Supplemental materials

Disrupted dorsal mid-insula activation during interoception across psychiatric disorders

1. *Additional details on record inclusion criteria*
   See **Table S1** for study details including interoceptive domain, contrast, and clinical category. Criterion 1 (interoception) was established according to previously published definitions of interoception (1, 2) : a sensing of the physiological condition or state of the body, including tickle, itch, skin temperature, hunger, thirst, heat, pain, and organ integrity. According to this definition, proprioceptive signals or any signals relating to sensing the outside environment through touch, taste, smell, sight, or hearing are not interoception. While many exteroceptive tasks studied in neuroimaging experiments may have interoceptive components (for example, viewing violent images could evoke visceral nausea), we included only tasks where the neuroimaging contrast itself was explicitly interoceptive, in an attempt to minimise the contribution of other neural systems to our results (in the same example, a contrast of violent and neural images would evoke various exteroceptive sensations in addition to any interoceptive components).

   In line with the transdiagnostic motivation behind our analysis, Criterion 2 (clinical group) was intended to capture an inclusive array of mental health problems, and included (for example) patients diagnosed with psychiatric disorders, patients with high levels of a clinically-significant trait (e.g. problem substance use; high anxiety), and recovered or weight-restored patients with anorexia nervosa. However, we excluded chronic pain and functional bowel disorders unless the patients were segregated according to a psychiatric measure (e.g. somatisation). Our clinical disorder keyword list was reviewed and finalized by a PhD-level clinical psychologist (Dalgleish) prior to searches.

   The full electronic search strategy for PubMed/MEDLINE (which can also be found on our preregistered protocol) combined (MRI OR "SPECT" OR "positron emission") with ("task" or "functional") via the Boolean operator AND.

   These terms were then combined with our clinical search terms via AND: (Psychiatric OR “Mood Disorder” OR Depress* OR Dysphori* OR Dysthymi* OR Bipolar OR Mania OR Manic OR Schiz* OR Psychosis OR Psychotic OR Delusional OR Paranoid OR Anxiety OR “Post traumatic stress disorder” OR PTSD OR Posttraumatic stress disorder OR Post-traumatic stress disorder OR “Acute stress disorder” OR Agoraphobia OR Phobia OR Panic OR “Obsessive compulsive” OR OCD OR Hoarding OR “Eating disorder” OR Anorexia OR Bulimia OR Binge eating OR Body dysmorphic OR Personality disorder OR Borderline OR Antisocial OR Narcissistic OR Histrionic OR Dependent OR Somatoform OR Somatic OR Substance use disorder OR Substance abuse OR Substance dependence OR Addiction OR Dependence OR oppositional defiant OR intermittent explosive OR sexual dysfunction)

Finally, the neuroimaging and clinical search terms were combined with interoceptive terms using the Boolean AND operator: (Interocept* OR "Visceral perception" OR "Heartbeat detection" OR "Affective touch" OR nocicepti* OR tickle OR thirst OR hunger OR "vasomotor flush" OR itch)

2. *Exploratory analyses of disorder groupings and hypo- and hyper-activation*

After conducting our primary analysis (see **Table S2**; **Table S3** for uncorrected results), for completeness only, we conducted a series of follow-up exploratory analyses. We first conducted an exploratory analysis to examine if the result was driven by foci representing hypo- (patients<controls; 97 foci) or hyper-activation (patients>controls; 180 foci). No clusters survived statistical correction (see **Table S4** for uncorrected results).

