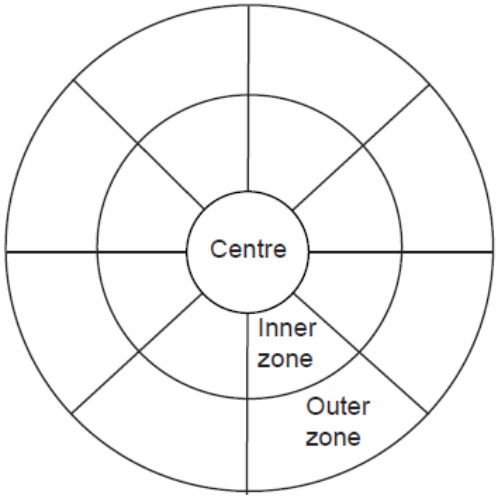
[Additional material]

Additional figures

a)



b)

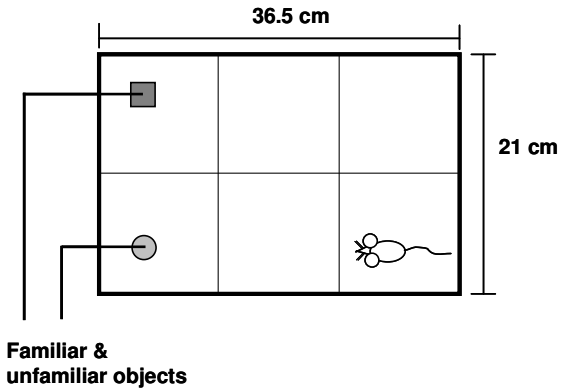


Figure A1: **Schematic drawing of the OF (a) and the ORT (b)**. a) Centre, inner and outer zone were divided by lines on the floor area. Extra lines were added to measure locomotor activity. b) After 24h familiarisation with one of the two objects, the familiar and an unfamiliar object were placed opposite the starting position.

Table A1 Overview of the (corrected) thresholds of significance used in the statistical analyses in experiment 1, Open Field.

	Behavioural category/physiology/ c-Fos	Behavioural/physiological parameter/brain area	ANOVA *	*Post hoc* comparison #	Data can be found in
Behaviour	Avoidance behaviour	Latency until the first center entry	0.0170 (q = 3)	0.0043 (q = 12)	Table A3/A4
		Total time spent in center		0.0019 (q = 27)	
		Total number of center entries		0.0019 (q = 27)	
	Risk assessment	Total number of stretched attends	0.0253 (q = 2)	0.0028 (q = 18)	
		Latency until first stretched attend		0.0064 (q = 8)	
	Locomotor activity	Total number of line crossings	0.0127 (q = 4)	0.0014 (q = 36)	
		Latency until first line crossing		0.0032 (q =16)	
		Total time spent immobile		0.0014 (q = 36)	
		Latency until the first immobility event		0.0032 (q =16)	
	Exploratory activity	Total number of rearings	0.0253 (q = 2)	0.0028 (q = 18)	
		Latency until first rearing		0.0064 (q = 8)	
	Arousal	Total time spent grooming	0.0170 (q = 3)	0.0019 (q = 27)	
		Latency until the first grooming event		0.0043 (q = 12)	
		Total number of fecal boli		0.0043 (q = 12)	
Blood plasma	Stress response	Corticosterone	0.0253 (q = 2)	0.0052 (q = 10)	Table A5
Brain	c-Fos	Medial prefrontal cortex	0.05 (q = 1)	0.0073 (q = 7)	Table A6
		Lateral septum	0.0170 (q = 3)	0.0024 (q = 21)	
		Bed nucleus of the stria terminalis	0.0170 (q = 3)	0.0024 (q = 21)	
		Hippocampus	0.05 (q = 1)	0.0073 (q = 7)	
		Hypothalamus	0.0253 (q = 2)	0.0037 (q = 14)	
		Amygdala	0.0253 (q = 2)	0.0037 (q = 14)	
		Periaqueductal gray	0.0127 (q = 4)	0.0018 (q = 28)	

* Calculating thresholds for the ANOVA: *i)* Behavioural parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of parameters per behavioural category. *ii*) Physiological parameters, $\alpha = 0.0253$ (data from vehicle-treated animals are used twice). *iii)* Brain parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of subdivisions per brain area. The q values are shown in parentheses.

Calculating thresholds for *post hoc* comparisons: *i)* Behavioural parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of parameters per behavioural category multiplied by the number of times a group is used for a meaningful comparison. *ii*) Physiological parameters, $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of meaningful comparisons between groups. *iii)* Brain parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of subdivisions per brain area multiplied by the times a group is used for meaningful comparisons.

Table A2 Overview of the (corrected) thresholds of significance used in the statistical analyses in experiment 2, Object recognition test.

