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DOI: 10.1503/jpn.130118

Emotion processing task

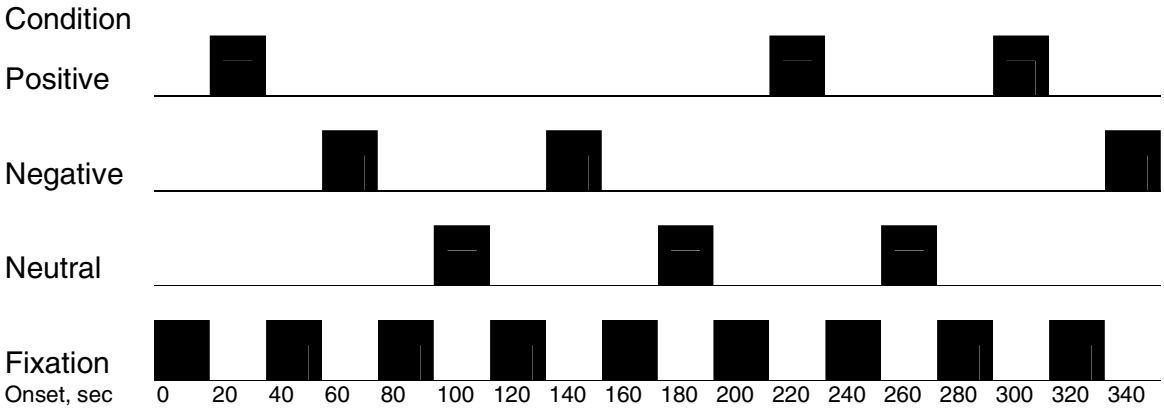
Emotion processing task design

Stimuli from the International Affective Picture System (IAPS[1]) were used to elicit negative and positive emotion processing.[2]

Box S1. List of IAPS image numbers in each form of the emotion processing task

Task Form A				Task Form B			
Positive	Neutral		Negative	Positive	Neutral		Negative
4525	2038	7040	1120	4505	2381	7025	1052
4660	2102	7041	1200	4656	2397	7052	1201
4681	2190	7050	1321	4659	2411	7056	1304
4687	2393	7053	1931	4668	2580	7059	1930
4698	2440	7080	1932	4670	2840	7060	3120
5621	2480	7090	3019	4677	5130	7110	3212
8001	2499	7100	5971	5629	5471	7150	3213
8034	2570	7185	6211	7405	5510	7175	3250
8158	2890	7187	6220	8030	5520	7179	6250
8163	7004	7205	6312	8179	5530	7224	6550
8178	7020	7217	6313	8185	5740	7490	6563
8180	7026	7233	6530	8186	7000	7705	6830
8206	7031	7235	9042	8193	7006	7900	6834
8492	7034	7491	9250	8370	7010	7950	8480
8496	7035	7700	9570	8490	7012	9360	9325

A block design was used with 3 blocks of arousing positively valanced pictures, 3 blocks of neutrally valanced pictures, 3 blocks of arousing negatively valanced pictures and 9 blocks of fixation crosses. Blocks of fixation crosses were followed by each IAPS picture block (see below). Emotional pictures were drawn from IAPS in accordance with the supplied normative ratings.[1] Each of the blocks consisted of 5 pictures that were presented for 4 seconds each. During all trials pictures were unique within and across sessions, with participants having been randomized to either of 2 forms of the task in their first session. Blocks of pictures were randomized within each form. Participants were trained using a PowerPoint presentation before entering the scanner. Images were displayed on an LCD screen and were viewed by participants through a mirror fixed to the fMRI scanner's head coil.



During the IAPS pictures, participants were asked to experience (or "feel") the emotions associated with the pictures and rate the valence of the pictures as 1) positive (thumb press), 2) neutral (index finger press) or 3) negative (middle finger press). In order to control for rating between emotional pictures and the fixation crosses, during presentation of the fixation crosses, participants were asked to rate the varying brightness of the backgrounds as 1) light (thumb press), 2) medium (index finger press) or 3) dark (middle finger press).

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Emotion processing task design analysis

The positive, neutral and negative categories were characterized with valence ratings ranging between 6.04 and 7.94, 4.10 and 6.50, and 1.33 and 3.90, respectively, and arousal ratings ranging between 6.31 and 7.48, 1.87 and 3.01, and 6.35 and 7.49, respectively. Compositional elements were not controlled in addition to the aforementioned constraints, as this was deemed impossible.