Next, again for completeness only, we disaggregated studies into three disorder groupings. Groupings were: substance use (K=9), encompassing substance use disorder (SUD) and problem substance use (PSU); eating disorders (K=13), encompassing remitted anorexia nervosa (rAN), anorexia nervosa (AN), remitted bulimia nervosa (rBN), and bingeing; affective and stress-related disorders (K=9), encompassing major depressive disorder (MDD), generalised anxiety disorder (GAD), post-traumatic stress disorder (PTSD), panic disorder (PD), low-resilience to stress/adversity (measured using the Connor-Davidson Resilience Scale), high anxiety (measured using the Anxiety Sensitivity Index); the two studies including patients with schizophrenia were not included in this follow-up analysis. Studies were categorised according to general clinical category (3), but note that some did not map on to distinct psychiatric diagnoses (e.g., low resilience to adversity); nevertheless, this study met our preregistered inclusion criteria according to both raters ("clinically-relevant traits"), and was therefore included.

In this exploratory analysis, only the affective disorders subgroup showed clusters surviving statistical correction: the left dorsal mid-insula (Z=5.08, p=0.00000019, peak: -36, -2, 14, Z=5.08; volume: 784mm^3) and the left entorhinal/perirhinal cortex (Z=5.46, p=0.000000024; peak: -20-18, -16, Z=5.46; volume: 784mm^3). However, this should not be strongly interpreted due to the lack of power in all disorder subgroups. See **Table S5** for uncorrected results.

A chi-squared test revealed that certain interoceptive domains were measured more in some clinical categories than others (X^2=35.72, p=0.003), such that studies investigating eating disorders (rAN, rBN, and AN) were most likely to have measured hunger-related processes (6 out of 12 eating disorder studies), studies investigating substance use (SUD and PSU) were most likely to have used a breathing load task (5 out of 9 SUD studies), and those in patients with affective disorders were most likely to have investigated pain processing (5 out of 9 affective disorder studies).

3. *Comparison with 'affect circuitry'*

In the first of our follow-up contrast and conjunction analyses, we tested if the interoceptive cluster we identified fell within established 'affect circuitry' in the brain. To conduct this analysis, we extracted 3867 relevant foci (N=3587) from a large database of affective tasks during neuroimaging (including fMRI and PET modalities) built for a previous meta-analysis (4). The 216 studies from which we extracted foci represented a whole-brain (not ROI) analysis, and the baseline for all contrasts was a neutral emotion (a criterion for the original 'affect circuitry' meta-analysis (4)). For a full description of the studies in this large database, see (4).

We first performed a standard ALE meta-analysis of these data to acquire a FWE cluster-corrected map of convergence of affect-related activation (p<0.05 FWE-corrected; initial cluster-forming threshold: p<0.001; 1000 threshold permutations). Next, we ran a contrast/conjunction analysis comparing this map with the thresholded map representing convergent activation across interoception tasks.

The contrast/conjunction analyses sought to identify convergent or divergent clusters with a minimum volume of 50mm^3 (p=0.05, 1000 p-value permutations).

No convergence of activation between the affect and interoception meta-analyses was found. Instead, significant differences in both subtractive directions (disrupted interoception minus affect circuitry, and affect circuitry minus disrupted interoception) are presented in **Figure 3 (main text)** and **Table S6.**

4. *Comparison with patterns of neural change following antidepressant medication*

For the comparison with patterns of neural change following antidepressant treatment, we used contrasts extracted from a previous meta-analysis of neuroimaging studies in patients with mood disorders before and after antidepressant therapy (selective serotonin reuptake inhibitor or selective noradrenaline reuptake inhibitors) (5). See **Table S7** for full sample characterisation including diagnosis, treatment, and imaging contrast.

We ran an ALE analysis on a subset of the original dataset: whole-brain results from studies in patients reporting the effects of a course of antidepressants treatment. We did not include those studies reporting results following acute antidepressant administration. When a study reported multiple post-treatment times, we included results obtained at the later date (for example, a 16 weeks scan, rather than 8 weeks). In the case of studies reporting multiple contrasts (fearful>neutral and sad>neutral), we included only the first contrast. We included results from within-subject analyses (pre- vs post-treatment), group-by-time interactions (placebo vs medication; pre- vs post-treatment), and mixed-design studies (K=24 studies total).

