>42</sub>;Aβ<sub>42</sub>P: protofibrillar Aβ<sub>42</sub>; B[a]P: Benzo[a]pyrene ; BDE-47: 2,2',4,4'-tetrabromodiphenyl ether;BMAA: β-N-

methyamino-L-alanine; BP1: benzophenone 1; CAF: caffeine; CBD: cannabidiol; CH<sub>3</sub>HgCl: methylmercury (II) chloride; CNS: central nervous system; CPF: chlorpyrifos; CPP: conditional place preference test; Cu: copper; CuCl<sub>2</sub>: copper chloride; CuSO<sub>4</sub>: copper sulphate; CVI: cerebroventricular injection; DA: dopamine; DI: discrimination index ; DM: deltamethrin; DOPAC: 3,4-dihydroxyphenylacetic acid ; dpf: day post fertilization; dpi: days post injection; DPZ: donepezil; EC: enriched chamber ; ES: electric shock; EW: exchange water/medium; GABA: gamma-aminobutyric acid ; Glu: glutamate; Gly: glycine; GPx: glutathione peroxidase; GSH: reduced glutathione; GST: glutathione S-transferase; HFD: high-fat diet; His: histidine; hpf: hours post fertilization; IHC: immunohistochemistry; LF: long-fin strain; LAT: locomotor activity test; LD: light-dark; LDLAT: light-dark locomotor activity test; MDA: malondialdehyde; MBT: mirror biting test; MCL-11:  $\alpha 4\beta 2$  nicotinic acetylcholine receptors (nAChRs) full agonist; MCL-117: nAChRs antagonist; MCL-28: nAChRs full agonist; MCL-54: nAChRs partial agonist; MnCl<sub>2</sub>: Manganese(II) chloride; mo: month; MPH: Methylphenidate; NBT Tg: NBT transgenic strain; NIC: Nicotine; NORT: novel object exploration test; PbAc: Lead acetate; PbCl<sub>2</sub>: Lead Chloride; PM: plus-maze test; Pq: paraquat; ROS: reactive oxygen species; SB: SB strain; SF: short-fin strain; SOD: superoxide dismutase; SPT: social preference test ; SRT: startle response test ; TBARS: thiobarbituric acid reactive substances; Tg: transgenic strain; TH: tyrosine hydrolase; THC:  $\Delta$ -9-tetrahydrocannabinol; TU: Tuebingen strain; VORT: virtual object recognition test; WT: wild-type; ZnCl<sub>2</sub>: Zinc chloride