A multivariate analysis of variance (MANOVA) demonstrated that there were no significant valence category × form effects, Wilk $\lambda = 0.967$, $F_{8, 222} = 0.474$, $p = 0.87$, indicating that valence, arousal, brightness (mean RGB; as determined by luminosity histogram plots in Adobe Photoshop), and contrast (standard deviation RGB) levels were equal between blocks of the same valence category across forms of the task.

Manipulation checks

This section contains the methods and results of the hormonal, behavioural and neurophysiological manipulation checks that were conducted to test for potential between-subject carry-over effects between treatment sessions.

Supplementary methods

Hormonal data analysis

First, participants provided saliva samples (1 mL) for estradiol and progesterone analysis before treatment administration at each session. The hormonal saliva samples were stored frozen until assay. On the day of assay, samples were thawed for determination of salivary progesterone and estradiol using commercially available kits (Salimetrics) according to the manufacturer's instructions. Thawed samples were centrifuged at 1500 × g for 15 minutes to collect clear saliva, which was used without further processing for all assays. All samples were brought to room temperature before adding to assay wells, and all samples were analyzed in duplicate. Hormonal menstrual phase was determined in accordance with previous research.[3,4] In order to check for equal proportions of participant menstrual phase within treatment sessions and equal proportions of participants using hormonal contraceptives in each order of treatment, χ^2 tests were conducted in SPSS Statistics software version 19. Hormone concentrations were entered in regression analyses to determine the associations between hormone levels and the individual percent signal changes extracted from the amygdala and inferior frontal gyrus (IFG) regions of interest (ROIs; the methods for obtaining the individual percent signal change values are described in the main article) associated with the emotion processing task.

Behavioural data analysis

Responses on the Positive Affect and Negative Affect Scales (PANAS;[5]) at each session before and 4 hours after treatment administration were assessed to examine change in subjective affect associated with participation. Potential treatment condition unblinding was determined by asking participants to guess which treatment they received and whether they experienced side effects at each session.

In order to check for manipulation of participant affect before and after treatment administration, between treatment sessions a repeated-measures MANOVA was performed with the PANAS data entered. To examine potential unblinding of treatment condition owing to guessing the treatment condition and experiencing side effects, χ^2 tests were performed. To examine the effect of guessing the drug condition and side effects on blood oxygen level–dependent (BOLD) activation during emotion processing under each treatment condition, a repeated-measures MANOVA, with the individual percent signal changes extracted from the ROIs for each condition entered as dependent variables.

To test for correct manipulation during the emotion processing task within treatment sessions, subjective ratings of each stimulus block were assessed along a negativity scale ranging from –1 to 1, with 1 corresponding to ratings of negative valence. A repeated-measures MANOVA was then conducted with the subjective ratings for each condition entered to test for changes in subjective ratings between treatment sessions. To examine the association between subjective ratings and BOLD activation during emotion processing under each treatment condition, simple regressions were performed. The dependent variables were the individual percent signal changes extracted from the ROIs for each condition, and the predictors were the IAPS ratings for each respective condition.

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Neurophysiological data analysis

As the task-related BOLD signal from pharmaco-fMRI studies may be confounded by drug-related cerebral blood flow effects,[6] a visual stimulation control analysis was devised. The fixation condition from the emotion processing experiment was used as the control, whereby participants' BOLD response of the fixation condition was compared between escitalopram and placebo conditions. The fixation contrasts from each treatment session were entered into a paired *t* test model at the second level. The calcarine cortex was identified as an ROI, as it was reliably activated by photic stimulation. Percent signal changes from the calcarine cortex ROI of each participant was extracted in order to determine the reliability of the photic stimulation. Significant differential effects in this ROI between treatments may indicate differences in cerebral blood flow effects.

Supplementary results

Hormonal results

The χ^2 tests demonstrated that participants were equally distributed between menstrual phases at the placebo ($\chi^2_2 = 0.500$, $p = 0.78$) and escitalopram ($\chi^2_2 = 2.000$, $p = 0.37$) treatment sessions. The number of participants who took hormonal contraceptives was equal to the number who did not. Hormonal contraceptive status was equally distributed between those who received placebo or escitalopram at their first session ($\chi^2_1 = 1.003$, $p = 0.32$).