After performing a standard ALE meta-analysis of these data (to acquire a FWE cluster-corrected map of convergence of changes following antidepressant treatment), we ran a conjunction analysis with the equivalent map from our differential interoception analysis.

We first ran an ALE meta-analysis of antidepressant change (again thresholded at a cluster-level family-wise- error (FWE)-corrected threshold of $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$; 1000 threshold permutations). Next, we ran a conjunction/contrasts analysis with the cluster-corrected map of convergence across interoceptive task. This conjunction/contrast analysis tested for clusters with minimum volume of $50mm^3$ ($p=0.05$, 1000 p-value permutations).

For completeness, although no significant convergence was found, significant differences between antidepressant changes and interoceptive disruptions, found in both subtractive directions, are presented in **Figure 4** (main text) and **Table S8**.

5. *Comparison with patterns of neural change following psychological therapy*

For the comparison with patterns of neural change following psychological therapy, we used contrasts extracted from a previous meta-analysis of neuroimaging studies in patients with various affective disorders before and after a course of psychotherapy (6). See **Table S9** for full sample characterisation including diagnosis, treatment, and imaging contrast.

Psychological interventions included mindfulness therapies, behavioural therapy, cognitive behavioural therapy, eye-movement displacement therapy, eclectic psychotherapy, exposure and restructuring, cognitive trauma therapy, affective bias modification-enhanced CBT, and psychodynamic therapy. We included in our analysis all studies repotting at least one coordinate from the original meta-analysis (K=17) (note ALE analysis does not incorporate studies with no findings).

As in the antidepressant comparison, we performed a standard ALE meta-analysis of these data to acquire a FWE cluster-corrected map of convergence of psychological treatment mechanisms activation. We then ran a conjunction analysis with the equivalent map from our disrupted interoception analysis.

Again, the psychological therapy change meta-analysis was thresholded at a cluster-level family-wise- error (FWE)-corrected threshold of $p<0.05$ (cluster-forming threshold at voxel-level $p<0.001$; 1000 threshold permutations). The subsequent conjunction/contrast analysis tested for clusters with a minimum volume of $50mm^3$ ($p=0.05$, 1000 p-value permutations). Neither convergence nor significant differences were found. For completeness, see **Table S10** for results contrasting uncorrected ALE maps thresholded at $p<0.001$).

Table S1. All included studies in transdiagnostic neuroimaging meta-analysis (K=33, N=1236)

First author	Year	Domain	Contrast	Clinical category	N (clinical)	N (controls)	Medication (1=yes)	Verbal access (1=yes)
Avery **(7)**	2014	interoceptive attention	heartbeat attention > exteroceptive attention	MDD	20	20	0	1
Bar **(8)**	2007	pain	thermal pain > baseline	MDD	13	13	0	0
Berk **(9)**	2015	breathing load	breathing load > baseline	SUD	15	18	0	0
Berner **(10)**	2018	breathing load	anticipation* breathing load*post-load	rAN	17	25	0	0
Berner **(11)**	2019	breathing load	anticipation* breathing load*post-load	rBN	25	24	0	0
Bischoff-Grethe **(12)**	2018	affective touch	soft touch > baseline	rAN	18	26	0	0
Coletta **(13)**	2009	hunger	fasted>fed* food>objects	Bingeing	10	9	0	0
Cui **(14)**	2016	heartbeat counting	heartbeat counting > tone counting	GAD	32	30	0	0
Davidovic **(15)**	2018	affective touch	gentle touch> static skin indentation	AN	25	25	1	0
de la Fuente-Sandoval **(16)**	2010	pain	thermal pain > thermal non-pain	Schizophrenia	12	13	0	0
Elman **(17)**	2018	pain	thermal pain> thermal non-pain	PTSD	12	12	1	0
Geuze **(18)**	2007	pain	thermal pain > baseline	PTSD	12	12	0	0
Haase **(19)**	2016	breathing load	breathing load > anticipation	SR	16	18	0	0
Han **(20)**	2018	pain	pain > baseline	BD	10	10	1	0
Kaye **(21)**	2020	hunger	hungry>sated * sucrose>water	rAN	26	22	0	0
Kerr **(22)**	2016	interoceptive attention	interoceptive > exteroceptive attention	AN	15	15	0	1
Linnman **(23)**	2013	pain	aversive shock > baseline	Schizophrenia	15	13	1	0
May **(24)**	2013	affective touch	gentle touch > skin indentation	SUD	25	17	0	0
May **(25)**	2020	breathing load	breathing load > baseline	SUD	13	34	0	0
McIntosh **(26)**	2020	breath hold	breath hold > baseline	PD	21	21	0	0
Migliorini **(27)**	2013	affective touch	soft touch > baseline	SUD	15	17	0	0
Pfleiderer **(28)**	2014	heartbeat counting	heartbeat counting> tone counting	Anxiety	24	24	0	0
Santel **(29)**	2006	hunger	hungry>sated* food>nonfood	AN	13	10	1	0
Stewart **(30)**	2014	breathing load	breathing load > baseline	SUD	20	22	NR	0
Stewart **(31)**	2015	affective touch	soft touch > no touch	PSU	18	15	0	0
Stewart **(32)**	2013	breathing load	breathing load > baseline	PSU	18	15	0	0

