Supporting Information

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SI Materials and Methods

Procedure. ***Prescanning session.*** Before the scanning session, participants performed the experiment once outside the scanner to familiarize themselves with the procedure. The same pictures were used in the prescanning and scanning sessions. Global valence and arousal ratings were obtained after each block of pictures only in the prescan session.

Orders of presentation. Each scan started with two control trials with only the fixation point. These trials controlled for potential habituation effects, allowing the RIII reflex to stabilize. After these two trials, the remaining 24 trials were presented in a pseudorandom order counterbalanced within and between subjects, consisting of six consecutive cycles, comprising each of the four experimental conditions (unpleasant, pleasant, neutral, or fixation). These cycles were ordered so that no experimental condition was presented twice consecutively. Two orders of presentation were created (order 2 being the inverse of order 1). The presentation of these two orders within a scanning session was counterbalanced across individuals.

Functional MRI Data Analyses. Imaging data were analyzed using SPM2 (www.fil.ion.ucl.ac.uk/spm/) for the preprocessing and SPM5 for the functional analyses. Preprocessing included slice-time correction and realignment. Anatomical and functional images were then spatially normalized to a standard stereotaxic space using the Montreal Neurological Institute (MNI) template. Subsequently, functional images were spatially smoothed using a Gaussian kernel of twice the voxel size (FWHM: $7 \times 7 \times 10$ mm).