The regression analyses on the percent signal changes for each task and treatment condition for the amygdala and IFG ROIs showed no significant predictive associations with progesterone or estradiol concentration (all $p > 0.05$). In addition, there was no differences of percent signal changes for each task and treatment condition between those who took hormonal contraceptives and those who did not (amygdala: $F_{1, 34} = 1.626$, $p = 0.21$; IFG: $F_{1, 34} = 0.414$, $p = 0.52$).

Behavioural results

With respect to the PANAS scales, the repeated-measures MANOVA demonstrated that there were no significant treatment or time × treatment effects (Wilk $\lambda = 0.937$, $F_{2, 34} = 1.151$, $p = 0.33$), indicating that there was no effect of treatment administration on subjective affect. Instead, a significant effect of time (Wilk $\lambda = 0.443$, $F_{2, 34} = 21.367$, $p < 0.001$, $\eta^2 = 0.557$) suggested that participation in the sessions, regardless of treatment, was associated with a change in affect. Follow-up repeated-measures ANOVAs revealed that positive affect significantly changed over participation in the sessions ($F_{1, 35} = 38.865$, $p < 0.001$, $\eta^2 = .526$), whereas negative affect did not change significantly ($F_{1, 35} = 2.022$, $p = 0.16$). Follow-up pairwise comparisons showed that there were no significant differences of affect between treatments at each time point (all $p > 0.05$). There were significant decreases between time points for both treatments on positive affect (all $p < 0.001$), but not negative affect (all $p > 0.05$). Post hoc analysis revealed that participants decreased ratings on the items "excited," "strong," "alert," "attentive," "active," "interested," "enthusiastic," "inspired" and "determined" from pre- to postsession, suggesting that participants became fatigued and habituated to the testing environment.

Correct treatment condition guessing (unblinding) occurred in 66% of the sample and occurred in a greater proportion than would be expected by chance ($\chi^2_1 = 4.000$, $p = 0.046$). Side effects occurred in 47% of the sample, yet did not occur in a greater proportion than would be expected by chance ($\chi^2_1 = 0.111$, $p = 0.74$). There was a significant association between the subjective experience of side effects and correct treatment guessing ($\chi^2_1 = 6.743$, $p = 0.009$).

The subjective ratings were successfully recorded in both treatment sessions for 33 of the participants: there were technical difficulties with the recording of the responses of the remaining participants. Under the escitalopram condition, participants rated the positive, negative and neutral IAPS images as positive (mean –0.48 ± standard deviation [SD] 0.51), negative (0.92 ± 0.14) and neutral (–0.03 ± 0.09), respectively. Under the placebo condition, participants also rated the positive, negative and neutral IAPS images as positive (mean –0.66 ± SD 0.34), negative (0.86 ± 0.20) and neutral (–0.03 ± 0.14), respectively. There was no significant effect of treatment on rating (Wilk $\lambda = 0.849$, $F_{3, 30} = 1.778$, $p = 0.17$).

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Under each treatment condition, the subjective ratings of positive, negative and neutral IAPS blocks did not predict percent signal change for the amygdala or IFG (all $p > 0.05$). There were no significant differences of percent signal changes for each task and treatment condition between those who correctly guessed treatment conditions and those who did not (amygdala: $F_{1, 32} = 0.102$, $p = 0.75$; IFG: $F_{1, 32} = 0.317$, $p = 0.57$), between those who experienced side effects (amygdala: $F_{1, 32} = 0.123$, $p = 0.73$; IFG: $F_{1, 32} = 0.075$, $p = 0.79$), or between those who guessed correctly and experienced side effects (amygdala: $F_{1, 32} = 0.575$, $p = 0.45$; IFG: $F_{1, 32} = 0.173$, $p = 0.68$).

Neurophysiological results

The calcarine cortex was activated by the fixation condition across all participants in both treatment sessions, as indicated by positive percent signal change values. There was no significant effect of treatment on fixation cross presentation in this region (at a $p < 0.05$, partial volume, family-wise error [FEW]–corrected).