Stewart **(33)**	2019	interoceptive attention	interoceptive > exteroceptive attention	SUD	60	30	1	1
Stewart **(34)**	2015	breathing load	anticipation* breathing load*post-load	PSU	19	21	0	0
Stopyra **(35)**	2020	hunger	hunger>satiety* viewing> distraction	AN	25	25	1	0
Strigo **(36)**	2013	pain	thermal pain> thermal non-pain	rAN	12	10	0	0
Strigo **(37)**	2008	pain	thermal pain> thermal non-pain	MDD	15	15	0	0
Vocks **(38)**	2011	hunger	hunger >satiety* drinking chocolate>water	AN	12	12	1	0
Wierenga **(39)**	2015	hunger	hunger>satiety* decision-making	rAN	23	17	0	1

*Interaction effects indicated with *. MDD=Major depressive disorder, AN=anorexia nervosa, rAN=recovered anorexia nervosa, , BD=bipolar disorder, rBN=recovered bulimia nervosa, GAD=generalised anxiety disorder, PD=panic disorder, PSU=problem substance use, PTSD=post-traumatic stress disorder, SR= stress resilience, SUD=substance use disorder, NR=Not reported*.

Table S2. Cluster-corrected results: transdiagnostic disrupted interoceptive activation (FWE cluster-corrected)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
Including all participants (K=33)						
L insula	-36	-2	14	928	4.47	0.0000038
Including only adults (K=27)						
L insula	-36	-2	14	1088	4.58	0.0000024
Including only affective and stress-related disorders (K=9)						
L insula	-36	-2	14	784	5.08	0.000000024
L parahipp. gyrus	-20	-18	-16	784	5.46	0.00000019

Thresholded at $p<0.05$, FWE cluster-corrected (cluster-forming threshold: $p<0.001$ uncorrected). MNI= Montreal Neurological Institute; L=left; parahipp.=parahippocampal

Table S3. Uncorrected results: transdiagnostic disrupted interoceptive activation (across all participants: K=33; N=1236)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L insula	-36	-2	14	888	4.44	0.00000458
	-42	-2	10		4.06	0.0000245
L perirhinal	-20	-18	-16	624	4.86	0.00000059
R MFG	-42	18	28	264	3.98	0.0000346
L cerebellum	-2	-40	-12	232	3.64	0.000137
R claustrum	32	-6	14	232	3.73	0.0000975
L cerebellum	-36	-66	-36	184	3.63	0.000144
MFG	-30	36	42	184	3.84	0.0000611
IFG	48	46	0	136	3.65	0.000131
L insula	-38	-24	22	96	3.44	0.000289
L cerebellum	-4	-38	-34	88	3.71	0.000104
L sgACC	-12	26	-22	88	3.47	0.000256
R DLPFC	26	48	22	88	3.55	0.000194
R Insula	44	-2	12	80	3.29	0.000502
L cerebellum	0	-60	-8	64	3.45	0.000285
R Insula	48	-4	-4	56	3.25	0.000585