	Behavioural category/physiology	Behavioural/physiological parameter	ANOVA *	Post hoc comparison #	Data can be found in
Behaviour	Object memory	Discrimination index	0.0102 (q = 5)	0.0015 (q = 35)	Table A7
		Latency until first exploration novel object			
		Latency until first exploration familiar object			
		Total time spent exploring novel object			
		Total time spent exploring familiar object			
	Risk assessment	Total number of stretched attends	0.05 (q = 1)	0.0073 (q = 7)	
	Locomotion	Total number of line crossings	0.0170 (q = 3)	0.0024 (q = 21)	
		Total time spent immobile			
		Latency until the first immobility event			
	General exploration	Total number of rearings	0.05 (q = 1)	0.0073 (q = 7)	
	Arousal/de-arousal	Total time spent grooming			
		Latency until the first grooming event	0.0253 (q = 2)	0.0037 (q = 14)	
Blood plasma	Stress response	Corticosterone	0.05 (q = 1)	0.0052 (q = 10)	Table A8

* Calculating thresholds for the ANOVA: *i)* Behavioural parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of parameters per behavioural category. *ii*) Physiological parameters, $\alpha = 0.05$.

Calculating thresholds for *post hoc* comparisons: *i)* Behavioural parameters: $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of parameters per behavioural category multiplied by the number of times a group is used for a meaningful comparison. *ii*) Physiological parameters, $\alpha = 1 - [1 - 0.05]^{1/q}$; q = number of meaningful comparisons between groups.

Table A3 Overview of behavioural parameters measured in the OF after vehicle, 1 mg/kg, 3 mg/kg or 5 mg/kg diazepam. The 30 min OF trial was divided in 6 time intervals of 5 min each. Data are shown per time interval, only latency and defecation data are shown once per OF trial.