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Table S1: Whole brain analysis of the average effect of treatment and stimulus conditions*

Cluster	Peak					
	p value					
equivk	Uncorrected	FWE–corrected	FDR–corrected	*F*	equivZ	ROI, mm *x,y,z*
20654	0	0	0	113.36	Inf	–22, –86, –6
	0	0	0	94.87	Inf	–26, –76, –6
	0	0	0	80.77	Inf	24, –84, –6
642	0	0	0	19.77	Inf	24, –38, 8
	0	0	0	16.18	7.8	24, –32, 22
	0	0	0	11.89	6.62	32, –48, 4
730	0	0	0	19.15	Inf	–20, –40, 10
	0	0	0	16.46	Inf	–18, –32, 24
	0	0	0	13.91	7.22	–32, –52, 4
337	0	0	0	15.16	7.55	14, –50, 14
226	0	0	0	14.97	7.5	0, 8, 18
	0	0	0	12.22	6.72	–6, 4, 22
284	0	0	0	14.18	7.29	–2, 4, 8
	0	0	0.003	9.93	5.97	8 –2 12
162	0	0	0	13.67	7.15	0, –38, –44
277	0	0	0	12.3	6.75	6, –26, –12
	0	0	0.001	10.4	6.13	22, –26, –4
	0	0	0.012	9.17	5.69	8, –10, –4
450	0	0	0.001	10.8	6.27	–30, 22, –6 Left IFG
	0	0	0.012	9.24	5.71	–34, 28, –16
358	0	0	0.001	10.42	6.14	40, 6, 32 Right IFG
	0	0.001	0.026	8.79	5.54	50, 26, 22
	0	0.002	0.056	8.33	5.36	42, 16, 24
101	0	0	0.003	9.88	5.95	–28, 0, –12 Left amygdala
120	0	0	0.011	9.28	5.73	–16, –58, 12
	0	0.017	0.391	7.24	4.9	–12, –52, 2
468	0	0	0.012	9.22	5.71	2, 60, 18
	0	0	0.014	9.09	5.66	6, 52, 26
	0	0.001	0.027	8.75	5.53	–4, 50, 22
35	0	0	0.012	9.21	5.7	–6, –24, –12
19	0	0.001	0.027	8.73	5.52	–20, –26, –8
60	0	0.001	0.029	8.69	5.5	–40, 8, 28
254	0	0.001	0.033	8.61	5.47	34, 30, –12
	0	0.005	0.134	7.84	5.16	36, 28, –4
	0	0.007	0.175	7.68	5.09	38, 20, –22
99	0	0.001	0.036	8.56	5.45	–34, 14, –32
	0	0.002	0.072	8.19	5.3	–38, 18, –26
61	0	0.002	0.056	8.33	5.36	–8, 20, 48
	0	0.007	0.175	7.68	5.09	–8, 8, 58
32	0	0.003	0.085	8.1	5.27	10, 20, 42
25	0	0.006	0.161	7.74	5.12	4, –26, –28
17	0	0.008	0.188	7.63	5.07	60, –24, –2
12	0	0.014	0.34	7.33	4.93	–50, 24, 20
6	0	0.024	0.522	7.07	4.82	–8, 24, 30

FDR = false discovery rate; FWE = family-wise error; IFG = inferior frontal gyrus; ROI = region of interest.
*$p < 0.05$, FWE–corrected; degrees of freedom = 2, 210

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Table S2: Region of interest (amygdala and IFG) analysis of the effect of stimulus conditions ($p < 0.05$, uncorrected, $k_{1,210} = 20$) (part 1 of 3)