Thresholded at $p<0.001$, uncorrected, minimum volume: $50mm^3$. L=left; R=right; MNI=Montreal Neurological Institute; MFG=middle frontal gyrus; IFG=inferior frontal gyrus; sgACC=subgenual anterior cingulate cortex; DLPFC=dorsolateral prefrontal cortex.

Table S4. Uncorrected results: exploratory analysis of hyper- and hypo-activation

Patient hyper-activation (Patients > Controls) (K=20)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L perirhinal	-20	-18	-16	688	5.12	0.00000015
R putamen	32	-6	14	488	4.22	0.0000123
R SFG	26	48	22	320	4.06	0.0000251
R IFG	48	46	0	312	4.01	0.0000305
L MFG	-44	18	28	288	4.01	0.0000303
L precentral gyrus	-50	-2	32	264	3.81	0.0000685
L MFG	-30	36	44	248	3.9	0.0000476
R Insula	50	-6	-6	232	3.7	0.000109
Culmen	0	-60	-8	200	3.86	0.0000575
R DLPFC	38	34	18	200	3.52	0.000218
R precentral gyrus	62	-4	36	144	3.34	0.00042
	58	0	36		3.33	0.000439
R amygdala	28	2	-18	112	3.35	0.000398
R thalamus	-8	32	26	112	3.47	0.000259
R putamen	12	-18	12	104	3.34	0.000425
L globus pallidus	32	-6	-10	80	3.34	0.000413

Patient hypoactivation (Controls>Patients) (K=21)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
Left insula	-36	-4	14	567	4.47	0.000004
Right insula	46	-2	12	560	3.97	0.0000353
Left precuneus	-34	-72	46	312	4.00	0.0000322
Left postcentral gyrus	-60	-12	16	264	3.72	0.000102
Left cingulate gyrus	-4	-4	48	264	3.76	0.0000858
Right precentral gyrus	60	-6	24	264	3.65	0.00013
Right subcallosal gyrus	20	16	-20	232	3.36	0.000388

Right putamen	24	20	-14	104	3.25	0.000587
Right amygdala	22	-4	-16	96	3.38	0.000361
Left culmen	-4	-40	-14	64	3.19	0.000713

Thresholded at $p<0.001$ uncorrected, minimum volume: $50mm^3$. R=right, L=left, MNI=Montreal Neurological Institute; SFG=superior frontal gyrus, IFG=inferior frontal gyrus, MFG=middle frontal gyrus DLPFC=dorsolateral prefrontal cortex.

Table S5. Uncorrected results: exploratory analysis of disorder subgroups

Affective and stress-related disorders (K=9)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L parahipp. gyrus	-20	-18	-16	784	5.46	0.00000002
L insula	-36	-2	14	784	5.08	0.0000002
R parahipp. gyrus	26	-2	-20	528	3.76	0.00008
R putamen	24	18	8	456	3.92	0.00004
R anterior cingulate	6	44	-4	272	3.86	0.00006
R putamen	32	-6	-10	216	3.61	0.0002
R IFG	28	30	-20	160	3.54	0.0002
L IFG	-50	40	-4	136	3.41	0.0003
L precentral gyrus	-48	-2	32	88	3.39	0.0003

Eating disorders (K=13)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L cingulate	-2	-2	48	400	3.87	0.00006
L MFG	-43	18	28	352	4.14	0.00002
L precentral gyrus	-54	-4	36	280	3.89	0.00005
R thalamus	12	-18	14	160	3.49	0.0002
R putamen	34	-20	12	160	3.52	0.0002
L SFG	-24	14	60	152	3.39	0.0004
	-20	8	58		3.22	0.0006
L caudate	-18	16	14	144	3.43	0.0003
L MFG	-30	38	42	120	3.36	0.0004
R precuneus	6	-48	58	88	3.29	0.0005
R IFG	42	52	0	80	3.34	0.0004
R cingulate	10	-20	30	72	3.33	0.0004

