

Table S1. Studies that have investigated the mechanism of action of gabazine in molluscs. All studies in molluscs have been done in gastropod molluscs. Target receptor: ion? = unknown which ion(s) the receptor is permeable to, hyper/depolarising? = unknown whether activation of the receptor results in hyperpolarisation (inhibitory) or depolarisation (excitatory). Administration method: bath application = animal/tissue/neuron sitting in the solution. Gabazine effect: the effect of gabazine on the behaviour measured or electrophysiological recording (neurotransmitter-induced hyper or depolarisation): - = no effect, X = completely blocked, ↓ = decrease, ↑ = increase.

Target receptor	Species Common name	Life stage	Gabazine conc. (uM)	Administration method	Method of measurement	Gabazine effect	Reference
Ionotropic GABA R (Cl ⁻ , hyper/depolarising?)	<i>Tritia obsoleta</i> Marine mud snail	Larvae	0.1, 1, 10, 100	Bath application	<i>In vivo</i> Percentage of larvae metamorphosing	-	Biscocho et al. (2018)
Ionotropic GABA R (ion?, hyperpolarising)	<i>Helix aspersa</i> Terrestrial snail	Not stated	10	Bath application then by micropipette	<i>In vitro</i> Electrophysiology	X	Vehovszky et al. (1989)
Ionotropic GABA R (ion?, depolarising)	<i>Helix aspersa</i> Terrestrial snail	Not stated	10	Bath application then by micropipette	<i>In vitro</i> Electrophysiology	↓	Vehovszky et al. (1989)
GABA R (type unknown)	<i>Nassarius obsoletus</i> Eastern mud snail (marine)	Larvae	1, 10 100, 1,000	Bath application	<i>In vivo</i> Percentage of larvae metamorphosing	- ↑	Welch (2015)

Table S2. Studies that have investigated the mechanism of action of picrotoxin in molluscs. All studies are in gastropod molluscs, apart from one study in a cephalopod mollusc (Chichery and Chichery, 1985). Target receptor: ion? = unknown which ion(s) the receptor is permeable to, hyper/depolarising? = unknown whether activation of the receptor results in hyperpolarisation (inhibitory) or depolarisation (excitatory). Administration method: superfusion = continuous flow over the outside of the tissue/neuron, perfusion = continuous flow through the tissue/neuron, bath application = animal/tissue/neuron sitting in the solution. Picrotoxin effect: The effect of picrotoxin on the behaviour measured or the electrophysiological recording (neurotransmitter-induced hyper or depolarisation): - = no effect, X = completely blocked, ↓ = decrease, ↑ = increase.

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Table S3. Explanatory variables, distribution family and link function as well as the priors used for the chosen model of each response variable in the gabazine experiment. Explanatory variables: * = interactive effect, + = additive effect. Priors: - = priors not applicable for this parameter, improper uniform = improper uniform priors were used (= uniform priors from infinity to -infinity).

Response variable	Explanatory variables	Family (link)	Intercept prior	Slope prior	sigma prior	shape prior
Time in Zone A (s)	CO2 * Drug	Gaussian (identity)	student_t(3, 316, 458.1)	improper uniform	student_t(3, 0, 458.1)	-
No. of visits to Zone A	CO2 * Drug + Mantle length	Negative binomial (log)	student_t(3, 1.4, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Proportion of squid that touched mirror softly	CO2 * Drug	Binomial (logit)	student_t(3, 0, 2.5)	improper uniform	-	-
Latency to first soft mirror touch (s)	CO2 * Drug	Gamma (log)	student_t(3, 3.7, 2.5)	improper uniform	-	gamma(0.01, 0.01)
No. of soft mirror touches	CO2 * Drug + Behavioural tank + Time of test	Negative binomial (log)	student_t(3, 2.9, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Proportion of squid that touched mirror aggressively	CO2 * Drug	Binomial (logit)	student_t(3, 0, 2.5)	improper uniform	-	-
Latency to first aggressive mirror touch (s)	CO2 * Drug + Behavioural tank + Time of test	Gamma (log)	student_t(3, 3.7, 2.5)	improper uniform	-	gamma(0.01, 0.01)
No. of aggressive mirror touches	CO2 * Drug	Negative binomial (log)	student_t(3, 2.9, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Active time (s)	CO2 * Drug	Gamma (log)	student_t(3, 5.3, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Total distance moved (cm)	CO2 * Drug	Gamma (log)	student_t(3, 6, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Average speed (cm/s)	CO2 * Drug	Gaussian (identity)	student_t(3, 2.1, 2.5)	improper uniform	student_t(3, 0, 2.5)	-

Table S4. Explanatory variables, distribution family and link function as well as the priors used for the chosen model of each response variable in the picrotoxin experiment. Explanatory variables: * = interactive effect, + = additive effect. Priors: - = priors not applicable for this parameter, improper uniform = improper uniform priors were used (= uniform priors from infinity to -infinity).