Behavioural parameter	Time interval ‡	ANOVA effects @	vehicle		1 mg/kg diazepam		3 mg/kg diazepam		5 mg/kg diazepam	
			BALB/c	129P3	BALB/c	129P3	BALB/c	129P3	BALB/c	129P3
Latency centre	1-6	ns	684.9 ± 221.2	487.1 ± 228.5	311.5 ± 215.0	89.6 ± 21.7	395.9 ± 130.8	598.4 ± 265.3	274.0 ± 119.0	248.1 ± 107.8
Centre duration	1	T	0.8 ± 0.7	2.0 ± 0.9	1.8 ± 0.7	1.8 ± 0.6	0.9 ± 0.6	0.5 ± 0.3	0.5 ± 0.2	0.5 ± 0.2
	2		1.2 ± 0.5	1.2 ± 2.4	1.4 ± 0.5	1.7 ± 0.4	0.7 ± 0.3	3.1 ± 2.7	0.7 ± 0.3	7.9 ± 6.3
	3		2.0 ± 0.7	1.6 ± 0.7	2.3 ± 0.7	1.8 ± 0.6	1.3 ± 0.3	2.0 ± 1.8	1.1 ± 0.5	1.0 ± 0.6
	4		3.0 ± 0.8	2.1 ± 0.9	1.9 ± 0.9	2.5 ± 1.1	2.0 ± 0.6	0.4 ± 0.2	1.7 ± 0.7	0.4 ± 0.2
	5		2.6 ± 0.8	2.8 ± 1.1	3.3 ± 1.4	2.6 ± 0.6	2.1 ± 0.6	0.3 ± 0.1	1.9 ± 0.6	1.7 ± 0.8
	6		2.3 ± 0.6	3.1 ± 1.1	1.6 ± 0.6	1.9 ± 0.8	2.0 ± 0.5	0.2 ± 0.1	1.3 ± 0.4	0.8 ± 0.4
Centre entries	1	T, T*S	1 (2)	3 (6)	5 (6)	3 (2)	1 (3)	1 (3)	2 (3)	2 (2)
	2		2 (7)	3 (5)	5 (6)	5 (4)	2 (4)	2 (1)	3 (3)	2 (2)
	3		8 (8)	4 (5)	8 (9)	2 (1)	3 (3)	0 (1)	3 (4)	0 (2)
	4		8 (9)	4 (6)	5 (4)	3 (3)	6 (8)	1 (1)	4 (3)	1 (1)
	5		6 (5)	5 (5)	9 (5)	4 (3)	9 (7)	0 (1)	4 (2)	1 (1)
	6		7 (6) †	4 (4)	5 (6)	5 (1)	7 (7)	1 (1)	3 (3)	1 (2)
Stretched attends	1	T, D, T*D	18 (22)	14 (35)	5 (6)	7 (6)	5 (7)	6 (7)	4 (2)	1 (3)
	2		4 (12)	2 (6)	0 (2)	0 (1)	0 (1)	0 (1)	0 (0) †	0 (1)
	3		2 (5)	0 (2)	0 (0)	0 (0)	0 (0) †	0 (3)	0 (0) †	0 (2)
	4		1 (4)	0 (2)	0 (0) †	0 (0)	0 (0) †	0 (3)	0 (0) †	0 (0)
	5		0 (3)	0 (1)	0 (0) †	0 (0)	0 (0) †	0 (0)	0 (0) †	0 (0)
	6		0 (0) †	0 (0) †	0 (1) †	0 (0)	0 (0) †	0 (1)	0 (0) †	0 (0)
Latency stretched attend	1-6	ns	16.5 ± 3.9	231.2 ± 224.1	8.8 ± 1.9	231.0 ± 224.1	291.0 ± 222.2	263.2 ± 165.3	19.1 ± 8.9	244.5 ± 222.3
Line crossings	1	S, T*S	146 (153)	105 (153)	286 (104)	181 (44)	134 (89)	53 (153)	217 (82)	41 (104)
	2		171 (107)	120 (78)	298 (90)	133 (64)	128 (139)	33 (57)	187 (82)	13 (77) ^
	3		213 (105)	123 (99)	268 (76)	114 (60)	200 (131)	23 (51)	176 (44)	30 (51)
	4		166 (133)	100 (76)	287 (71)	137 (72)	251 (173)	50 (73)	192 (54)	60 (47)
	5		221 (103)	122 (77)	256 (94)	118 (95)	333 (106)	39 (55) ^	213 (49)	59 (45) ^
	6		230 (75) †	116 (86) ^	287 (140)	117 (73)	363 (163) †	14 (52) ^	240 (87)	51 (48) ^
Latency line cross	1-6	ns	45.8 ± 11.0	11.8 ± 3.0	13.0 ± 3.1	8.1 ± 1.1	18.0 ± 6.0	35.1 ± 6.8	19.0 ± 3.6	33.2 ± 17.0
Immobility duration	1	S, D, S*D	5.0 ± 4.3	0.3 ± 0.3	0.0 ± 0.0	0.6 ± 0.3	5.7 ± 2.9	30.1 ± 10.8 ^*	7.7 ± 5.0	32.6 ± 9.2 ^*
	2		0.3 ± 0.2	2.1 ± 1.8	0.6 ± 0.6	2.2 ± 1.1	6.2 ± 5.2	32.5 ± 11.1 ^*	6.4 ± 3.8	45.2 ± 13.8 ^*
	3		0.0 ± 0.0	1.3 ± 0.7	0.4 ± 0.3	1.5 ± 1.0	10.2 ± 9.2	44.3 ± 11.6	5.3 ± 3.6	40.7 ± 13.2 ^*
	4		5.6 ± 5.6	3.2 ± 2.5	0.4 ± 0.3	1.6 ± 1.0	2.7 ± 1.9	32.2 ± 12.1 ^*	1.3 ± 1.2	33.8 ± 13.2 ^*
	5		1.2 ± 0.8	0.6 ± 0.4	0.4 ± 0.4	2.5 ± 1.3	0.8 ± 0.6	27.7 ± 9.9 ^*	2.4 ± 2.4	24.5 ± 10.4 ^*
	6		0.5 ± 0.3	5.3 ± 4.9	0.4 ± 0.4	0.6 ± 0.4	4.1 ± 4.0	38.5 ± 12.1	4.2 ± 2.7	33.5 ± 11.5
Latency immobility	1-6	D	778.2 ± 240.9	830.7 ± 212.6	1286.3 ± 34.7	600.7 ± 217.4	300.9 ± 218.1	343.6 ± 22.9*	596.7 ± 231.2	141.5 ± 60.9 *
Rearings	1	T, D. T*D	2 (3)	2 (9)	6 (17)	5 (6)	1 (3)	0 (0)	1 (2)	1 (1)
	2		3 (21)	9 (17)	27 (46)	10 (12)	2 (11)	1 (2)	3 (9)	0 (2)
	3		19 (34)	9 (10)	43(40) †	21 (17)	4 (22)	1 (3)	5 (9)	1 (4)
	4		26 (30)	16 (16)	33 (45) †	25 (25)	6 (14)	2 (4)	7 (5)	2 (4)
	5		32 (30) †	15 (17)	49 (28) †	27 (33)	6 (23)	2 (4)	7 (6)	2 (12)
	6		37 (36) †	16 (23)	45 (43) †	31 (9)	9 (21)	2 (10) *	13 (15)	2 (11) *
Latency rearing	1-6	ns	349.9 ± 102.1	263.9 ± 108.3	341.6 ± 140.1	127.4 ± 22.6	300.5 ± 55.9	795.2 ± 242.7	337.9 ± 72.6	678.5 ± 210.7

[Table A3 continues on next page]

[Table A3 continued]

