Supplementary Figure 1
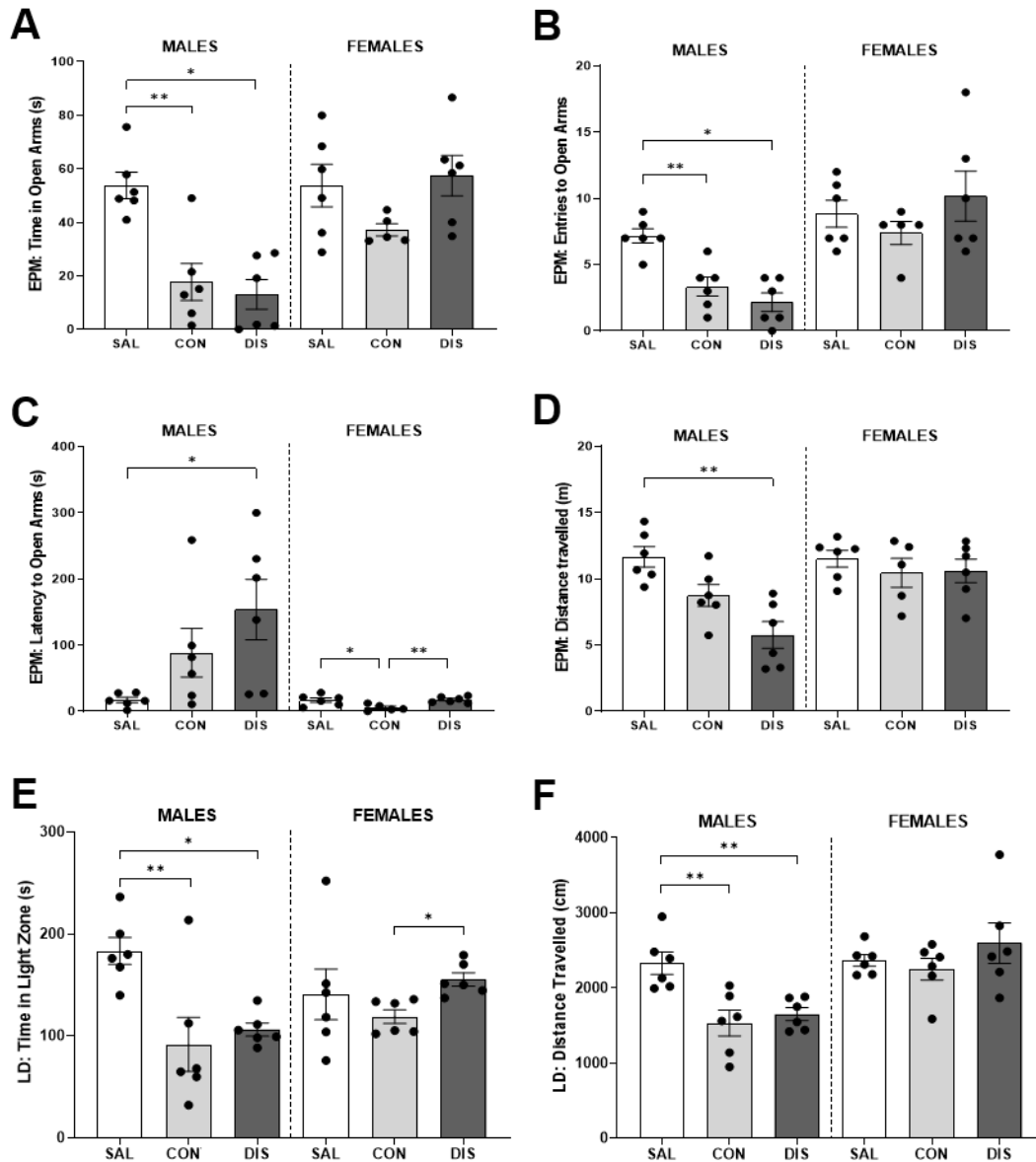