Differential modulation of valence and arousal in high-alexithymic and low-alexithymic individuals

Alexander Heinzel[a], Ralf Schäfer[b], Hans-Wilhem Müller[a], Andre Schieffer[a], Ariane Ingenhag[a], Georg Northoff[c], Matthias Franz[b] and Hubertus Hautzel[a]

High-alexithymic individuals are characterized by an impaired ability to identify and communicate emotions whereas low-alexithymic individuals have a wide-ranging ability to deal with emotions. This study examined the hypothesis that valence and arousal modifications of emotional stimuli differentially modulate cortical regions in high-alexithymic and low-alexithymic individuals. To this end, 28 high-alexithymic and 25 low-alexithymic individuals were investigated with event-related fMRI using visual emotional stimuli. We found differential neural activations in the dorsal anterior cingulate, the insula and the amygdala. We suggest that these differences may account for the impaired ability of high-alexithymic individuals to appropriately handle emotional stimuli. *NeuroReport* 21:998–1002 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Introduction

Alexithymia is a psychological construct representing a personality trait that is normally distributed in the general population [1]. It is comparable with other psychological constructs such as intelligence. It describes the inability to identify and differentiate the emotional aspects of social interactions. Thus, a pronounced inability (high alexithymia) does not represent a psychological disorder in itself, but is considered to be a risk factor associated with chronic pain, somatoform disorders, addictive disorders, anxiety and depression [1–3]. The identification of the neural correlates of high alexithymia might therefore contribute to an improved diagnosis and treatment of associated disorders.

With respect to the neural correlates, Lane et al. [4] reported a decreased activity in the anterior cingulate of high-alexithymic individuals [5]. They suggested that the emotional response in these individuals is associated with impoverished conscious experience of emotion caused by an altered function of the anterior cingulate.

In contrast, Berthoz et al. [6] found decreased cingulate activation in high-alexithymics for negative emotional stimuli, but an increased cingulate activation for positive emotional stimuli. Kano et al. [7] reported decreased activity in cingulate only for emotional stimuli with angry face expressions, but not for sad or happy faces. Finally, Meriau et al. [8] discovered a positive correlation of the Toronto Alexithymia Scale (TAS-20) score and anterior cingulate activity.

In addition, Kano et al. [7] and also Reker et al. [9] identified the altered neural processing in the right and left insula in high-alexithymic individuals. However, other studies did not confirm these findings [6,8].

Likewise, results regarding the amygdala activity are controversial. Some studies did not reveal any altered activity in the amygdala [6–8], whereas other observations challenge these findings [9].

The aim of our study was to investigate the neural correlates of emotional processing in a well-defined sample of 29 high-alexithymic and 25 low-alexithymic male individuals. In contrast to earlier studies, we applied a parametric design. This allowed us to include individual valence and arousal ratings of the emotional stimuli. Arousal (i.e. the intensity with which emotional stimuli are perceived) and valence (i.e. how positive or how negative emotional stimuli are perceived) represent the core features of emotional processing. Our design permits the neural correlates of these features to be addressed separately.

Thus, we aim to identify the neural correlates of emotional valence and arousal processing in individuals with high and low alexithymia by directly relating individual self-reports to neural processing. On the basis of the earlier studies, we hypothesized altered neural processing in the anterior cingulate, insula and amygdala.

Methods

A total of 28 high-alexithymic and 25 low-alexithymic individuals participated in this study. Classification was based on the sum score of the German version of the

TAS-20 [10]. The definition of high and low alexithymia was based on a large representative random sample of the general German population [1]. According to this sample, the 33rd percentile (sum score = 45) was used as a cut-off for low alexithymics and the 66th (sum score = 52) for high alexithymics. Moreover, all the individuals completed the Beck depression inventory to exclude the individuals with clinically relevant depression (Beck depression inventory score > 12) [11]. Only right-handed male individuals aged 20–40 years with a German high school diploma were included. None of the individuals had any history of psychiatric, neurological or severe medical illness. After receiving a detailed explanation of the study's design and any potential risks, all individuals gave their written informed consent. The study was approved by the institutional review board of the University of Düsseldorf.