Grooming duration	1	ns	1.5 ± 0.5	1.6 ± 0.6	1.6 ± 1.3	0.0 ± 0.0	0.4 ± 0.2	0.3 ± 0.3	2.8 ± 1.3	2.9 ± 0.9
	2		2.8 ± 1.3	3.9 ± 1.2	0.3 ± 0.3	3.5 ± 2.9	5.0 ± 2.4	6.0 ± 1.5	6.8 ± 3.8	6.1 ± 2.4
	3		4.2 ± 1.4	3.1 ± 1.7	2.4 ± 1.7	4.9 ± 3.9	1.8 ± 0.7	11.3 ± 6.3	7.2 ± 4.1	11.2 ± 3.5
	4		3.7 ± 1.3	5.7 ± 2.3	0.3 ± 0.2	3.1 ± 2.0	2.0 ± 0.4	9.4 ± 2.9	6.0 ± 2.6	9.9 ± 3.5
	5		2.4 ± 0.9	3.7 ± 2.5	0.5 ± 0.3	3.4 ± 2.4	6.4 ± 1.2 †	4.6 ± 1.3	4.9 ± 1.7	6.3 ± 2.3
	6		2.4 ± 1.0	5.3 ± 2.2	0.1 ± 0.1	3.8 ± 3.2	6.7 ± 2.4	10.4 ± 3.3	8.2 ± 1.9	7.7 ± 2.5
Latency self-groom	1-6	ns	372.9 ± 56.2	443.5 ± 73.0	652.1 ± 135.7	439.6 ± 41.0	521.6 ± 172.2	754.7 ± 213.2	393.4 ± 83.6	757.1 ± 181.6
Defecation	1-6	D	13 (3)	8 (2)	5 (7)	9 (4)	4 (2) *	5 (4)	9 (5)	4 (5)

Data are represented as mean ± SEM for continuous numerical data, for discrete numerical data on the ordinal scale the results are represented as median with in parentheses IQR. Multivariate repeated measures ANOVA was performed with time interval as within factor and strain and dose as between factor. Latencies and defecation parameter were analyzed with a two-way ANOVA with strain and dose as main factors.

‡ The open field test of 30 minutes was divided in 6 bins of 5 minutes each (time interval). Number and duration of a specific behavioural parameter were calculated per time interval except for the latency and defecation, which is given only once per whole trial.

@ Significant ANOVA effects: S = strain effect; T = time interval effect; D = dose effect; T*S interaction; T*D interaction; S*D interaction; ns = non-significant. Thresholds of significance used for the ANOVA analyses, according to the Dunn- Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A1 for the corrected P values).

Significant *post hoc* differences are shown as: * = vs. vehicle, ^ = vs. BALB/c, † = vs. time interval 1. Thresholds of significance used for *post hoc* comparisons can also be found in Table A1

Table A4 Overview of behavioural parameters measured in the OF after vehicle, 3 mg/kg, 10 mg/kg or 30 mg/kg MPEP. For behavioural analyses, the 30 min OF trial was divided in 6 time intervals of 5 min each. Data are shown per time interval, only latency and defecation data are shown once per OF trial.

