Study or Subgroup	Fluoxetine Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
1.2.1 Higher doses										
Iñiguez 2010 20 mg	5.62	3.34	8	22.07	13.1	8	5.9%	-1.63 [-2.80, -0.45]	2010	
Homberg 2011 12 mg	13.84	8.87	10	23.78	9.28	10	6.4%	-1.05 [-2.00, -0.10]	2011	
Vorhees 2011 10 mg	21.58	15.99	20	25.45	15.72	20	7.0%	-0.24 [-0.86, 0.38]	2011	
Yoo 2013 10 mg	5.56	5.17	5	14.78	11.63	5	5.5%	-0.93 [-2.27, 0.42]	2013	
Amodeo 2015 Female 10 mg	41.34	13.1	9	46.77	10.55	9	6.4%	-0.43 [-1.37, 0.50]	2015	
Amodeo 2015 Male 10 mg	39.52	14.38	9	43.15	8.31	9	6.4%	-0.29 [-1.22, 0.64]	2015	
Sonei 2017 7.5 mg	5.37	4.29	8	12.9	3.24	8	5.7%	-1.87 [-3.11, -0.64]	2016	
Subtotal (95% CI)			**69**			**69**	**43.3%**	**-0.79 [-1.26, -0.32]**		

Heterogeneity: Tau² = 0.15; Chi² = 9.64, df = 6 (P = 0.14); I² = 38%

Test for overall effect: Z = 3.31 (P = 0.0009)

Study or Subgroup	Fluoxetine Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
1.2.2 Lower doses										
Oh 2009 B6 strain 3 mg	4.22	1.11	36	11.6	2.34	34	6.6%	-4.02 [-4.85, -3.19]	2009	
Oh 2009 SW strain 3 mg	6.08	1.97	29	6.53	2.44	31	7.2%	-0.20 [-0.71, 0.31]	2009	
Vorhees 2011 3 mg	22	15.99	20	25.45	15.72	20	7.0%	-0.21 [-0.84, 0.41]	2011	
Warren 2011 5 mg	30.77	9.3	7	34.36	12.34	7	6.1%	-0.31 [-1.36, 0.75]	2011	
Amodeo 2015 Female 5 mg	48.58	13.74	9	46.77	10.55	9	6.4%	0.14 [-0.78, 1.07]	2015	
Amodeo 2015 Male 5 mg	44.42	13.1	9	43.15	8.31	9	6.4%	0.11 [-0.81, 1.04]	2015	
Sadegzadeh 2020 Male 5 mg	40.61	24.96	8	38.47	17.14	8	6.3%	0.09 [-0.89, 1.08]	2020	
Sadegzadeh 2020 Female 5 mg	49.17	17.89	8	29.91	17.89	8	6.1%	1.02 [-0.04, 2.08]	2020	
Zolfaghari 2021 5 mg	14.25	5.19	7	36.46	6.79	7	4.4%	-3.44 [-5.27, -1.61]	2021	
Subtotal (95% CI)			**133**			**133**	**56.7%**	**-0.70 [-1.68, 0.29]**		

Heterogeneity: Tau² = 2.00; Chi² = 93.98, df = 8 (P < 0.00001); I² = 91%

Test for overall effect: Z = 1.39 (P = 0.16)

Study or Subgroup	Fluoxetine Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
Total (95% CI)			**202**			**202**	**100.0%**	**-0.77 [-1.36, -0.17]**		

Heterogeneity: Tau² = 1.20; Chi² = 104.13, df = 15 (P < 0.00001); I² = 86%

Test for overall effect: Z = 2.53 (P = 0.01)

Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.86), I² = 0%

Forest plot of effects of chronic fluoxetine at higher (7.5-20 mg/kg/day) or lower (3-5 mg/kg/day) doses vs. vehicle on anxiety-like behavior in naive animals measured as time spent in the open arms of the EPM. Note: Significance of the results was unchanged when effects of fluoxetine in the dose of 20 mg instead of 10 mg from Amodeo's et al. study were included in the higher dose subgroup (Online Resource ESM_4).