DATA SUPPLEMENT 1

Supplementary methods

All imaging data were collected at the Oxford Centre for Clinical Magnetic Resonance Research using a Siemens Sonata scanner operating at 1.5 T. Functional MRI scans consisted of 24 high-resolution T_2*-weighted echo-planar image slices (repetition time 3000 ms, echo time 54 ms, matrix 128×128, $1.5 \times 1.5 \times 4.5$ mm voxels). A high-resolution structural scan (repetition time 12 ms, echo tme 5.65 ms, voxel size 1 mm^3) was also acquired to facilitate co-registration of fMRI data into standard space.

Functional MRI data were preprocessed and analysed using FSL (version 3.2β, http://www.fmrib.ox.ac.uk/fsl; Smith *et al*, 2004). Preprocessing included within-participant image realignment (Jenkinson *et al*, 2002), non-brain removal (Smith, 2002), spatial normalisation to a standard template (Montreal Neurological Institute 152 stereotactic template) using an affine procedure (Jenkinson & Smith, 2001) and spatial smoothing using a Gaussian kernel (5 mm full-width-half-maximum). The time series in each session was high pass-filtered (to a maximum of 0.025 Hz). FSL was used to compute individual participant analyses in which the time series were prewhitened to remove temporal autocorrelation (Woolrich *et al*, 2001). Six experimental conditions were modelled, covert/overt fear, covert/overt happy and covert/overt neutral. Each condition was modelled separately by convolving trials with a canonical haemodynamic response function (Friston *et al*, 1994*a*; Boynton *et al*, 1996). Temporal derivatives were included as covariates of no interest to increase statistical sensitivity. All analyses were performed at the group level using mixed-effects analyses (Woolrich *et al*, 2004). Z (Gaussian T) statistic images were thresholded using clusters determined by Z=2.7 and a corrected cluster significance of P=0.05 (Friston *et al*, 1994*b*).

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DATA SUPPLEMENT 2

Table DS2.1 Demographic details. The two groups were matched with respect to age, verbal IQ and gender.

Measure	Placebo (n=12)	Reboxetine (n=12)
Age, mean (s.d.)	25 (7)	24 (4)
Verbal IQ[1], mean (s.d.)	109 (4)	11 (4)
Gender, M/F	6/6	6/6

1. Nelson (1991).

Table DS2.2 Subjective state ratings before and after 7 days of randomly assigned double-blind intervention with reboxetine or placebo

Measure	Placebo (n=12)				Reboxetine (n=12)			
	Before treatment		After treatment		Before treatment		After treatment	
	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.
Beck Depression Inventory (Beck *et al*, 1961)	4.33	3.23	3.46	2.38	3.50	2.80	3.33	3.11
State–Trait Anxiety Inventory (Spielberger *et al*, 1970)								
State Anxiety	45.25	3.33	42.83	5.09	45.50	4.58	46.50	4.23
Trait Anxiety	43.33	3.22	42.58	2.87	46.00	3.81	46.08	3.67
Positive and Negative Affective Schedule[1] (Watson *et al*, 1988)								
Positive	31.43	5.89	29.19	4.58	32.50	7.23	31.43	5.89
Negative	13.04	2.16	12.09	1.28	13.50	1.88	13.04	2.16
Befindlichkeits Scale[1,2] (von Zerrsen *et al*, 1974)								
Mood	15.91	7.07	17.44	5.05	15.57	6.38	13.81	3.15
Energy	5.17	1.46	6.72	1.69	6.17	2.08	5.48	1.02
Buss–Durkee Hostility Inventory (Buss & Durkee, 1957)	24.50	8.31	25.17	8.56	27.73	8.97	24.82	7.51
Social Adaptation Self-Evaluation Scale (Bos *et al*, 1997)	45.18	5.21	44.63	4.74	45.00	6.76	44.83	6.79

1. Ratings taken daily throughout the 7-day period. Values represent ratings before treatment and mean ratings over days 2–7 (after treatment).
2. There was no significant main effect of group or time. We did, however, observe a significant group-by-time interaction (F (1,22)=6.72, P=0.017). *Post hoc* analyses revealed that this was owing to the reboxetine group endorsing fewer descriptions of low energy after treatment (independent measures: before treatment, t_{22}=1.36, P=0.188, after treatment, t_{22}=−2.173, P=0.04).

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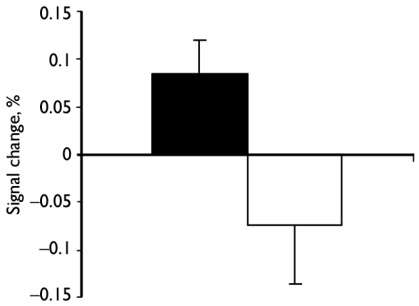

Fig. DS3.1 Right amygdala response to covert fear.
Bars show mean, error bars s.e.m. ■, Placebo fear; □, reboxetine fear; *P=0.03.

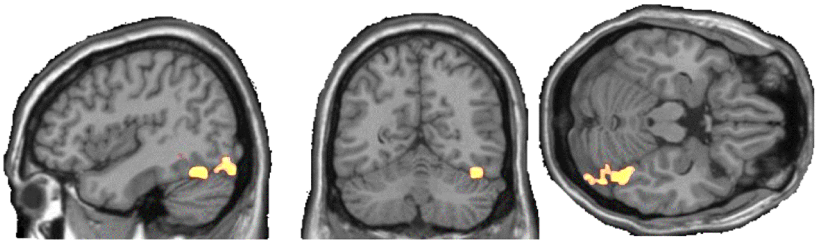

Fig. DS3.2 Increased activation under reboxetine in the right fusiform gyrus associated with the contrast between covert happy and covert neutral faces. Montreal Neurological Institute coordinates x=44, y=−59, z=20; threshold, Z=2.7; P=0.05, corrected.

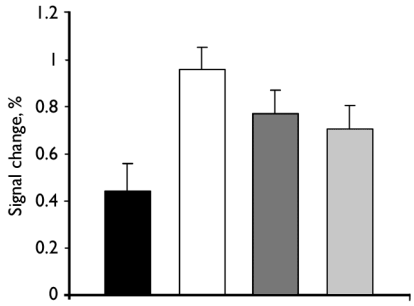

Fig. DS3.3 Percentage signal change to covert happy and neutral facial expressions. Bars show mean, error bars s.e.m. ■, Placebo happy; □, reboxetine happy; ■, placebo neutral; □, reboxetine neutral; *P=0.003.