Behavioural parameter	Time interval ‡	ANOVA effects @	vehicle		3 mg/kg MPEP		10 mg/kg MPEP		30 mg/kg MPEP	
			BALB/c	129P3	BALB/c	129P3	BALB/c	129P3	BALB/c	129P3
Latency centre	1-6	S	684.9 ± 221.2	487.1 ± 228.5	453.6 ± 154.9	565.5 ± 272.0	1250.5 ± 106	184.5 ±120.3^	525.5 ±279.0	125.1 ± 39.4^
Centre duration	1	T	0.8 ± 0.7	2.0 ± 0.9	0.7 ± 0.4	1.4 ± 0.6	0.6 ± 0.4	2.1 ± 0.6	1.9 ± 0.9	1.1 ± 0.2
	2		1.2 ± 0.5	1.2 ± 2.4	0.6 ± 0.3	1.6 ± 0.6	1.0 ± 0.7	2.9 ± 0.6	2.5 ± 1.6	3.2 ± 0.5
	3		2.0 ± 0.7	1.6 ± 0.7	0.8 ± 0.4	1.9 ± 1.1	0.6 ± 0.4	2.6 ± 0.8	1.9 ± 0.8	3.2 ± 0.5
	4		3.0 ± 0.8	2.1 ± 0.9	3.5 ± 1.0	2.0 ± 0.6	1.2 ± 0.9	3.0 ± 0.6	3.5 ± 1.0	4.2 ± 1.1
	5		2.6 ± 0.8	2.8 ± 1.1	3.8 ± 1.0	2.0 ± 0.7	1.4 ± 0.8	3.6 ± 1.3	2.4 ± 0.7	2.8 ± 0.5
	6		2.3 ± 0.6	3.1 ± 1.1	3.0 ± 0.7	2.6 ± 1.6	1.4 ± 0.8	2.1 ± 0.5	3.2 ± 1.2	2.6 ± 0.5
Centre entries	1	T	1 (2)	3 (6)	0 (4)	2 (3)	0 (1)	6 (4)	3 (5)	5 (4)
	2		2 (7)	3 (5)	0 (2)	3 (4)	0(3)	7 (2)	3 (7)	9 (4)
	3		8 (8)	4 (5)	2 (3)	2 (6)	0 (3)	7 (4)	5 (7)	12 (6)
	4		8 (9)	4 (6)	4 (3)	5 (8)	0 (4)	8 (3)	7 (11)	10 (4)
	5		6 (5)	5 (5)	6 (4)	5 (7)	1 (5)	6 (2)	5 (8)	8 (4)
	6		7 (6)	4 (4)	6 (2)	4 (9)	2 (6)	5 (3)	8 (4)	9 (2)
Stretched attends	1	T, T*S	18 (22)	14 (35)	26 (21)	11 (20)	23 (14)	5 (10)	16 (31)	4 (3) ^
	2		4 (12)	2 (6)	5 (8)	2 (16)	9 (13)	0 (0)	3 (15)	0 (0)
	3		2 (5)	0 (2)	0 (2)	1 (9)	10 (15)	0 (0) ^	1 (5)	0 (0)
	4		1 (4)	0 (2)	0 (2)	0 (3)	10 (14)	0 (0) ^	0 (5)	0 (0)
	5		0 (3) †	0 (1)	0 (0)	0 (10)	5 (11)	0 (0)	1 (4)	0 (0)
	6		0 (0) †	0 (0) †	0 (0)	0 (8)	0 (7)	0 (0)	0 (5)	0 (0)
Latency stretched attend	1-6	ns	16.5 ± 3.9	231.2 ± 224.1	10.2 ± 2.7	230.6 ± 224.2	5.8 ± 1.0	231.8 ± 224.0	232.0 ±224.0	231.6 ± 224.1
Line crossings	1	T*S	146 (153)	105 (153)	105 (68)	140 (210)	89 (115)	199 (46)	189 (127)	204 (42)
	2		171 (107)	120 (78)	104 (53)	135 (141)	93 (86)	159 (36)	169 (99)	183 (64)
	3		213 (105)	123 (99)	129 (56)	137 (68)	114 (58)	144 (63)	174 (90)	152 (37)
	4		166 (133)	100 (76)	177 (50)	145 (82)	118 (104)	127 (58)	205 (121)	156 (50)
	5		221 (103)	122 (77)	166 (64)	137 (70)	131 (128)	130 (59)	149 96)	159 (24)
	6		230 (75) †	116 (86)	192 (35)	133 (96)	174 (129)	131 (63)	221 (130)	138 (52)
Latency line cross	1-6	S	45.8 ± 11.0	11.8 ± 3.0	16.5 ± 3.2	21.0 ± 8.3	29.3 ± 9.9	5.4 ± 1.3	12.4 ± 2.3	7.3 ± 1.1
Immobility duration	1	ns	5.0 ± 4.3	0.3 ± 0.3	1.8 ± 1.8	5.6 ± 2.7	0.0 ± 0.0	0.0 ± 0.0	0.2 ± 0.2	0.4 ± 0.4
	2		0.3 ± 0.2	2.1 ± 1.8	0.3 ± 0.3	4.0 ± 1.9	0.2 ± 0.2	0.1 ± 0.1	0.0 ± 0.	0.5 ± 0.5
	3		0.0 ± 0.0	1.3 ± 0.7	2.0 ± 1.3	5.4 ± 3.4	0.4 ± 0.4	0.0 ± 0.0	0.1 ± 0.3	0.2 ± 0.1
	4		5.6 ± 5.6	3.2 ± 2.5	2.2 ± 2.2	5.9 ± 4.2	0.4 ± 0.4	0.1 ± 0.1	0.6 ± 0.4	0.2 ± 0.1
	5		1.2 ± 0.8	0.6 ± 0.4	0.4 ± 0.4	1.8 ± 0.8	1.1 ± 0.8	0.3 ± 0.3	0.2 ± 0.2	0.1 ± 0.1
	6		0.5 ± 0.3	5.3 ± 4.9	0.3 ± 0.3	3.0 ± 1.9	1.5 ± 1.1	0.3 ± 0.3	0.4 ± 0.2	0.0 ± 0.0
Latency immobility	1-6	D	778.2 ± 240.9	830.7 ± 212.6	1087.3 ± 51.2	526.0 ± 206.0	1559.2 ±64.8*	1531.7±175.7*	832.9 ± 12.6	1070.6 ± 248.7
Rearings	1	T	2 (3)	2 (9)	1 (2)	5 (6)	2 (4)	4 (4)	2 (14)	6 (9)
	2		3 (21)	9 (17)	6 (8)	12 (11)	1 (6)	10 (11)	10 (17)	7 (8)
	3		19 (34)	9 (10)	12 (14)	16 (15)	4 (13)	17 (9)	11 (18)	14 (15)
	4		26 (30)	16 (16)	18 (14)	15 (17)	7 (16)	13 (9)	28 (27)	18 (22)
	5		32 (30) †	15 (17)	32 (14)	25 (31)	9 (20)	28 (3) †	22 (22)	18 (21)
	6		37 (36) †	16 (23)	52 (16) †	20 (43)	12 (27)	27 (22) †	30 (17)	17 (16) †
Latency rearing	1-6	S	349.9 ± 102.1	263.9 ± 108.3	269.0 ± 72.9	233.5 ± 110.9	635.9 ± 262.4	234.2 ± 102.4	151.2 ± 51.4	200.5 ± 107.8