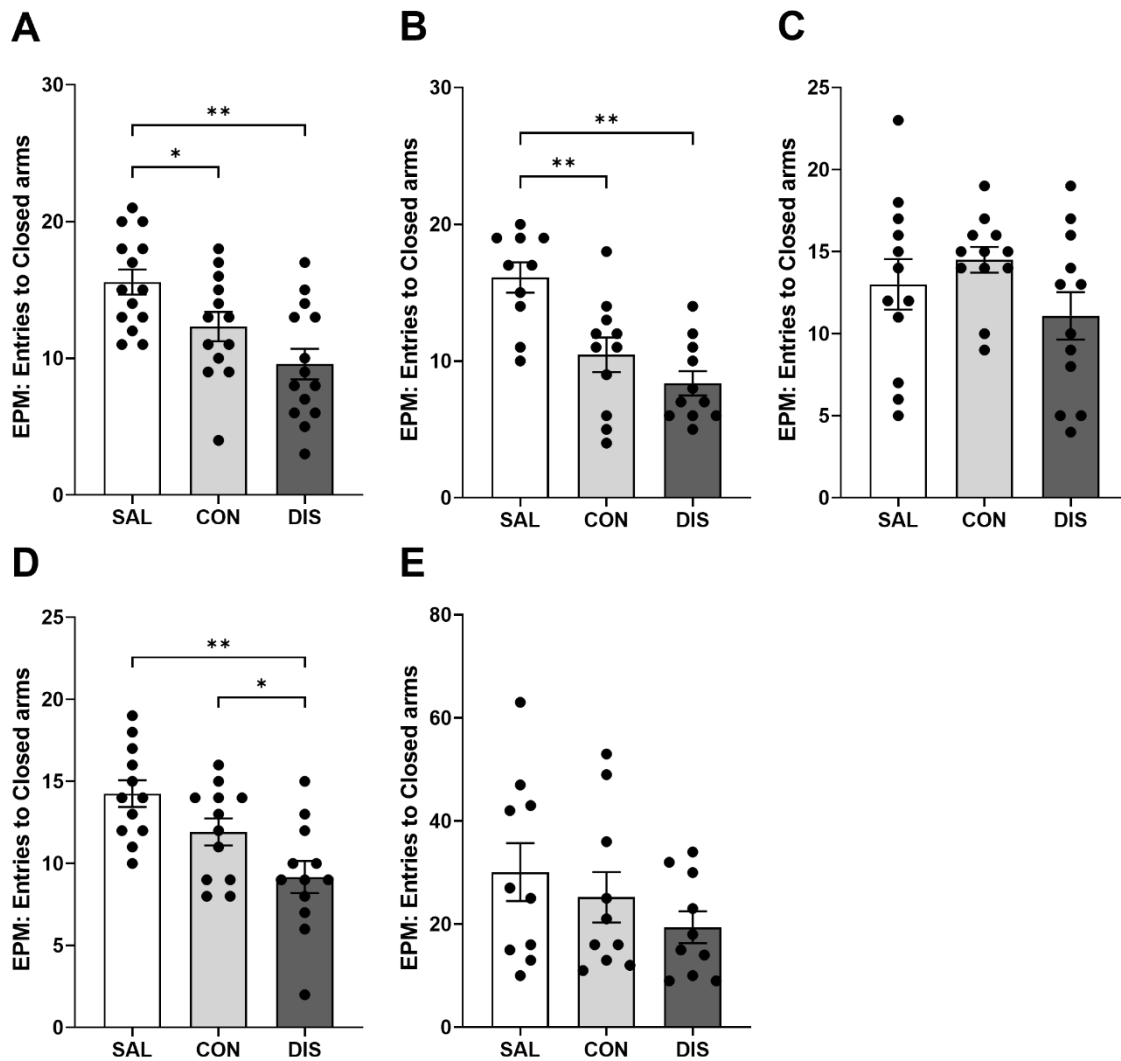