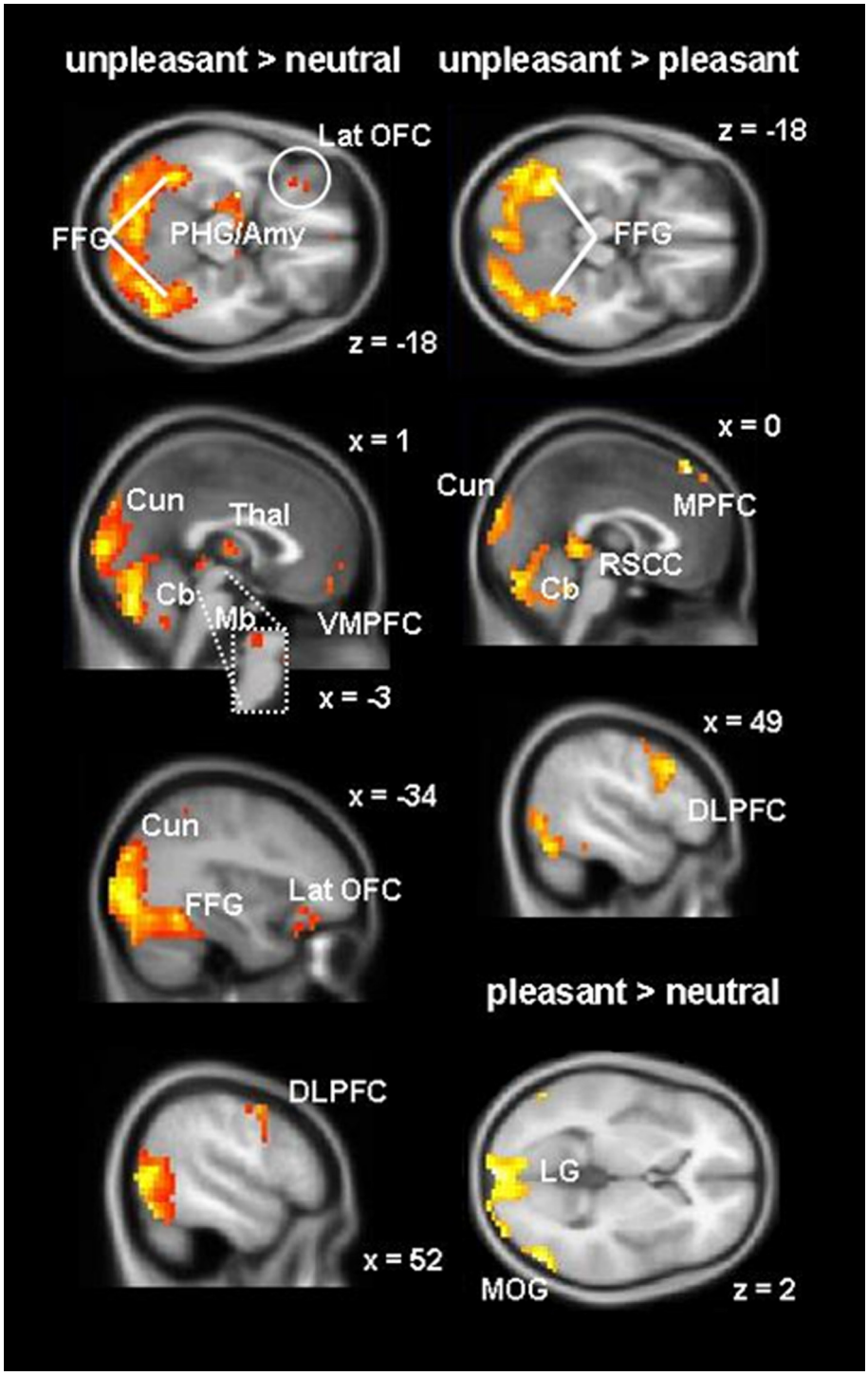

Fig. S1. Main effects of emotional pictures. Unpleasant pictures elicited stronger activations than neutral pictures in the bilateral fusiform gyrus (FFG), left parahippocampal gyrus (PHG) and amygdala (Amy), left lateral orbitofrontal cortex (OFC), ventromedial prefrontal cortex (VMPFC), dorsolateral prefrontal cortex (DLPFC), cuneus (Cun), cerebellum (Cb), midbrain (Mb), and thalamus (Thal). Unpleasant pictures elicited stronger activations than pleasant pictures in the Cun, Cb, retrosplenial cingulate cortex (RSCC), medial prefrontal cortex (MPFC), and DLPFC. Pleasant pictures elicited stringer activations than neutral pictures the right lingual gyrus (LG) and middle occipital gyrus (MOG). Activations were thresholded at $P < 0.005$ for display purposes (see Table S4).