Substance abuse disorders (K=9)

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L postcentral gyrus	-60	-14	16	168	3.69	0.0001

	-58	-22	16		3.48	0.0002
L caudate	-2	4	12	80	3.61	0.0002
R insula	36	-4	14	64	3.35	0.0004
L fusiform	-38	-78	-12	56	3.48	0.0003
R precuneus	8	-74	56	56	3.53	0.0002

Thresholded at $p<0.001$ uncorrected, minimum volume: $50mm^3$. R=right, L=left, MNI=Montreal Neurological Institute; SFG=superior frontal gyrus, IFG=inferior frontal gyrus, MFG=middle frontal gyrus; parahipp=parahippocampal.

Table S6. Cluster-corrected results: significant differences between disrupted interoception and affect circuitry

Contrast: Disrupted interoception minus affect circuitry

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L insula	-34	-4	16	872	3.29	<0.001
L entorhinal	-20	-18	-20	272	2.75	0.003

Contrast: Affect circuitry minus disrupted interoception

L claustrum/Insula	-27	13.3	-10.8	30064	3.29	<0.001
	-33.7	25.7	-7.7		3.29	<0.001
	-16	-34	-2		2.75	0.003
	-20	-33	0		2.65	0.004
	18	6	-12		2.58	0.005
	11.3	-3.3	-20.7		2.01	0.022
	14.4	-4.4	-18.8		1.67	0.047
	16	1	-21		1.73	0.042
	-48	18	14		2.14	0.016
	-52	20	12		2.12	0.017
	-20	-6	-10		1.88	0.03
R cerebellum	40.4	-61.8	-15	8464	3.29	<0.001
	46.8	-66.6	7		3.09	0.001
	43.7	-67.1	1.1		2.20	0.014
	44	-84	-6		2.65	0.004
	44	-78	-3		2.33	0.01
	48	-84	-9		2.51	0.006
	42	-78	-2		2.46	0.007
L MTG	-53.5	-62.5	10.5	4096	2.88	0.002
	-46.7	-80.7	7.3		2.37	0.009
	-45.5	-78.5	13.5		2.46	0.007
	-44	-82	6		2.46	0.007
SFG	0	57.5	26.9	3880	3.29	<0.001
	0	63	14		2.51	0.006
R IFG	56	24	-6	2944	3.29	<0.001

	57.3	31.3	-2.7		3.09	0.001
	52.5	29.5	-9.5		2.88	0.002
	44.7	32.7	-12		2.58	0.005
L fusiform	-44	-53	-13	2296	2.33	0.01
	-44	-52	-16		2.51	0.006
R STG	51.7	-28.9	1.1	1392	3.29	<0.001
	55	-36	7		2.88	0.002
	66	-42	8		2.14	0.016
R cingulate	6.7	20	36.7	1128	2.88	0.002
	0	19	36		2.75	0.003
R IFG	48	12	22	888	2.88	0.002
	43.6	10.4	32		2.41	0.008
R precentral gyrus	42	8	30	360	2.46	0.007
	44	8	30		2.37	0.009
R IFG	52	12	22	200	2.65	0.004
	52	18	32		2.46	0.007
R IFG	54	15	27	160	2.05	0.02
L cingulate	-4	18	36	152	2.33	0.01
R cingulate	10	22	36	144	2.65	0.004
R cingulate	42	4	34	120	2.17	0.015
R precentral gyrus	44	4	30		2.01	0.022
R MFG	56	18	32	72	2.12	0.017
R IFG	52	10	22	64	2.41	0.008
L cingulate	-2	20	34	64	2.33	0.01
R MFG	58	18	32	56	1.98	0.024

Initial ALE analyses for both analyses were thresholded at $p<0.05$, FWE cluster-corrected (cluster-forming threshold: $p<0.001$ uncorrected); subsequent conjunction/contrast analysis thresholded at $p<0.05$, 1000 p value permutations, minimum cluster size=50m^3. L=left;R=right; MNI=Montreal Neurological Institute; MTG=middle temporal gyrus; MFG=middle frontal gyrus; IFG=inferior frontal gyrus; STG=superior temporal gyrus; SFG=superior frontal gyrus.