We used 50 positive, 50 negative and 50 neutral images taken from the International Affective Picture System (IAPS). To inhibit neural activation associated with task-related cognitive processing we used a picture viewing task. To control for a constant level of attention, the individuals had to press a button with their right index finger as soon as they recognized the picture appearing on the screen. All the IAPS pictures were presented for 4 s during event-related fMRI followed by a fixation cross of randomly varied duration (6, 6.5, 7, 7.5, 8 s). The different IAPS types were pseudo-randomized within and across runs.

Subjective ratings were analyzed by the two two-factor analyses of variance using the between-individuals factor group (high/low alexithymia) and the within-individuals factor valence (first analysis) and arousal (second analysis). Analyses were performed with SPSS (SPSS Inc., Chicago, Illinois, USA), version 10.0.

MR measurements were made on a 1.5 T Siemens Sonata scanner at Forschungszentrum Jülich, using a standard head coil and a scanning protocol developed to enhance statistical inference in the amygdala [12].

Arousal and valence ratings of the pictures were made immediately after the fMRI session outside the scanner. The IAPS pictures were now presented in a different order. Valence assessment ranged on a continuum from very negative (1) to very positive (9), arousal assessment ranged on a continuum from low (1) to high (9) arousal [13].

Image processing and statistical analyses were carried out using MATLAB 7.4.0 and SPM5 (*www.fil.ion.ucl.ac.uk*). Images were corrected for differences in slice acquisition time, realigned to the first volume, corrected for motion artifacts, mean-adjusted by proportional scaling, resliced and normalized into standard stereotactic space (cluster size $2 \times 2 \times 2\,mm^3$) and smoothed with an 8-mm full-width-at-half-maximum Gaussian kernel. Time series were high-pass filtered to eliminate low-frequency drifts (cut-off 128 s). Preprocessed fMRI data were analyzed using the general linear model. A linear parametric modulation approach was applied [14]. We defined the onsets of the picture presentations as a regressor with two parametric regressors (valence, arousal). The resulting parameter estimates of the parametric regressors indicate the correlation between observed BOLD signal and individual subjective ratings.

Individual-specific activations were calculated and then passed to a second-level random effects analysis using one-sample *t*-tests for the whole group (main effect) as well as separately for both the subgroups. Finally, exclusive masking (masked at $P = 0.05$ uncorrected) of the results of low-alexithymic with those of high-alexithymic individuals, and vice versa, was applied for arousal and valence.

The statistical threshold for significant activations was set to P less than 0.05. False discovery rate-corrected for multiple comparisons with an additional cluster-size threshold of $k > 10$ voxels. Then we performed a small volume correction based on our hypotheses for the anterior cingulate, insula and amygdala. Regions were defined using the AAL regions of the WFU Pick Atlas version 1.02 (*http://fmri.wfubmc.edu/*).

Results
Behavioral results
High-alexithymic individuals (mean valence/arousal ratings): negative stimuli 2.57 (SD 0.8)/4.76 (SD 1.66), positive stimuli 7.18 (SD 0.76)/4.41 (SD 1.52), neutral stimuli 5.44 (SD 0.75)/2.01 (SD 1.02).

Low-alexithymic individuals (mean valence/arousal ratings): negative stimuli 2.32 (SD 0.69)/5.22 (SD 1.06) positive stimuli 7.14 (0.72)/4.25 (SD 1.34), neutral stimuli 5.57 (SD 0.46)/2.0 (SD 1.0).

The analyses revealed a significant effect for the factor valence (F = 564.75, d.f. = 2/106, $P < 0.0001$) and the factor arousal (F = 184.41, d.f. = 2/106, $P < 0.0001$). The pair-wise testing revealed a significant difference between the subjective valence ratings for negative versus positive, positive versus neutral, and negative versus neutral stimuli ($P < 0.0001$). Moreover, there was a significant difference between the subjective arousal ratings for negative versus neutral and for positive versus neutral ($P < 0.0001$), but no significant difference for positive versus negative stimuli. In both the analyses, there was no significant effect for the factor group or the interaction of the factors.

Functional magnetic resonance imaging results
Valence
Main effect: There was a positive correlation (the higher the valence ratings the stronger the BOLD signal) with individual valence ratings in the anterior cingulate and the insula. No correlation was found in the amygdala (Table 1).