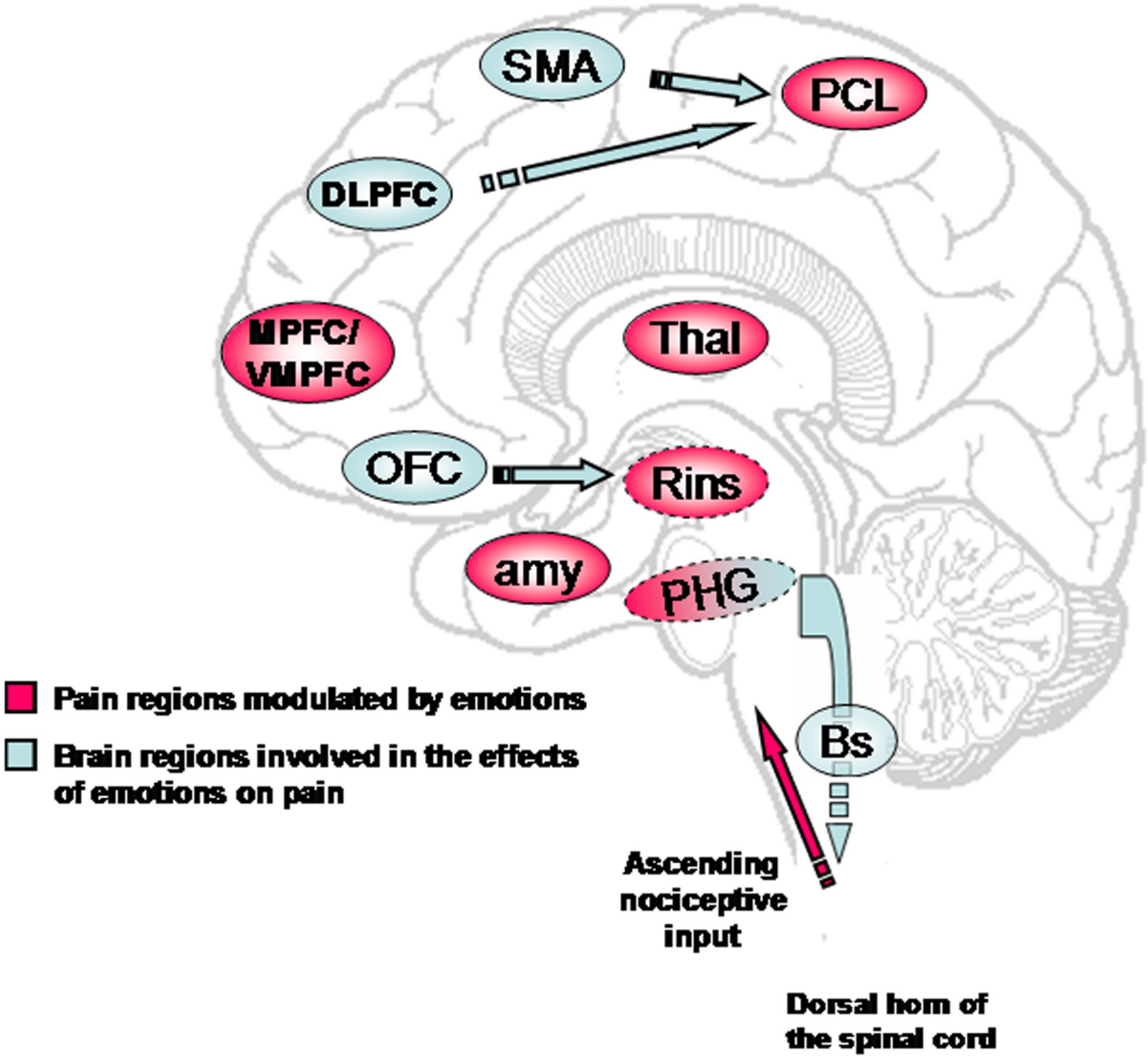

Fig. S2. Brain regions involved in the emotional modulation of pain in this study. Regions in red reflect pain-related activations that were higher in the context of unpleasant vs. pleasant pictures. Regions in blue were identified as possible mediators of the effects of emotions on pain by the psychophysiological interaction (PPI) analysis and by the picture blocks analyses. Blue arrows indicate possible corticocortical and descending modulatory pathways. Note that this figure only summarizes the results and that additional regions might also be involved in the emotional modulation of pain. Bs, brainstem; Rins, right insula; SMA, supplementary motor area.

Table S1. Brain activation peaks related to the painful stimulations and pictures

Region of activation	BA	Side*	*t*	*x*, *y*, *z***
Electrical stimulations				
Postcentral gyrus/Paracentral lobule	1–3, 5	L	8.20	−7, −41, 75
Precuneus/Postcentral gyrus	1–3/5/7	R	7.18	7, −48, 75
Precentral gyrus/SMA	4/6	L	10.40	−7, −13, 80
Cingulate cortex				
Anterior	24	L	12.47	7, 24, 40
Mid	24	L	6.44	−7, −3, 40
Dorsal	32	L	13.73	−3, 14, 50
Insula	—	L	11.67	−34, 17, 0
	—	R	10.91	38, 14, 0
Parietal operculum	40	L	10.73	−55, −24, 20
	40	R	8.77	69, −24, 20
Parahippocapal gyrus	28/35	L	6.22	−28, −28, −5
		R	6.30	21, −21, −10
Inferior frontal gyrus	45	R	10.18	41, 38, 5
Middle frontal gyrus	10/11	L	7.61	−41, 45, 20
		R	11.22	38, 42, 30
Medial orbitofrontal gyrus	25	L	8.68	−21, 21, −15
		R	11.51	13, 7, −10
Thalamus	—	L	5.68	10, 0, 0
	—	R	6.46	−10, 0, 0
Hypothalamus	—	—	6.32	−7, −10, −15
Pons	—	R	7.30	3, −38, −30
Cerebellum				
Culmen	—	L	8.20	3, −58, −5
Uvula of vermis	—	—	9.58	3, −83, −25
Tonsils	—	L	9.86	−31, −52, −45
	—	R	6.06	28, −41, −50
Pictures				
Inferior occipital gyrus	18	L	9.55	−31, −86, −10
	18	R	6.24	34, −86, 0
Fusiform gyrus		L	6.80	−31, −61, −10
		R	7.37	34, −65, −15

Peaks of activity thresholded at $P < 0.05$ corrected for multiple comparisons for the global search volume (626.38 resels), using random field theory (RFT).
*R, right ipsilateral side; L, left contralateral side.
**Coordinates are reported in MNI space.