	Cluster				Peak					
	p value				*p* value					
Factor	Uncorrected	FWE–corrected	FDR–corrected	equivk	Uncorrected	FWE–corrected	FDR–corrected	*F*	equivZ	ROI, mm x,y,z
Main effect										
				196	0	0	0	22.14	5.89	–26, –2, –12 Left amygdala
					0	0	0	22	5.87	–28, 0, –16
				1547	0	0	0	22.13	5.89	–36, 26, –2 Left IFG
					0	0	0	18.26	5.33	–32, 28, –4
					0	0	0	18.17	5.32	–40, 24, –6
					0	0.001	0	14.83	4.76	–44, 20, –6
					0	0.044	0.005	10.33	3.88	–44, 16, 24
					0	0.071	0.008	9.71	3.74	–46, 12, 24
					0	0.124	0.014	8.97	3.56	–48, 16, 20
					0	0.157	0.018	8.66	3.49	–52, 36, –2
					0	0.163	0.018	8.6	3.47	–52, 32, –4
					0	0.193	0.022	8.37	3.41	–50, 36, –6
					0.001	0.532	1	6.75	2.98	–60, 12, 16
					0.006	0.891	1	5.33	2.54	–54, 8, 8
					0.006	0.918	1	5.17	2.49	–50, 30, 18
				1411	0	0	0	19.91	5.58	36, 26, –2 Right IFG
					0	0	0	18.99	5.44	48, 28, –4
					0	0	0	17.74	5.25	36, 24, 4
					0	0.001	0	15.95	4.96	44, 22, –2
					0	0.003	0	13.76	4.57	52, 24, 22
					0	0.019	0.002	11.38	4.1	44, 18, 24
					0	0.159	0.018	8.64	3.48	54, 26, 14
					0.002	0.638	1	6.37	2.87	52, 34, 18
					0.013	0.984	1	4.46	2.24	56, 36, 12
					0.031	1	1	3.52	1.87	40, 40, –14
				248	0	0	0	19.07	5.46	26, –2, –18 Right amygdala
Positive versus neutral										
Increased										
	0.039	0.255	0.125	1453	0	0	0	5.97	5.73	–36, 26, –4 Left IFG
					0	0	0	5.62	5.42	–32, 28, –4
					0	0	0	5.5	5.31	–40, 24, –6
					0	0.001	0	4.92	4.78	–44, 20, –6
					0	0.028	0.006	4.04	3.96	–42, 14, 22
					0	0.055	0.013	3.83	3.76	–46, 12, 24
					0	0.14	0.027	3.52	3.46	–44, 16, 6
					0	0.174	0.033	3.44	3.39	–46, 34, –10
					0.001	0.255	0.05	3.28	3.24	–48, 26, 20
					0.001	0.286	0.052	3.23	3.19	–50, 32, –2
					0.001	0.322	0.059	3.18	3.14	–50, 30, 18
					0.001	0.34	0.061	3.16	3.12	–48, 16, 12
					0.003	0.66	0.469	2.77	2.75	–44, 46, –8
					0.008	0.904	0.469	2.41	2.39	–52, 26, 12
	0.046	0.292	0.125	1347	0	0	0	5.59	5.4	36, 24, 4 Right IFG
					0	0.001	0	4.99	4.85	44, 22, –2
					0	0.002	0.001	4.7	4.58	50, 24, 22
					0.004	0.729	0.469	2.69	2.66	52, 34, 18
					0.004	0.762	0.469	2.65	2.62	56, 36, 10
					0.011	0.937	0.469	2.32	2.3	46, 52, 2

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Table S2: Region of interest (amygdala and IFG) analysis of the effect of stimulus conditions ($p < 0.05$, uncorrected, $k_{1,210} = 20$) (part 2 of 3)