Table 1 Results of correlation analyses of BOLD signal with individual valence and arousal ratings for predefined ROIs

| | Anatomical region | | | | | | | | | | | | | | | | |
| | Anterior cingulate | | | | | | Insula | | | | | | Amygdala | | | | |
	BA	CS	Z	Peak (x, y, z)			BA	CS	Z	Peak (x, y, z)			CS	Z	Peak (x, y, z)		
Arousal main effect	32	412	3.89	0	44	−5	47	78	4.98	26	19	−14	102	5.09	22	−1	−16
							47	33	3.46	36	29	1	61	4.2	−16	−8	−12
							13	18	3.33	38	−6	−6					
							47	95	4.94	−30	19	−17					
Arousal low alexithymics	24	13	3.12	0	35	5	47	48	4.18	−28	19	−19					
							47	43	3.61	126	17	−15					
							13	11	3.43	38	−8	−6					
Arousal LAXL masked by HAXL							13	11	3.43	38	−8	−6					
							47	25	3.34	30	19	−19					
Arousal high alexithymics	32	679	4.24	−4	43	12	47	64	4.63	34	29	1	95	6.25	22	−3	−13
	10						47	29	4.6	626	19	−14	93	5.92	−16	−6	−2
							47	54	3.88	−44	15	−5					
							47	32	3.47	−30	19	−17					
Arousal HAXL masked by LAXL	32	585	4.24	−4	43	12	47	58	5.21	34	29	1	41	5.21	22	−3	−13
	10	24	2.91	8	37	−8	47	81	3.74	26	23	−10	81	5.13	−16	−6	−12
							47	54	3.88	−44	15	−5					
Valence main effect	32	914	4.62	6	45	−1	13	35	3.23	−36	2	6					
Valence low alexithymics	32	75	4.22	−4	38	16	13	13	3.48	−34	−15	15					
	32	64	3.75	−4	45	−1											
Valence LAXL masked by HAXL	32	62	4.22	−4	38	16	13	13	3.48	−34	−15	15					
Valence high alexithymics	32	60	4.13	8	35	−9											
Valence HAXL masked by LAXL	32	51	4.13	8	35	−9											

The presented values refer to the peak voxel (Talairach-coordinates). Activations are only reported if they survived a threshold of $P < 0.05$. False discovery rate-corrected and $k > 10$. First and second column represent simple correlation analyses third and forth represent exclusive masking ($P = 0.05$, uncorrected) of first and second column. BA, Brodmann area; CS, cluster size; HALX, individuals with high degrees of alexithymia; LALX, individuals with low degrees of alexithymia.

Low alexithymia: There was a positive correlation in the dorsal anterior cingulate and insula. Exclusive masking with the respective results of high-alexithymic individuals showed significant activation in the dorsal anterior cingulate (Fig. 1a and b).

High alexithymia: There was a positive correlation in the dorsal anterior cingulate. Exclusive masking showed significant activation in the same region.

Arousal
Main effect: There was a positive correlation (the higher the arousal ratings the stronger the BOLD signal) in the anterior cingulate, the right and left insula as well as in both amygdalae (Table 1).

Low alexithymia: There was a positive correlation in the ventral anterior cingulate and insula. Exclusive masking showed significant correlation in the insula (Fig. 1c).

High alexithymia: There was an extended positive correlation in the anterior cingulate covering the dorsal and a smaller ventral part, in the right and left insula as well as in the right and left amygdala. Moreover, exclusive masking showed significant activation in the same regions (Fig. 1d–f).

There was no significant negative correlation with arousal or valence in the predefined regions.

Discussion
Anterior cingulate
In accordance with the literature [2,15,16], we found positive correlations of individual valence and arousal ratings with neural activity in the anterior cingulate for the combined group analysis.

In addition, in the subgroup of high alexithymics we found a correlation with individual arousal and valence ratings that survived masking with the respective results of the low alexithymics, whereas in the low-alexithymic individuals we only found a correlation with valence after masking. The peak activation for both the groups is located in the dorsal anterior cingulate. This region has been associated with cognitive processing related to emotional processing such as the cognitive control of emotional processing or emotional decision making [17]. In particular, activation of the dorsal anterior cingulate cortex has been repeatedly observed during the regulation of emotional responses [18,19]. Beauregard *et al.* [18] found that, specifically, the attempted inhibition of arousal was associated with anterior cingulate activation. Therefore, it may be speculated that the anterior cingulate activity represents an effort on the part of the high-alexithymic individuals to down-regulate the arousal of the emotional stimuli, for example, by recruiting additional cognitive resources. This fits in with the observation that high-alexithymic individuals tend to suppress emotions as their main strategy of emotion regulation [20].