Table S7. Details of studies included in antidepressant therapy versus interoception contrast analysis

First author	Year	Diagnosis	Intervention	N patients	Task	Contrast	Imaging
Benedetti**(40)**	2009	MDD	SNRI	8	emotion	negative>positive	fMRI
Davidson**(41)**	2003	MDD	SNRI	12	emotion	negative>neutral	fMRI
Frodl**(42)**	2011	MDD	SNRI	11	emotion	sad>shapes	fMRI
Kalin**(43)**	1997	MDD	SNRI	2	emotion	negative>neutral	fMRI
Lopez-Sola**(44)**	2010	MDD	SNRI	13	pain	painful>nonpainful	fMRI
Robertson**(45)**	2007	MDD	SNRI	10	emotion	sad>neutral	fMRI
Schaefer**(46)**	2006	MDD	SNRI	9	social	social interaction>other	fMRI
Anand**(47)**	2007	MDD	SSRI	12	emotion	negative emotion>fixation	fMRI
Arnone**(48)**	2012	social phobia	SSRI	30	emotion	sad>neutral	fMRI
Cornelius**(49)**	2010	MDD	SSRI	6	emotion	fear>shape	fMRI
Fales**(50)**	2009	MDD	SSRI	23	emotion	fear>neutral	fMRI
Fu**(51)**	2004	MDD	SSRI	13	emotion	sad>fixation	fMRI
Godlewska**(52)**	2012	MDD	SSRI	42	emotion	fear>happy	fMRI
Hoehn-Saric**(53)**	2004	GAD	SSRI	6	emotion	worry>neutral	fMRI
Maslowsky**(54)**	2010	GAD	SSRI	7	emotion	angry>fixation	fMRI
Phan**(55)**	2012	social phobia	SSRI	21	emotion	fear>happy	fMRI
Rosenblau**(56)**	2012	MDD	SSRI	12	emotion	negative>positive	fMRI
Ruhe**(57)**	2012	MDD	SSRI	16	emotion	fear>scrambled faces	fMRI
Stoy**(58)**	2012	MDD	SSRI	15	reward	loss>neutral	fMRI
Tao**(59)**	2012	adolescent MDD	SSRI	19	emotion	fear>neutral	fMRI
Victor**(60)**	2010	MDD	SSRI	10	emotion	sad>neutral	fMRI
Wang**(61)**	2012	MDD	SSRI	18	emotion	negative>neutral	fMRI
Samson**(62)**	2011	MDD	SSRI/SNRI	10	emotion	sad>baseline	fMRI

MDD=Major depressive disorder; GAD=generalized anxiety disorder; fMRI=functional magnetic resonance imaging; SSRI=selective serotonin reuptake inhibitor; SNRI=selective noradrenaline reuptake inhibitor.

Table S8. Cluster-corrected results: contrast between disrupted interoception and neural changes following treatment with antidepressant medication (cluster corrected, $p<0.05$)

Contrast: Disrupted interoception minus antidepressant mechanisms

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L insula	-42	2	10	408	2.33	0.01

Contrast: Antidepressant mechanisms minus disrupted interoception

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L medial GP	-15	-6	-10.5	408	2.23	0.013
L amygdala	34	-6	-22	256	1.87	0.031
		-4	-22		1.85	0.032
	33	0	-24		1.84	0.033
R amygdala	-22	2	-22	256	2.23	0.013

Initial ALE maps for both analyses were thresholded at $p<0.05$ FWE cluster-corrected (cluster-forming threshold: $p<0.001$ uncorrected); subsequent conjunction/contrast analysis thresholded at $p<0.05$, 1000 *p* value permutations. L=left; R=right; MNI=Montreal Neurological Institute; GP=globus pallidus.