Effect of discontinuation from 12 days of once-daily paroxetine treatment in male and female mice on the elevated plus maze (EPM; 300 s) and the light/dark box (LDB; 300 s). Bars represent the mean ± SEM values for time spent in open arms (males: p=0.0309 SAL vs CON, p=0.0030 SAL vs DIS) (A), entries to open arms (males: p=0.0285 SAL vs CON, p=0.0009 SAL vs DIS) (B), latency to enter the open arms (males: p=0.0157 SAL vs DIS; females: p=0.0355 SAL vs CON, p=0.0189 CON vs DIS) (C) and distance travelled (males: p=0.0001 SAL vs DIS) (D) on the EPM, and time spent in the light zone (males: p=0.0058 SAL vs CON, p=0.0231 SAL vs DIS; females: p=0.00110 CON vs DIS) (F) and distance travelled (males: p=0.0069 SAL vs CON, p=0.0049 SAL vs

DIS) (G) on the LDB. SAL, Saline (males n=6, females n=6); CON, Continuation (males n=6, females n=5, one female mouse excluded due to technical issues during testing); DIS, Discontinuation (males n=6, females n=6). Individual values are indicated by dots. Kruskal-Wallis followed by post-hoc Fisher's LSD, * $p < 0.05$, ** $p < 0.01$.

Supplementary Figure 2

Effect of discontinuation from paroxetine or citalopram treatment in male mice on the closes arm entries on the elevated plus maze (EPM; 300 s). Bars represent the mean ± SEM values for number of entries to the closed arms following discontinuation from 12-days once-daily paroxetine (p=0.0336 SAL vs CON, p=0.0002 SAL vs DIS) (A), 28-days of once-daily paroxetine (p=0.0012 SAL vs CON, p<0.0001 SAL vs DIS) (B), 7-days once-daily paroxetine (C), 12-days twice-daily paroxetine (p=0.0002 SAL vs DIS, p=0.0331 CON vs DIS) (D) and 12-days twice-daily citalopram (E). SAL, Saline (n=10-14); CON, Continuation (n=10-14); DIS, Discontinuation (n=10-14). Individual values are indicated by dots. One-way ANOVA followed by post-hoc Fisher's LSD, * p<0.05, ** p<0.01.

Supplementary Table 1

Effect of Saline (SAL), Continuation (CON) or Discontinuation (DIS) treatments with 12-days once-daily paroxetine in male and female mice. LMA, locomotor activity (60 min); AOF, aversive open field (600 s). Each value is a mean ± S.E.M.

Parameter	MALES (n=6/group)				FEMALES (n=6/group)			
	Kruskal Wallis	Group (mean ± SEM)			Kruskal Wallis	Group (mean ± SEM)		
		SAL	CON	DIS		SAL	CON	DIS
LMA								
Total beam breaks	H(2)=1.906 p=0.408	2325 ± 239	1974 ± 163	1857 ± 147	H(2)=4.433 p=0.108	2677 ± 140	2314 ± 181	3274 ± 461
Total rearings	H(2)=2.854 p=0.251	175 ± 17	165 ± 10	191 ± 5	H(2)=1.556 p=0.484	162 ± 19	179 ± 14	196 ± 13
AOF								
Time in centre (s)	H(2)=0.737 p=0.715	13.7 ± 2.5	24.2 ± 9.3	11.2 ± 3.0	H(2)=0.924 p=0.652	11.1 ± 1.5	14.9 ± 4.6	22.3 ± 7.5
Distance travelled (m)	H(2)=3.591 p=0.170	50.1 ± 4.5	40.3 ± 5.1	45.5 ± 3.7	H(2)=0.947 p=0.640	58.8 ± 3.7	54.0 ± 6.6	74.5 ± 16.2

Supplementary Table 2

Effect of Saline (SAL), Continuation (CON) or Discontinuation (DIS) treatments with 28-day once-daily paroxetine in male mice. LMA, locomotor activity (60 min); AOF, aversive open field (600 s); LDB, light/dark box (600 s). 1 mouse excluded from the LMA onwards due to receiving the wrong injection the night before; 1 mouse excluded from the LMA due to issues with the photobeam box during testing. Each value is a mean ± S.E.M., and the statistical outcomes of pairwise comparisons were: SAL vs DIS $*p<0.05$; SAL vs CON $†p<0.05$, $††p<0.01$.

| | ANOVA/ | Paroxetine (n=12/group) | | |
| | | Group (mean ± SEM) | | |
	Kruskal Wallis	SAL	CON	DIS
LMA				
Total beam breaks	$F_{(2,31)}=3.872$ $p=0.032$	2522 ± 154	2061 ± 148 $†$	2044 ± 110 $*$
Total rearings	$F_{(2,31)}=0.336$ $p=0.717$	167.2 ± 14.5	181.5 ± 8.7	169.3 ± 15.5
AOF				
Time in centre (s)	$F_{(2,32)}=2.327$ $p=0.114$	11.9 ± 1.0	8.5 ± 1.6	7.8 ± 1.7
Distance travelled (m)	$F_{(2,32)}=10.01$ $p<0.001$	64.6 ± 4.7	40.1 ± 3.0 $††$	49.8 ± 4.0 $*$