Fig. 1
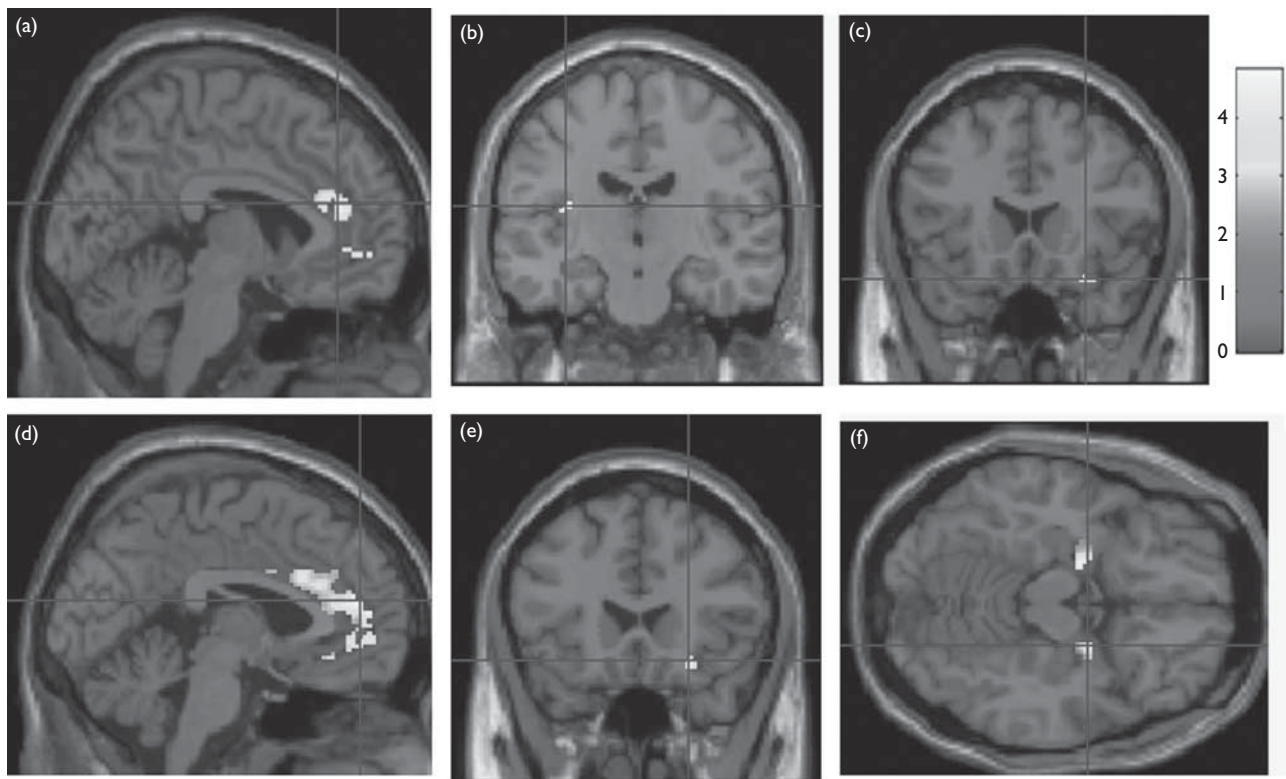
Images show statistical parametric (T) maps overlaid on a single individual's normalized brain in the MNI stereotactic space. Clusters are displayed with $P<0.05$ (False discovery rate-corrected) and $k>10$ voxels threshold. The crosses show the activation peaks (Table 1). (a–c) Low-alexithymic individuals: correlations between the observed BOLD response and individual valence (left and middle) and arousal (right) ratings exclusively masked ($P=0.05$ uncorrected) with the respective correlation for high-alexithymic individuals. (d–f) High-alexithymic individuals: Correlation between the observed BOLD response and individual arousal ratings exclusively masked ($P=0.05$ uncorrected) with the respective correlation for low-alexithymic individuals.