Table S9. Details of studies included in psychological therapy versus interoception contrast analysis

First author	Year	Diagnosis	Intervention	N patients	Task	Contrast	Imaging
Mansson**(63)**	2013	SAD	ABM	13	emotion	disgust>neutral	fMRI
Lindauer**(64)**	2008	PTSD	BEP	10	emotion	symptom provocation	SPECT
Yamanishi**(65)**	2009	OCD	BT	33	resting	resting	SPECT
Felmingham**(66)**	2007	PTSD	CBT	8	emotion	fearful>neutral	fMRI
Furmark**(67)**	2002	social phobia	CBT	6	emotion	anxiogenic public speaking	PET
Goldapple**(68)**	2004	MDD	CBT	14	resting	resting	PET
Goldin**(69)**	2012	SAD	CBT	24	emotion	negative self-referential>self	fMRI
Kircher**(70)**	2013	PD	CBT	42	emotion	fear-conditioned> non-conditioned	fMRI
Klumpp**(71)**	2013	SAD	CBT	14	emotion	fearful>happy	fMRI
Prasko**(72)**	2004	PD	CBT	6	resting	resting	PET
Sakai**(73)**	2006	PD	CBT	11	resting	resting	PET
Sankar**(74)**	2015	MDD	CBT	16	emotion	negative attitudes>neutral	fMRI
Yoshimura**(75)**	2014	MDD	CBT	23	emotion	negative self-referential>verbal	fMRI
Aupperle**(76)**	2013	PTSD	CBT (CTT)	14	emotion	negative>positive	fMRI
Mansson**(77)**	2013	SAD	CBT (iCBT)	13	emotion	disgust>neutral	fMRI
Goldin**(78)**	2010	SAD	mindfulness	14	emotion	negative self-belief>fixation	fMRI
Holzel**(79)**	2013	GAD	mindfulness	15	emotion	angry>neutral	fMRI
Keedwell**(80)**	2009	MDD	variety	12	emotion	sad>fixation	fMRI

MDD=Major depressive disorder, GAD=generalized anxiety disorder, PD=panic disorder, PTSD=post-traumatic stress disorder, OCD=Obsessive-compulsive disorder, SAD=social anxiety disorder; fMRI=functional magnetic resonance imaging; PET=positron emission tomography; SPECT=single photon emission tomography; CBT=cognitive behavioral therapy; iCBT=internet-based CBT; CTT=cognitive trauma therapy; BT=behavioral therapy; ABM=affective bias modification; BEP=brief eclectic psychotherapy.

Table S10. Uncorrected results: contrast between disrupted interoception and neural changes following treatment with psychological therapy

Contrast: Disrupted interoception minus psychological therapy mechanisms

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
L insula						
	-42	-4	10	544	2.18	0.015
	-46	-2	12		2.11	0.018
	-42	2	8		2.07	0.019
Culmen						
	0	-42	-12	216	2.21	0.014
L culmen						
	-0.8	-59.2	-7.2	88	2.35	0.009

Contrast: Psychological therapy mechanisms minus disrupted interoception

Region	MNI coordinates			Volume (mm^3)	*Z*	*P*
	x	*y*	*z*			
R DMPFC						
	7	61.5	16.5	904	2.68	0.0037
	11	59	15		2.56	0.0052

Initial ALE maps thresholded at $p<0.001$ uncorrected, minimum volume: $50mm^3$; subsequent conjunction/contrast analysis thresholded at $p<0.05$, 1000 p value permutations. L=left; R=right; MNI=Montreal Neurological Institute; DMPFC=dorsomedial prefrontal cortex.

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