Response variable	Explanatory variables	Family(link)	Intercept	Slope	sigma	shape
Time in Zone A (s)	CO ₂ * Drug + Behavioural tank + Time of test	Gaussian (identity)	student_t(3, 677, 315.8)	improper uniform	student_t(3, 0, 315.8)	-
No. of visits to Zone A	CO ₂ * Drug + System	Negative binomial (log)	normal(0, 8)	normal(0, 2.5)	-	gamma(0.01, 0.01)
Proportion of squid that touched mirror softly	CO ₂ * Drug	Binomial (logit)	student_t(3, 0, 2.5)	improper uniform	-	-
Latency to first soft mirror touch (s)	CO ₂ * Drug	Gamma (log)	student_t(3, 4.4, 2.5)	improper uniform	-	gamma(0.01, 0.01)
No. of soft mirror touches	CO ₂ * Drug + Mantle length	Negative binomial (log)	student_t(3, 2.8, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Proportion of squid that touched mirror aggressively	CO ₂ * Drug	Binomial (logit)	student_t(3, 0, 2.5)	improper uniform	-	-
Latency to first aggressive mirror touch (s)	CO ₂ * Drug + System	Gamma (log)	normal(0, 10)	normal(0, 2.5)	-	gamma(0.01, 0.01)
No. of aggressive mirror touches	CO ₂ * Drug + Number of acclimation days + Date introduced to treatment tank	Negative binomial (log)	student_t(3, 3.1, 2.5)	improper uniform	-	gamma(0.01, 0.01)
Active time (s)	CO ₂ * Drug	Gaussian (identity)	student_t(3, 297.8, 206.5)	improper uniform	student_t(3, 0, 206.5)	-
Total distance moved (cm)	CO ₂ * Drug	Gaussian (identity)	student_t(3, 737.1, 641.1)	improper uniform	student_t(3, 0, 641.1)	-
Average speed (cm/s)	CO ₂ * Drug	Gaussian (identity)	student_t(3, 2.4, 2.5)	improper uniform	student_t(3, 0, 2.5)	-

References

- Arshavsky, Y. I., Deliagina, T., Gamkrelidze, G., Orlovsky, G., Panchin, Y. V., Popova, L. and Shupliakov, O. (1993). Pharmacologically induced elements of the hunting and feeding behavior in the pteropod mollusk *Clione limacina*. I. Effects of GABA. *Journal of Neurophysiology* **69**, 512-521.
- Biscocho, D., Cook, J. G., Long, J., Shah, N. and Leise, E. M. (2018). GABA is an inhibitory neurotransmitter in the neural circuit regulating metamorphosis in a marine snail. *Developmental Neurobiology* **78**, 736-753.
- Chichery, R. and Chichery, M.-P. (1985). Motor and behavioural effects induced by putative neurotransmitter injection into the optic lobe of the cuttlefish, *Sepia officinalis*. *Comparative Biochemistry and Physiology Part C: Comparative Pharmacology* **80**, 415-419.
- Jing, J., Vilim, F. S., Wu, J.-S., Park, J.-H. and Weiss, K. R. (2003). Concerted GABAergic actions of *Aplysia* feeding interneurons in motor program specification. *Journal of Neuroscience* **23**, 5283-5294.
- Magoski, N. S. and Bulloch, A. G. (1999). Dopamine activates two different receptors to produce variability in sign at an identified synapse. *Journal of Neurophysiology* **81**, 1330-1340.
- Moccia, F., Di Cristo, C., Winlow, W. and Di Cosmo, A. (2009). GABA A-and AMPA-like receptors modulate the activity of an identified neuron within the central pattern generator of the pond snail *Lymnaea stagnalis*. *Invertebrate Neuroscience* **9**, 29-41.
- Norekian, T. P. and Satterlie, R. A. (1993). FMRFamide and GABA produce functionally opposite effects on prey-capture reactions in the pteropod mollusk *Clione limacina*. *The Biological Bulletin* **185**, 248-262.
- Norekian, T. P. (1999). GABAergic excitatory synapses and electrical coupling sustain prolonged discharges in the prey capture neural network of *Clione limacina*. *Journal of Neuroscience* **19**, 1863-1875.
- Norekian, T. P. and Malyshev, A. Y. (2005). Coordinated excitatory effect of GABAergic interneurons on three feeding motor programs in the mollusk *Clione limacina*. *Journal of Neurophysiology* **93**, 305-315.
- Piggott, S. M., Kerkut, G. and Walker, R. (1977). The actions of picrotoxin, strychnine, bicuculline and other convulsants and antagonists on the responses to acetylcholine glutamic acid and gamma-aminobutyric acid on *Helix* neurones. *Comparative Biochemistry and Physiology Part C: Comparative Pharmacology* **57**, 107-116.
- Rubakhin, S., Szücs, A. and Rozsa, K. (1996). Characterization of the GABA response on identified dialysed *Lymnaea* neurons. *General Pharmacology* **27**, 731-739.
- Vehovszky, A., Bokisch, A. J., Krogsgaard-Larsen, P. and Walker, R. J. (1989). Pharmacological profile of gamma-aminobutyric acid (GABA) receptors of identified central neurones from *Helix aspersa*. *Comparative Biochemistry and Physiology Part C: Comparative Pharmacology* **92**, 391-399.
- Welch, M. (2015). Where do Nitergic and GABAergic neurons lie in the metamorphic pathway of *Nassarius obsoletus*? *PhD thesis*, University of North Carolina at Greensboro, Greensboro, North Carolina.
- Wu, J.-S., Jing, J., Diaz-Rios, M., Miller, M. W., Kupfermann, I. and Weiss, K. R. (2003). Identification of a GABA-containing cerebral-buccal interneuron-11 in *Aplysia californica*. *Neuroscience Letters* **341**, 5-8.
- Yarowsky, P. and Carpenter, D. (1978a). A comparison of similar ionic responses to gamma-aminobutyric acid and acetylcholine. *Journal of Neurophysiology* **41**, 531-541.
- Yarowsky, P. and Carpenter, D. (1978b). Receptors for gamma-aminobutyric acid (GABA) on *Aplysia* neurons. *Brain Research* **144**, 75-94.