In contrast to our results, Lane's group reported an arousal-dependent positive correlation between the Levels of Emotional Awareness Scale (LEAS) scorings (high LEAS scoring corresponds to low scoring in the TAS-20) and dorsal anterior cingulate activity in women [4,5]. However, the results are only partly comparable as they did not apply the TAS-20. Moreover, the difference might be sex-related. It has been shown that the caudal anterior cingulate is more active in men than in women during instructed cognitive down-regulation of emotional processing [21] and that the relationship between LEAS and dorsal anterior cingulate activity is stronger in women than in men [5].

Insula

In the combined group analysis we found positive correlations of individual valence and arousal ratings with the insula activity. These findings are in line with imaging studies showing an insula involvement in valence [15,22] and arousal processing [23]. Regarding the subgroups, a correlation of the insula signal with valence and arousal ratings was found in the low-alexithymic individuals. In contrast, for the high-alexithymic group this correlation was only observed with arousal ratings. These findings confirm an altered processing in the insula in high-alexithymic individuals. As the insula is associated with internal monitoring of bodily responses and internal evaluation of emotions [24], altered insula function may – together with the anterior cingulate – account for the alexithymia-related disturbances of emotional processing.

Amygdala

Our results show amygdala activation during arousal processing in high but not in low-alexithymic individuals. In contrast, the amygdala was not involved in valence processing of either group. Reker *et al.* [9] also found altered processing in the amygdala, but reported a negative correlation with the TAS-20. However, in contrast to our paradigm their study focused on unconscious automatic brain reactivity using masked emotional faces and did not differentiate between arousal and valence processing.

Other groups did not find changes in amygdala activation in high-alexithymics [6,7]. This fits in with our results on valence processing and might therefore imply that those results should be related to valence processing rather than to arousal processing.

Imaging studies demonstrated that cognitive reappraisal of emotional scenes may lead to a decrease [19] or increase [25] of amygdala activity. Based on our results, one may speculate that the cognitive control of an emotional experience is altered in high-alexithymic individuals: the amygdala activity might not be properly down-regulated or, on the other hand, might even be enhanced by cognitive processes. Meriau *et al.* [8] found an increased coupling between the dorsal anterior cingulate and amygdala in individuals with high TAS-20 scores. They suggested that the increased effective connectivity of the anterior cingulate and amygdala may reflect an increased affective influence on the dorsal anterior cingulate. In addition, they reported a decreased coupling of the dorsal anterior cingulate and the ventrolateral prefrontal cortex. The latter brain area was related to emotional-cognitive interactions and down-modulation of emotional arousal by judgment [13,19]. Psychologically, this may result in an increased experience of emotional arousal without being able to deal cognitively with this experience.

Thus, in high-alexithymic individuals these connectivity changes may explain the enhanced arousal-driven activity in the dorsal anterior cingulate and amygdala and may account for the impairment in identifying and communicating their emotional state.

It has to be noted that rating of emotional stimuli may only be regarded as indirect evidence of emotional experience as it has been argued that direct access to subjective experiential data such as emotional experience may be impossible in principle [16]. Thus, it cannot be ruled out that the rating of emotional stimuli may also include the expression of emotion. One option for measuring the experienced emotion more accurately might be a correlation of autonomic nervous responses such as skin conductance to the emotional attributes of valence and arousal.

Conclusion
The correlations of neural activations with individual arousal and valence ratings revealed differences in the dorsal anterior cingulate, the insula and the amygdala. We suggest that these altered activations may account for the impaired ability of high-alexithymic individuals to appropriately handle emotional stimuli.

Acknowledgements

References
1 Franz M, Popp K, Schaefer R, Sitte W, Schneider C, Hardt J, *et al.* Alexithymia in the German general population. *Soc Psychiatry Psychiatr Epidemiol* 2008; **43**:54–62.

2 Franz M, Schaefer R, Schneider C, Sitte W, Bachor J. Visual event-related potentials in subjects with alexithymia: modified processing of emotional aversive information? *Am J Psychiatry* 2004; **161**:728–735.

3 Taylor GJ, Bagby RM. New trends in alexithymia research. *Psychother Psychosom* 2004; **73**:68–77.

4 Lane RD, Ahern GL, Schwartz GE, Kaszniak AW. Is alexithymia the emotional equivalent of blind sight? *Biol Psychiatry* 1997; **42**:834–844.

5 McRae K, Reiman EM, Fort CL, Chen K, Lane RD. Association between trait emotional awareness and dorsal anterior cingulate activity during emotion is arousal-dependent. *Neuroimage* 2008; **41**:648–655.