	Cluster				Peak					
	p value				*p* value					
Factor	Uncorrected	FWE–corrected	FDR–corrected	equivk	Uncorrected	FWE–corrected	FDR–corrected	*F*	equivZ	ROI, mm x,y,z
					0.014	0.963	0.469	2.22	2.21	44, 54, 6
					0.021	0.989	1	2.04	2.03	46, 50, –2
					0.023	0.991	1	2	1.99	38, 42, –14
					0.026	0.994	1	1.95	1.95	42, 44, –14
	0.759	0.997	1	36	0.011	0.94	0.469	2.31	2.3	20, 2, –18 Right amygdala
Decreased										
Negative versus neutral										
Increased										
	0.431	0.962	1	192	0	0	0	6.51	6.2	–28, 0, –16 Left amygdala
					0	0	0	6.16	5.9	–26, –2, –12
					0	0.16	0.026	3.47	3.42	–16, –6, –18
	0.028	0.194	0.067	1668	0	0	0	6.05	5.8	46, 30, –2 Right IFG
					0	0	0	5.5	5.31	36, 26, –2
					0	0	0	5.33	5.16	36, 30, 0
					0	0	0	5.21	5.05	38, 24, –6
					0	0.004	0.001	4.56	4.45	52, 24, 26
					0	0.007	0.001	4.43	4.32	44, 14, 26
					0	0.212	0.037	3.36	3.31	52, 34, 18
					0.002	0.487	0.091	2.97	2.94	44, 34, –14
					0.006	0.835	0.241	2.54	2.52	40, 40, –14
					0.006	0.844	1	2.52	2.5	54, 38, 12
	0.368	0.938	0.426	248	0	0	0	5.97	5.73	26, –2, –18 Right amygdala
	0.033	0.22	0.067	1568	0	0	0	5.63	5.42	–36, 26, –2 Left IFG
					0	0.012	0.002	4.27	4.18	–46, 14, 0
					0	0.026	0.005	4.06	3.98	–50, 24, –4
					0	0.043	0.007	3.91	3.83	–52, 32, –4
					0	0.044	0.007	3.9	3.83	–52, 36, –2
					0	0.045	0.007	3.89	3.82	–44, 16, 24
					0	0.066	0.01	3.77	3.71	–46, 12, 24
					0	0.068	0.01	3.76	3.7	–50, 36, –6
					0	0.101	0.015	3.63	3.57	–50, 18, 22
					0	0.177	0.037	3.43	3.38	–46, 32, –10
					0.001	0.306	0.054	3.21	3.16	–48, 8, 16
					0.001	0.335	0.091	3.16	3.12	–60, 16, 16
					0.001	0.41	0.091	3.07	3.03	–54, 8, 8
					0.002	0.494	0.091	2.97	2.93	–58, 12, 12
	0.759	0.997	1	36	0.002	0.531	0.241	2.92	2.89	44, 52, –4 Right IFG
					0.003	0.675	0.241	2.76	2.73	46, 52, 2
Decreased	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Positive versus negative										
Increased										
	0.601	0.989	0.733	90	0.009	0.913	0.476	2.39	2.37	–50, 36, 22 Left IFG
					0.012	0.955	0.476	2.26	2.25	–48, 40, 20
Decreased										
	0.426	0.96	0.461	196	0	0	0	5.58	5.38	–24, –4, –12 Left amygdala
	0.369	0.939	0.461	247	0	0.006	0.004	4.44	4.34	26, –2, –18 Right amygdala
					0	0.009	0.004	4.36	4.27	24, 4, –16

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Table S2: Region of interest (amygdala and IFG) analysis of the effect of stimulus conditions ($p < 0.05$, uncorrected, $k_{1,210} = 20$) (part 3 of 3)

	Cluster				Peak					
	p value				*p* value					
Factor	Uncorrected	FWE–corrected	FDR–corrected	equivk	Uncorrected	FWE–corrected	FDR–corrected	*F*	equivZ	ROI, mm x,y,z
	0.476	0.973	1	159	0	0.194	0.061	3.39	3.35	–60, 12, 16 Left IFG
					0.002	0.557	0.171	2.89	2.86	–40, 8, 6
					0.003	0.697	0.202	2.73	2.7	–56, 8, 6
					0.004	0.707	0.215	2.72	2.69	–36, 8, 10
					0.017	0.979	0.653	2.13	2.12	–52, 8, 2
	0.561	0.986	1	109	0.001	0.393	0.124	3.09	3.05	52, 10, –4 Right IFG
					0.002	0.572	0.171	2.88	2.85	52, 10, 2
	0.632	0.992	1	77	0.006	0.832	0.304	2.54	2.52	50, 30, –4 Right IFG
					0.023	0.991	0.653	2	2	38, 32, 0
					0.033	0.997	1	1.84	1.84	48, 30, 4
					0.034	0.998	1	1.82	1.82	44, 28, 6

FDR = false discovery rate; FWE = family-wise error; IFG = left inferior frontal gyrus; NS = not significant; ROI = region of interest.

Table S3: Region of interest (amygdala and IFG) analysis of the effect of treatment conditions ($p < 0.05$, uncorrected, $k_{210} = 20$)

	Cluster				Peak					
Factor	*p* value FWE–corrected	*p* value FDR–corrected	equivk	p(unc)	*p* value FWE–corrected	*p* value FDR–corrected	*t*	equivZ	p(unc)	ROI, mm *x,y,z*
Escitalopram versus placebo										
Increased										
	0.99	0.69	59	0.681	0.96	0.81	2.26	2.24	0.012	–38, 30, –2 L IFG
					0.96	0.81	2.25	2.24	0.013	–40, 30, 2
					0.99	0.81	2.02	2.01	0.022	–34, 30, –4
	> 0.99	> 0.99	33	0.771	> 0.99	0.81	1.9	1.9	0.029	–48, 40, –2 L IFG
					> 0.99	> 0.99	1.72	1.72	0.043	–46, 38, –6
	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Decreased										

FDR = false discovery rate; FWE = family-wise error; L IFG = left inferior frontal gyrus; NS = not significant; ROI = region of interest.