Table S2. Shock-related activations modulated by pleasant and unpleasant vs. neutral pictures

Region of activation	BA	Side*	*t*	*x*, *y*, *z***
Pain during unpleasant > pleasant pictures				
Insula	—	R	4.26	34, 7, 10
Paracentral lobule	5/6	—	5.28	0, −24, 60
Parahippocampal gyrus	28/35	L	4.92	28, −34, −20
	28/35	R	4.15	−24, −45, −15
Lingual gyrus	17	R	5.02	14, −89, 0
Pain during unpleasant > neutral pictures				
Superior frontal gyrus	8	R	6.47	−17, 58, 25
Dorsolateral prefrontal gyrus	10	R	5.07	−45, 14, 45
Pain during neutral > pleasant pictures				
Parahippocampal gyrus	28/35	L	8.94	−24, −45, −5
	28/35	R	4.42	28, −34, −20
Cuneus	18	L	5.50	−10, −103, 15

A priori regions are thresholded at $P < 0.05$ corrected for multiple comparisons using RFT (pain directed search volume = 109.58 resels). Other regions are thresholded at $P < 0.05$, corrected for multiple comparisons using RFT (global search volume = 626.38 resels).
*R, right ipsilateral side; L, left contralateral side.
**Coordinates are reported in MNI space.

Table S3. Brain regions correlating with pain ratings and RIII reflex modulation during unpleasant vs. pleasant pictures

Region of activation	BA	Side*	*t*	*x*, *y*, *z***
Correlation with pain ratings modulation				
Insula	—	R	4.47	45, 17, −5
Medial prefrontal cortex	10	L	3.96***	−14, 48, 0
Lingual gyrus	17	L	6.88	−10, −86, 0
	17	R	4.40	14, −96, −5
Cerebellar nodule	—	L	4.56	−10, −62, −20
Correlation with RIII reflex modulation				
Medial thalamus	—	L	6.95	−7, −17, 10
Amygdala	—	L	6.78	−17, −7, −20
	—	R	7.95	21, −10, −30
Brainstem	—	L	5.31	−10, −21, −25
Perigenual cingulate	25	L	5.27	−7, 28, −15
Ventromedial prefrontal cortex	10/11	R	4.24	3, 51, −15
Medial prefrontal cortex	10	L	4.59	−14, 58, 5
Dorsolateral prefrontal cortex	9	L	6.45	−55, 14, 35
Postcentral gyrus	2	L	5.55	−58, −28, 50
Cerebellar nodule	—	L	4.85	−7, −62, −30
Superior occipital gyrus	19	L	6.85	−38, −89, 25
	19	R	5.66	31, −83, 45

A priori regions are thresholded at $P < 0.05$ corrected for multiple comparisons using RFT (pain-directed search volume = 109.58 resels). Other regions are thresholded at $P < 0.05$, corrected for multiple comparisons using RFT (global search volume = 626.38 resels).
*R, right ipsilateral side; L, left contralateral side.
**Coordinates are reported in MNI space.
***$P < 0.005$, uncorrected.

