

**Table S1.** Effects of an i.p. injection of  $\alpha$ -casozepine ( $\alpha$ -CZP), YLGYL, and diazepam (on the anxiety-induced c-Fos immunoreactivity (positive cells/0.04 mm<sup>2</sup>) in different areas of mice brains (n = 4/group). Mice were injected with either vehicle,  $\alpha$ -CZP (1 mg/kg), YLGYL (0.5 mg/kg), or diazepam (1 mg/kg) 90 mins before culling. Data are mean  $\pm$  SEM. Results were analysed using a one-way ANOVA to detect the effects of treatment (\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001) and a Bonferroni post-hoc test was performed to compare the effect of  $\alpha$ -CZP, YLGYL and diazepam to the vehicle (+p < 0.05, ++p < 0.01, +++)p < 0.001).

	Vehicle	$\alpha$ -CZP	YLGYL	Diazepam	ANOVA	
					F(3,11)	(p-value)
<b>Prefrontal cortices</b>						
<i>Global</i>	7.59 $\pm$ 0.61	6.47 $\pm$ 0.27	5.81 $\pm$ 0.41	2.15 $\pm$ 0.16 +++	33.262	8.21E-06 ***
Frontal association cortex	4.45 $\pm$ 0.33	4.92 $\pm$ 0.18	3.86 $\pm$ 0.49	1.85 $\pm$ 0.24 +++	14.661	3.69E-04 ***
Prelimbic cortex	8.28 $\pm$ 0.60	7.84 $\pm$ 0.85	6.98 $\pm$ 0.42	2.49 $\pm$ 0.14 +++	27.389	2.11E-05 ***
Medial orbital cortex	11.18 $\pm$ 1.09	9.15 $\pm$ 0.60	10.52 $\pm$ 0.96	2.91 $\pm$ 0.13 +++	22.654	5.19E-05 ***
Ventral orbital cortex	10.03 $\pm$ 0.90	8.12 $\pm$ 1.19	9.87 $\pm$ 0.74	2.96 $\pm$ 0.09 +++	19.242	0.00011 ***
Lateral orbital cortex	8.56 $\pm$ 0.85	6.54 $\pm$ 0.62	7.28 $\pm$ 0.50	1.83 $\pm$ 0.17 +++	25.734	2.84E-05 ***
Dorsolateral orbital cortex	6.05 $\pm$ 0.23	5.77 $\pm$ 0.29	5.32 $\pm$ 0.52	1.45 $\pm$ 0.05 +++	45.99	1.63E-06 ***
<b>Amygdala</b>						
<i>Global</i>	2.56 $\pm$ 0.14	6.21 $\pm$ 0.08 +++	3.64 $\pm$ 0.34	2.16 $\pm$ 0.39	51.173	9.47E-07 ***
Anterior cortical nucleus	3.65 $\pm$ 0.31	7.82 $\pm$ 1.30 +	10.25 $\pm$ 1.00 ++	1.54 $\pm$ 0.21	21.771	6.25E-05 ***
Posterolateral cortical nucleus	3.71 $\pm$ 0.49	7.39 $\pm$ 0.29 +++	8.93 $\pm$ 0.73 +++	1.72 $\pm$ 0.29 +	53.659	7.43E-07 ***
Basolateral nucleus	1.49 $\pm$ 0.05	4.17 $\pm$ 0.11 +++	1.91 $\pm$ 0.15	1.11 $\pm$ 0.23	89.916	5.07E-08 ***
Basomedial nucleus	2.88 $\pm$ 0.39	6.60 $\pm$ 0.38 +++	3.41 $\pm$ 0.54	1.78 $\pm$ 0.33	28.829	1.65E-05 ***
Central nucleus	2.33 $\pm$ 0.41	4.17 $\pm$ 0.20	1.93 $\pm$ 0.25	6.59 $\pm$ 1.25 ++	11.663	0.00133 **
Medial nucleus	3.29 $\pm$ 0.26	9.38 $\pm$ 0.49 ++	4.48 $\pm$ 0.62	2.63 $\pm$ 0.24	61.17	3.79E-07 ***
<b>Nucleus of the Tractus Solitarius</b>	9.03 $\pm$ 1.54	11.25 $\pm$ 1.90	8.42 0.64	21.24 $\pm$ 3.45 ++	8.5315	0.00328 **
<b>Periaqueductal Grey</b>	6.68 $\pm$ 0.65	6.01 $\pm$ 0.96	7.03 $\pm$ 0.86	3.13 $\pm$ 0.53 +	6.0371	0.01101 *
<b>Raphe magnus nucleus</b>	1.61 $\pm$ 0.17	3.18 $\pm$ 0.05 +++	5.35 $\pm$ 0.43 +++	1.20 $\pm$ 0.08	82.797	7.83E-08 ***