6 Berthoz S, Artiges E, Van De Moortele PF, Poline JB, Rouquette S, Consoli SM, *et al.* Effect of impaired recognition and expression of emotions on frontocingulate cortices: an fMRI study of men with alexithymia. *Am J Psychiatry* 2002; **159**:961–967.

7 Kano M, Fukudo S, Gyoba J, Kamachi M, Tagawa M, Mochizuki H, *et al.* Specific brain processing of facial expressions in people with alexithymia: an H2 15O-PET study. *Brain* 2003; **126**:1474–1484.

8 Meriau K, Wartenburger I, Kazzer P, Prehn K, Lammers CH, van der ME, *et al.* A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision making. *Neuroimage* 2006; **33**:1016–1027.

9 Reker M, Ohrmann P, Rauch AV, Kugel H, Bauer J, Dannlowski U, *et al.* Individual differences in alexithymia and brain response to masked emotion faces. *Cortex* 2010; **46**:658–667.

10 Bach M, Bach D, de ZM, Serim M, Bohmer F. Validation of the German version of the 20-item Toronto Alexithymia Scale in normal persons and psychiatric patients. *Psychother Psychosom Med Psychol* 1996; **46**:23–28.

11 Kuhner C, Burger C, Keller F, Hautzinger M. Reliability and validity of the revised beck depression inventory (BDI-II). Results from German samples. *Nervenarzt* 2007; **78**:651–656.

12 Stocker T, Kellermann T, Schneider F, Habel U, Amunts K, Pieperhoff P, *et al.* Dependence of amygdala activation on echo time: results from olfactory fMRI experiments. *Neuroimage* 2006; **30**:151–159.

13 Grimm S, Schmidt CF, Bermpohl F, Heinzel A, Dahlem Y, Wyss M, *et al.* Segregated neural representation of distinct emotion dimensions in the prefrontal cortex – an fMRI study. *Neuroimage* 2006; **30**: 325–340.

14 Buchel C, Holmes AP, Rees G, Friston KJ. Characterizing stimulus-response functions using nonlinear regressors in parametric fMRI experiments. *Neuroimage* 1998; **8**:140–148.

15 Viinikainen M, Jaaskelainen IP, Alexandrov Y, Balk MH, Autti T, Sams M. Nonlinear relationship between emotional valence and brain activity: evidence of separate negative and positive valence dimensions. *Hum Brain Mapp* 2010; **31**:1030–1040.

16 Heinzel A, Northoff G. Emotional feeling and the orbitomedial prefrontal cortex: theoretical and empirical considerations. *Philosophical Psychology* 2009; **22**:443–464.

17 Mohanty A, Engels AS, Herrington JD, Heller W, Ho MH, Banich MT, *et al.* Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function. *Psychophysiology* 2007; **44**:343–351.

18 Beauregard M, Levesque J, Bourgouin P. Neural correlates of conscious self-regulation of emotion. *J Neurosci* 2001; **21**:RC165.

19 Ochsner KN, Bunge SA, Gross JJ, Gabrieli JD. Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *J Cogn Neurosci* 2002; **14**:1215–1229.

20 Swart M, Kortekaas R, Aleman A. Dealing with feelings: characterization of trait alexithymia on emotion regulation strategies and cognitive-emotional processing. *PLoS One* 2009; **4**:e5751.

21 Domes G, Schulze L, Bottger M, Grossmann A, Hauenstein K, Wirtz PH, *et al.* The neural correlates of sex differences in emotional reactivity and emotion regulation. *Hum Brain Mapp* 2010; **31**:758–769.

22 Small DM, Gregory MD, Mak YE, Gitelman D, Mesulam MM, Parrish T. Dissociation of neural representation of intensity and affective valuation in human gustation. *Neuron* 2003; **39**:701–711.

23 Phan KL, Taylor SF, Welsh RC, Ho SH, Britton JC, Liberzon I. Neural correlates of individual ratings of emotional salience: a trial-related fMRI study. *Neuroimage* 2004; **21**:768–780.

24 Phan KL, Wager T, Taylor SF, Liberzon I. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 2002; **16**:331–348.

25 Ochsner KN, Ray RD, Cooper JC, Robertson ER, Chopra S, Gabrieli JD, *et al.* For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage* 2004; **23**: 483–499.