Table S4. Brain activation to pleasant and unpleasant pictures

			Unpleasant vs. neutral pictures		Pleasant vs. neutral pictures		Unpleasant vs. pleasant pictures*	
Region of activation	BA	Side**	*t*	*x, y, z****	*t*	*x, y, z****	*t*	*x, y, z****
Cuneus	18	L	8.17	−14, −100, 15	—	—	—	—
	18/19	R	8.61	14, −100, 20	5.32	17, −100, 25	4.56	3, −100, 10
Lingual gyrus	17/18	R	—	—	4.99	3, −90, 5	—	—
Middle occipital gyrus	19	L	8.78	−48, −82, 0	5.25	−52, −69, 5	6.97	−48, −83, −5
	19	R	8.90	41, −79, 5	5.06	55, −72, 0	4.56	52, −72, −5
Fusiform gyrus	37	L	7.66	−38, −55, −15	—	—	6.55	−34, −58, −20
	37	R	8.66	48, −62, −25	—	—	5.32	38, −52, −15
Superior parietal lobule	7	L	4.77	−24, −58, 70	—	—	3.79	−31, −65, 60
	7	R	4.80	28, −55, 55	—	—	—	—
Retrosplenial cortex	26/29–30	R	—	—	—	—	5.49	3 −41, 0
Thalamus	—	—	4.31	0, −17, 10	—	—	—	—
Thalamus/Pulvinar	—	R	4.89	17, −27, 0	—	—	—	—
Amygdala	—	L	4.93	−17, −7, −25	—	—	3.22	−10, −10, −20
		R	3.84****	24, −7, −20	—	—	—	—
Parahippocampal gyrus	28/35	L	4.59	−17, −17, −20	—	—	—	—
	28/35	R	4.02****	28, −28, −5	—	—	—	—
Orbitofrontal cortex	47	L	4.73	−38, 24, −25	—	—	—	—
Middle temporal gyrus	—	—	—	—	—	—	4.13	58, −38, −10
Ventromedial prefrontal cortex	10/11	—	4.06	0, 52, −15	—	—	—	—
Medial prefrontal cortex	8	—	—	—	—	—	6.84	0, 38, 55
Premotor cortex	6/8	R	5.22	52, 3, 50	—	—	—	—
Midbrain	—	R	4.79	3, −31, −5	—	—	—	—
Cerebellum								
Culmen	—	L	—	—	—	—	—	—
	—	R	—	—	—	—	—	—
Nodule	—	—	—	—	—	—	4.30	0, −45, −30
Tuber of vermis	—	R	7.87	0, −79, −30	—	—	4.95	−3, −86, −25
Declive	—	—	—	—	—	—	5.76	−45, −72, −25
Pyramis	—	L	—	—	—	—	5.36	−14, −76, −50
	—	R	—	—	—	—	5.15	10, −79, −45

Peaks of activity thresholded at $P < 0.05$ corrected for multiple comparisons for the pictures-directed search volume (153.12 resels), using RFT. Peaks of activity falling out of a priori defined regions are thresholded at $P < 0.05$ corrected for multiple comparisons for the global search volume (626.38 resels).

*There were no significant peaks for the pleasant vs. unpleasant contrast.

**R, right ipsilateral side; L, left contralateral side.

***Coordinates are reported in MNI space.

****$P < 0.005$, uncorrected.

Table S5. Results of the psychophysiological interaction (PPI) analyses

Region of activation	BA	Side*	*t*	*x*, *y*, *z***
Regions correlating with the effects of unpleasant vs. pleasant pictures on the right insula				
Tail of caudate/lateral geniculate body of thalamus	—	L	4.12	−24, −28, 5
Orbitofrontal cortex	11	R	3.74***	21, 41, −15
Subgenual cingulate cortex	25	—	3.22***	0 10, −10
Middle occipital gyrus	19	L	4.49	−17, −103, 20
	19	R	5.13	28, −96, 20
Regions correlating with the effects of unpleasant vs. pleasant pictures on the paracentral lobule				
Thalamus	—	L	3.40***	−3, −21, 15
Brainstem	—	—	3.41***	3, −38, −50
Tail of caudate/lateral geniculate body of thalamus	—	L	4.42	−24, −28, 0
Dorsolateral prefrontal cortex	45	L	4.66	−55, 28, 15
Supplementary motor area	6	L	4.65	−7, −17, 80
Parahippocampal gyrus	28/35	L	3.80***	−21, −31, −20
	28/35	R	3.74***	21, −59, −10
Fusiform gyrus	18	L	4.11	−24, −72, −15
	18	R	5.01	34, −65, −20
Cuneus	18	L	7.56	−24, −103, 10
	18	R	4.88	7, −100, 5

A priori regions are thresholded at $P < 0.05$ corrected for multiple comparisons using RFT (pain-directed search volume = 109.58 resels). Other regions are thresholded at $P < 0.05$, corrected for multiple comparisons using RFT (global search volume = 626.38 resels).

*R, right ipsilateral side; L, left contralateral side.

**Coordinates are reported in MNI space.

***$P < 0.005$, uncorrected.

Table S6. Mean (± SD) valence and arousal ratings

	SAM ratings under experimental conditions			
	Pleasant	Unpleasant	Neutral	No picture
Valence	7.38 (±0.96)	2.07 (±0.68)	4.86 (±0.86)	4.83 (±0.85)
Arousal	5.56 (±0.94)	6.29 (±1.37)	2.83 (±1.30)	2.36 (±1.66)

Recorded using a computerized version of the self-assessment manikin (1). Valence: 1, unpleasant; 9, pleasant; arousal: 1, low arousal; 9, high arousal.