[Table A4 continues on next page]

[Table A4 continued]

Grooming duration	1	S, D	1.5 ± 0.5	1.6 ± 0.6	2.8 ± 1.5	9.5 ± 3.3	9.7 ± 5.7	1.9 ± 0.6	1.0 ± 0.4	4.0 ± 1.2
	2		2.8 ± 1.3	3.9 ± 1.2	1.6 ± 0.6	5.3 ± 1.7	5.4 ± 1.6	10.6 ± 4.2	7.6 ± 2.2	3.1 ± 1.4
	3		4.2 ± 1.4	3.1 ± 1.7	6.0 ± 2.8	7.4 ± 2.3	0.7 ± 0.4	8.9 ± 3.6	5.9 ± 1.0	10.5 ± 3.3
	4		3.7 ± 1.3	5.7 ± 2.3	1.3 ± 0.6	10.0 ± 4.4	12.1 ± 4.9	8.9 ± 2.1	5.5 ± 2.0	8.6 ± 3.2
	5		2.4 ± 0.9	3.7 ± 2.5	3.7 ± 1.3	9.7 ± 4.9	4.0 ± 1.9	6.1 ± 3.4	11.0 ± 4.4	12.4 ± 3.5
	6		2.4 ± 1.0	5.3 ± 2.2	2.8 ± 1.0	4.3 ± 1.9	5.9 ± 2.5	5.5 ± 1.6	3.6 ± 1.3	10.2 ± 3.8
Latency self-groom	1-6	ns	372.9 ± 56.2	443.5 ± 73.0	479.5 ± 119.0	539.5 ± 44.9	415.0 ± 47.0	448.0 ± 62.3	414.7 ± 33.3	226.1 ± 38.4
Defecation	1-6	S	13 (3)	8 (2)	7 (4)	8 (7)	10 (4)	8 (2)	12 (9)	6 (3) ^

Data are represented as mean ± SEM for continuous numerical data, for discrete numerical data on the ordinal scale the results are represented as median with in parentheses IQR. Multivariate repeated measures ANOVA was performed with time interval as within factor and strain and dose as between factor. Latencies and defecation parameter were analyzed with a two-way ANOVA with strain and dose as main factors.

‡ The open field test of 30 minutes was divided in 6 bins of 5 minutes each (time interval). Number and duration of a specific behavioural parameter were calculated per time interval except for the latency and defecation, which is given only once per whole trial.

@ Significant ANOVA effects: S = strain effect; T = time interval effect; D = dose effect; T*S interaction; T*D interaction; S*D interaction; ns = non-significant. Thresholds of significance used for the ANOVA analyses, according to the Dunn- Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A1 for the corrected P values).

Significant *post hoc* differences are shown as: * = vs. vehicle, ^ = vs. BALB/c, † = vs. time interval 1. Thresholds of significance used for *post hoc* comparisons can also be found in Table A1

Table A5: Overview of CORT levels before (basal) and after behavioural testing (non-basal) in the OF after diazepam or MPEP treatment.

		ANOVA	BALB/c		129P3	
		effects @	basal	non-basal	basal	non-basal
diazepam	vehicle	B, S, D, S*D	191.8 ± 27.4	391.5 ± 35.4 *	265.3 ± 45.0	445.9 ± 29.5 *
	1 mg/kg diazepam		245.8 ± 57.5	372.3 ± 34.8	221.4 ± 67.9	253.3 ± 54.4
	3 mg/kg diazepam		282.6 ± 53.6	263.8 ± 32.4	163.7 ± 7.8a	551.1 ± 128.2 *
	5 mg/kg diazepam		183.6 ± 30.4	211.3 ± 34.6b	232.3 ± 36.9a	589.5 ± 100.7 # *
MPEP	vehicle	B, S	191.8 ± 27.4	391.5 ± 35.4 *	265.3 ± 45.0	445.9 ± 29.5 *
	3 mg/kg MPEP		159.6 ± 22.3	398.0 ± 44.6 *	293.0 ± 53.8	446.8 ± 85.0
	10 mg/kg MPEP		179.4 ± 26.7	353.0 ± 37.8 *	293.7 ± 75.5	375.4 ± 82.5
	30 mg/kg MPEP		131.8 ± 10.6	425.3 ± 81.6 *	194.3 ± 30.3	460.3 ± 110.7

Data are presented as mean nmol/l ± SEM. Multivariate repeated measures ANOVA was performed with basal/non-basal as within factor and strain and dose as between factor.