Appendix 1 to Outhred T, Das P, Felmingham KL, et al. Impact of acute administration of escitalopram on the processing of emotional and neutral images: a randomized crossover fMRI study on healthy females. *J Psychiatry Neurosci* 2014

DOI: 10.1503/jpn.130118

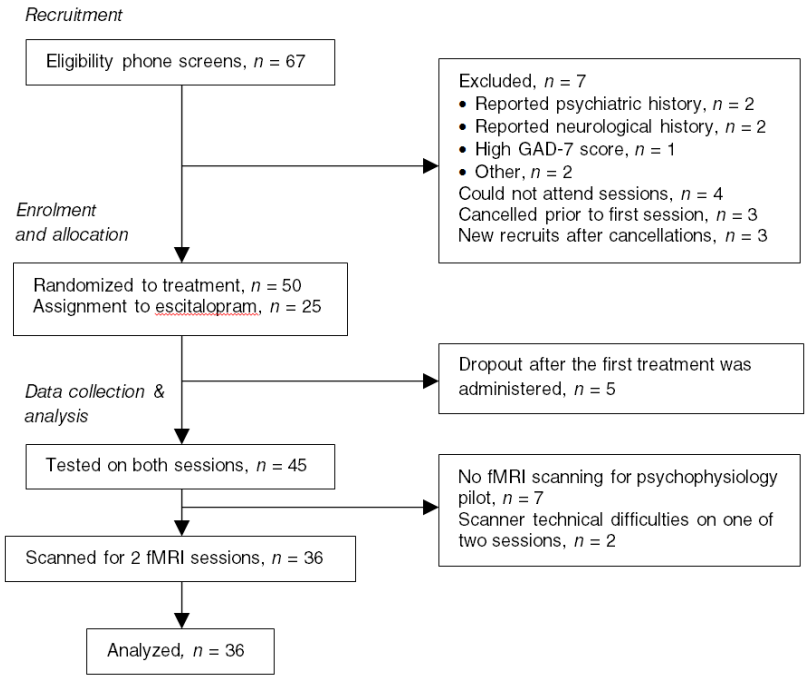

Fig. S1: Depicts, according to CONSORT guidelines, participant attrition from the experiment and the reasons and various stages at which they were excluded.

Appendix 1 to Outhred T, Das P, Felmingham KL, et al. Impact of acute administration of escitalopram on the processing of emotional and neutral images: a randomized crossover fMRI study on healthy females. *J Psychiatry Neurosci* 2014

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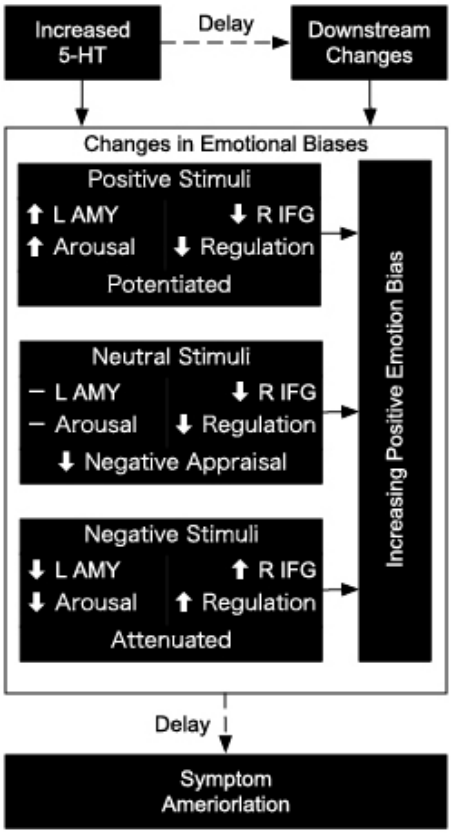

Fig. S2: An extended cognitive neuropsychological model of antidepressant action. The neurophysiological changes in emotional bias associated with acute administration of antidepressant medication may be explained, at least in part, by the modulation of amygdala (AMY) and inferior frontal gryus (IFG) during positive, negative, and neutral stimuli, consistent with an increasing positive bias. 5-HT = serotonin; L = left; R = right.

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