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Effect of chronic pre-treatment with fluoxetine on anxiety response in a 3D spatial navigation test

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In previous studies (1, 2), we demonstrated that different strains of mice express fear and anxiety when exposed to an unfamiliar open space. In a 3D maze, which is a modified version of the radial arm maze, avoidance of the distal segment of the arms of the maze is used as an indicator of anxiety. Balb/c mice required four to five sessions to venture onto the distal part of the arms of the maze while C57/BL6J and CD-1 mice require one to two sessions, respectively. In the present study, we examined whether fluoxetine would facilitate crossing onto the distal part of the arms in BALB/c mice in 3 test sessions, one session a day. The drug was administered i.p. at 20 mg/kg for two weeks, and was continued to be injected to mice 30 min before exposure to the test apparatus during the subsequent 3 days. The maze (Grey PVC, 5 mm thick) consists of nine arms radiating from a central platform. Each arm (51 cm x 11.2 cm) is made from two segments, extended from a nonagonal shaped central hub. The first segment of an arm (15.2 cm x 11.2 cm) directly attached to the central platform can be tilted and constitutes a bridge that allows access to the second segment (35 cm x 11.2 cm) of the arm. In the present experiment, the bridge to each arm forms a slope which is inclined upward by about 40º. All parts of the maze apparatus are unprotected; hence mice are exposed to a complete open space. All data are expressed as mean ± s.e.m. Differences among group means values for each measurement were tested for significance with two-way ANOVA followed up with Newman–Keuls post-hoc comparisons. Results were considered significant with $p \leq 0.05$. All experiments were performed with full ethical approval under the Animals (Scientific Procedures) Act 1986

As shown in the table below, fluoxetine appears to facilitate crossings onto the distal part of the maze, hence indicating reduced anxiety in the first session of exposure to the open space.

	LAT. A	LAT. B	NUM. B	DUR. B	NUM. A	DUR. A
Saline	666.70 ±53.30	12.00 ±2.21	24 ±3.59	462.44 ±24.57	0.63 ±0.63	4.34 ±4.34
Fluoxetine	437.53 ±103.53	6.82 ±1.28	30.25 ±5.03	326.73 ±56.22	5.38 ±2.04	105.55 ±41.72
	p<0.05	p<0.05	p>0.10	p<0.04	p<0.04	p<0.03

Mean (± s.e.m.) of latency of first crossing onto an arm (LAT.), number (NUM.) and duration (DUR.) of crossings onto the bridges (B) and arms (A) of the maze.

In the second and third session, the number of crossings onto and time spent in the arms increased and the latency of first entry onto an arm decreased in both groups. There were significant differences between sessions 1 and 3 in each group on these parameters ($p<0.05$). Balb/c treated mice made many crossings onto the arms of the maze in the second (7.13 ±2.7) and third (21.38± 2.8) session. This reduced anxiety, in sessions 2 and 3, can only be accounted for by the day to day handling of mice for injection of saline over two weeks period. This handling could have masked the effect of fluoxetine

1. Ennaceur et al. (2011) Neuropharmacology 61: 981-991;
2. Ennaceur (2011) Behavioural Brain Research 223: 203– 210