@ Significant ANOVA effects: B = basal/non-basal effect; S = strain effect; D = dose effect; S*D interaction. Threshold of significance used for the ANOVA analyses, according to the Dunn- Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A1 for the corrected P values)

Significant *post hoc* effects are shown as: * = vs. vehicle, # = vs. BALB/c. Thresholds of significance used for *post hoc* comparisons can also be found in Table A1.

Table A6: Overview of c-Fos positive cells after behavioural testing in the OF after treatment with vehicle, 1 mg/kg diazepam or 10 mg/kg MPEP.

Brain area	subdivision	ANOVA effects @	BALB/c vehicle	BALB/c 1 mg/kg diazepam	BALB/c 10 mg/kg MPEP	129P3 vehicle	129P3 1 mg/kg diazepam	129P3 10 mg/kg MPEP
Medial prefrontal cortex	PrL	S, Tr, S*Tr	157.8 ± 18.5	97.9 ± 6.8 *	93.6 ± 17.6 *	65.4 ± 14.9 #	47.4 ± 11.2 #	105.7 ± 11.3 *
Lateral septum	LSD	S, Tr	47.6 ± 10.8	18.8 ± 10.8	21.9 ± 9.9	11.8 ± 7.4 #	4.0 ± 3.0	6.3 ± 2.3
	LSI	ns	35.4 ± 9.7	22.0 ± 5.4	20.4 ± 3.8	19.1 ± 5.7	18.4 ± 4.9	16.9 ± 4.5
	LSV	Tr	64.9 ± 20.2	26.6 ± 4.5	22.9 ± 7.6 *	48.4 ± 14.8	36.9 ± 15.3	17.7 ± 9.5 *
Bed nucleus stria terminalis	BSTMA	ns	62.3 ± 7.6	37.9 ± 12.2	67.5 ± 11.0	40.6 ± 7.7	48.8 ± 5.6	82.9 ± 14.3
	BSTLP	S*Tr	62.6 ± 11.1	38.5 ± 6.2	51.0 ± 8.0	29.0 ± 5.0	58.4 ± 10.5	71.6 ± 11.1 *
	BSTMV	ns	23.2 ± 2.9	27.6 ± 6.2	22.9 ± 5.2	19.8 ± 5.4	30.6 ± 6.6	58.0 ± 18.0
Hippocampus	DG	S	72.3 ± 12.2	73.2 ± 10.9	73.8 ± 10.2	25.0 ± 6.0 #	25.5 ± 4.3 #	48.2 ± 14.7
Hypothalamus	PVN	S, Tr , S*Tr	101.3 ± 20.6	44.8 ± 8.5 *	75.9 ± 11.4	120.5 ± 20.7	58.0 ± 16.0	20.6 ± 5.8 # *
	DMH	S, Tr	138.8 ± 33.4	114.9 ± 19.4	53.9 ± 17.4 *	89.9 ± 8.0	61.5 ± 8.2 *	40.0 ± 5.8 *
Amygdala	BLA	S*Tr	51.9 ± 9.1	39.2 ± 5.9 *	41.1 ± 5.2	42.9 ± 4.9	18.1 ± 2.6 *	31.3 ± 3.2 *
	cAmy	ns	35.5 ± 8.6	34.2 ± 5.8	28.8 ± 8.0	40.7 ± 5.6	18.7 ± 3.4	21.9 ± 4.7
Periaqueductal gray	dlPAG	ns	119.9 ± 13.9	77.6 ± 8.9	56.0 ± 14.1	63.4 ± 10.3	63.9 ± 7.9	69.9 ± 6.7
	dmPAG	ns	2.2 ± 26.3	57.7 ± 22.1	31.8 ± 12.7	35.8 ± 14.0	52.6 ± 18.9	43.5 ± 15.2
	lPAG	ns	108.9 ± 14.1	85.7 ± 12.3	66.1 ± 17.1	106.2 ± 19.9	105.5 ± 13.8	76.7 ± 4.5
	vlPAG	Tr	85.4 ± 13.7	60.2 ± 5.8	46.9 ± 7.0 *	98.9 ± 21.9	70.6 ± 7.1	56.5 ± 4.4 *

Abbreviations: PrL (prelimbic cortex), LSD (dorsal lateral septum), LSI (intermediary lateral septum), V (ventral lateral septum), BSTMA (bed nucleus of the stria terminalis, medial anterior part), BSTLP (bed nucleus of the stria terminalis, lateral posterior part), BSTMV (bed nucleus of the stria terminalis, medial ventral part), DG (dentate gyrus), PVN (paraventricular nucleus), DMH (dorsal medial hypothalamus), BLA (basolateral amygdala), cAmy (central nucleus of the amygdala), dlPAG (dorsolateral part of periaqueductal grey), dmPAG (dorsomedial part of the periaqueductal grey), lPAG (lateral part of the periaqueductal grey) and the vlPAG (ventrolateral part of the periaqueductal grey).

Results are represented as the mean number of c-Fos positive cells per mm^2 (± SEM). A two-way ANOVA was performed with strain and treatment as main factors.