Supplementary Table 3

Effect of Saline (SAL), Continuation (CON) or Discontinuation (DIS) treatments with 12-days twice-daily paroxetine in male mice. LMA, locomotor activity (60 min); AOF, aversive open field (600 s); FC, fear conditioning; CS, conditioned stimulus. 1 SAL and 1 CON mouse excluded due to technological issues on training day. Each value is a mean ± S.E.M., and the statistical outcomes of pairwise comparisons were: SAL vs DIS *p<0.01; SAL vs CON †p<0.05.

	Paroxetine (n=11-12/group)		
	ANOVA/	Group (mean ± SEM)	
	Kruskal Wallis	SAL	CON	DIS
LMA				
Total beam breaks	$F_{(2,33)}=0.073$, p=0.929	1913.7 ± 161.7	1906.8 ± 137.4	1839.5 ± 134.3
Total rearings	$F_{(2,33)}=1.293$, p=0.288	190.4 ± 10.4	170 ± 10.4	173.1 ± 6.3
AOF				
Time in centre (s)	$F_{(2,32)}=2.167$, p=0.1306	6.6 ± 0.9	3.8 ± 1.0	5.7 ± 1.0
Distance travelled (m)	$F_{(2,33)}=5.560$, p=0.0083	28.3 ± 1.8	21.6 ± 1.7 [†]	21.4 ± 1.5 *
FC				
Training day				
Δ Freezing (%)	$F_{(2,31)}=2.549$, p=0.0944	5.6 ± 1.8	-0.6 ± 1.8	2.4 ± 2.1
Test day				
Pre-CS freezing (%)	$F_{(2,31)}=0.2451$, p=0.7842	19.2 ± 6.6	25.6 ± 8.1	22.4 ± 4.0
Post-CS freezing (%)	$F_{(2,31)}=0.1248$, p=0.8831	39.3 ± 7.5	38.2 ± 8.9	43.1 ± 5.6
Δ Freezing (%)	$F_{(2.31)}=0.3106$, p=0.7353	19.9 ± 5.9	14.6 ± 4.5	19.03 ± 4.6

Supplementary Table 4

Effect of Saline (SAL), Continuation (CON) or Discontinuation (DIS) treatments with 12-days twice-daily citalopram in male mice. LMA, locomotor activity (60 min); AOF, aversive open field (600 s); FC, fear conditioning. Each value is a mean ± S.E.M.

	ANOVA/ Kruskal Wallis	Citalopram (n=10/group)		
		Group (mean ± SEM)		
		SAL	CON	DIS
LMA				
Total beam breaks	$F_{(2,27)}$=0.7999, p=0.4598	2491.0 ± 131.1	2190.0 ± 261.5	2298.0 ± 260.4
Total rearings	$F_{(2,27)}$=1.6710, p=0.0276	202.3 ± 6.6	156.1 ± 16.2	171.4 ± 10.0
AOF				
Time in centre (s)	$F_{(2,27)}$=0.4738, p=0.6279	9.1 ± 1.2	9.3 ± 1.0	8.9 ± 1.0
Distance travelled (m)	$F_{(2,27)}$=0.6227, p=0.5440	37.4 ± 3.0	32.3 ± 2.3	32.3 ± 3.1
FC				
Training day				
Δ Freezing (%)	$F_{(2,27)}$=0.9676, p=0.3928	6.8 ± 2.4	12.8 ± 3.1	8.0 ± 4.0
Test day				
Pre-CS freezing (%)	$F_{(2,27)}$=2.247, p=0.1073	17.0 ± 5.2	43.5 ± 9.0	26.3 ± 9.9
Post-CS freezing (%)	$F_{(2,27)}$=2.932, p=0.0704	60.5 ± 6.0	75.8 ± 5.3	53.3 ± 26.6
Δ Freezing (%)	$F_{(2,27)}$=1.215, p=0.3124	43.5 ± 6.5	33.3 ± 7.1	27.0 ± 8.9