@ Significant ANOVA effects: S = strain effect; Tr = treatment effect; S*Tr interaction effect; ns = non-significant. Thresholds of significance used for ANOVA analyses, according to the Dunn- Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A1 for the corrected P values).

Significant *post hoc* differences are shown as: * = vs. vehicle # = vs. BALB/c. Thresholds of significance used for *post hoc* comparisons can also be found in Table A1.

Table A7: **Overview of behavioural parameters measured in the object recognition test.**

		BALB/c			129P3		
	ANOVA effects @	vehicle	diazepam	MPEP	vehicle	diazepam	MPEP
Discrimination Index (DI)	S	0.28 ± 0.06	0.20 ± 0.08	0.31 ± 0.04	-0.05 ± 0.15 #	0.06 ± 0.05	0.16 ± 0.08
Latency novel object [sec]	ns	23.1 ± 4.4	21.2 ± 2.6	51.4 ± 8.1	18.0 ± 3.3	24.8 ± 5.2	28.5 ± 4.7
Latency familiar object [sec]	ns	23.5 ± 5.1	18.9 ± 2.4	43.7 ± 9.6	23.8 ± 5.4	31.4 ± 5.6	32.3 ± 6.8
Time novel object [%]	ns	7.1 ± 1.3	5.8 ± 1.2	5.5 ± 0.9	4.3 ± 0.9	5.9 ± 0.7	5.6 ± 0.6
Time familiar object [%]	ns	4.0 ± 0.7	4.1 ± 0.9	2.8 ± 0.4	4.1 ± 0.5	5.0 ± 0.4	4.1 ± 0.5
Stretched attends [nr]	Tr	5.5 (4.5)	6.0 (6.5)	17.5 (12.5)	11.0 (11.0)	12.0 (5.5)	5.0 (6.5)
Line crossings [nr]	S	159.5 (68.0)	176.0 (35.5)	149.5 (38.5)	91.0 (94.0) #	60.0 (67.5) #	69.0 (56.0) #
Immobility duration [%]	S	0.5 ± 0.3	0.3 ± 0.1	0.3 ± 0.2	11.8 ± 4.5 #	23.4 ± 5.4 #	11.7 ± 3.4 #
Latency immobility	S	425.7 ± 75.5	405.3 ± 76.5	479.8 ± 74.5	169.7 ± 37.3 #	140.3 ± 29.8 #	190.7 ± 30.4 #
Rearings [nr]	S	85.5 (30.5)	126.0 (38.0)	77.5 (74.0)	30.0 (75.0)	10.0 (27.5)	19.0 (28.0)
Grooming [%]	ns	2.2 ± 0.5	1.3 ± 0.4	1.6 ± 0.4	2.1 ± 0.4	1.1 ± 0.3	1.8 ± 0.3
Latency groom [sec]	Tr	189.5 ± 20.4	300.9 ± 37.5 *	172.7 ± 11.2	223.7 ± 44.4	302.6 ± 41.4 *	188.2 ± 27.7 *

Data are presented as mean ± SEM for continuous data, for discrete data on the ordinal scale the results are presented as median with in parentheses IQR. Two-way ANOVA was performed using strain and treatment as main factors.

@ Significant ANOVA effects: S = strain effect; T = time interval effect; D = dose effect; T*S interaction; T*D interaction; S*D interaction; ns = non-significant. Thresholds of significance used for the ANOVA analyses, according to the Dunn- Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A2 for the corrected P values).

Significant *post hoc* differences are shown as: * = vs. vehicle, ^ = vs. BALB/c, † = vs. time interval 1. Thresholds of significance used for *post hoc* comparisons can also be found in Table A2.

Table A8: Overview of CORT levels before (basal) and after behavioural testing (non-basal) in the ORT after diazepam or MPEP treatment

	ANOVA	BALB/c		129P3	
	effects @	basal	non-basal	basal	non-basal
vehicle	B, S	136.4 ± 16.6	402.6 ± 136.7 *	270.9 ± 45.3	1059.3 ± 159.8 # *
1 mg/kg diazepam		172.3 ± 20.7	438.9 ± 82.7	325.4 ± 86.1	774.2 ± 164.1
10 mg/kg MPEP		153.0 ± 14.3	389.5 ± 69.9	382.3 ± 109.8	108.9 ± 47.3

Data are presented as mean nmol/l ± SEM. Multivariate repeated measures ANOVA was performed with basal/non-basal as within factor and strain and treatment as between factor.

@ Significant ANOVA effects: B = basal/non-basal effect; S = strain effect. Threshold of significance used for the ANOVA analyses, according to the Dunn-Šidák correction for multiple comparisons (see Experimental procedures 2.8 and Table A2 for the corrected P values)

Significant *post hoc* effects are shown as: * = vs. vehicle, # = vs. BALB/c. Thresholds of significance used for *post hoc* comparisons can also be found in Table A2.