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DOI: https://doi.org/10.1159/000358090

Original Paper

Neuropsychobiology

Neuropsychobiology 2014;69:95–106
DOI: 10.1159/000358090

Received: July 1, 2013
Accepted after revision: December 16, 2013
Published online: February 27, 2014

Brain Activation Associated with Pride and Shame

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Key Words

Pride · Shame · Guilt · Amygdala · Medial prefrontal cortex · Insula · Functional magnetic resonance imaging

Abstract

Background: Self-referential emotions such as shame/guilt and pride provide evaluative information about persons themselves. In addition to emotional aspects, social and self-referential processes play a role in self-referential emotions. Prior studies have rather focused on comparing self-referential and other-referential processes of one valence, triggered mostly by external stimuli. In the current study, we aimed at investigating the valence-specific neural correlates of shame/guilt and pride, evoked by the remembrance of a corresponding autobiographical event during functional magnetic resonance imaging. ***Method:*** A total of 25 healthy volunteers were studied. The task comprised a negative (shame/guilt), a positive (pride) and a neutral condition (expecting the distractor). Each condition was initiated by a simple cue, followed by the remembrance and finished by a distracting picture. ***Results:*** Pride and shame/guilt conditions both activated typical emotion-processing circuits including the amygdala, insula and ventral striatum, as well as self-referential brain regions such as the bilateral dorsomedial prefrontal cortex. Comparing the two emotional conditions, emotion-processing circuits were more activated by pride than by shame, possibly due to either hedonic experiences or stronger involvement of the participants in positive self-referential emotions due to a self-positivity bias. However, the ventral striatum was similarly activated by pride and shame/guilt. In the whole-brain analysis, both self-referential emotion conditions activated medial prefrontal and posterior cingulate regions, corresponding to the self-referential aspect and the autobiographical evocation of the respective emotions. ***Conclusion:*** Autobiographically evoked self-referential emotions activated basic emotional as well as self-referential circuits. Except for the ventral striatum, emotional circuits were more active with pride than with shame.

Introduction

Self-referential emotions are directed to the experiencing persons themselves [1, 2]. Typically, they particularly comprise pride as a positive emotion, and guilt and shame on the negative side. The differentiation of guilt and shame and the general function of self-referential emotions are subjects of a longstanding and ongoing debate [1–3]. According to some theories [1–3], guilt addresses the *actions* of an individual, whereas shame is related to the individual *as a whole*. However, this differentiation is controversial [3] as guilt and shame arise together quite often [3]. In addition, some authors emphasize sequential effects [2] of guilt and shame. The aspects differentiating between these two emotions are rather inconsistent [3]. When comparing the so-called 'basic emotions', comprising joy/happiness, sadness, anger, disgust and fear [4–7], with self-referential emotions, the following differences can be found:

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– self-referential emotions are said to be more complex [1];
– self-referential emotions are said to require complex preconditions such as language-based self-representations of the subject and theory of mind [1];
– self-referential emotions develop later in childhood than basic emotions [1, 6, 8], although guilt/shame behavior can be observed already in 2- to 3-year-old children [3].

However, basic and self-referential emotions overlap in many other aspects: both are associated with characteristic, stably elicited facial and bodily expression patterns even in congenitally blind human beings [9], and their neurobiological circuits are parallel to and overlapping with basic emotions [10, 11].

The neurofunctional networks involved in basic emotions generally comprise the amygdala, insula, anterior cingulate cortex, ventral striatum, prefrontal cortex (PFC) and hypothalamus as well as midbrain regions [12–14]. These networks show a wide overlap with respect to valence, and some authors even question any valence specificity in emotional networks [15]; the amygdala, for instance, is more prominently influenced by arousal than by valence [16, 17]. Because fear is strongly associated with high arousal, fear seemingly activates the amygdala more strongly than other negative and positive emotions [14].

Compared with studies on basic emotions, research on the neurofunctional correlates of self-referential emotions is rather sparse. Conceptually, self-referential emotions are composed of: (a) an emotional aspect, at least if they are elicited; (b) a self-reflecting, self-evaluating and self-conscious aspect; and often (c) a sociocognitive component such as violation of social-moral norms and regulation of interpersonal behavior [2, 18]. Consequently, we expected self-referential emotions to activate (a) networks involved in the generation of basic emotions, covering the amygdala, insula and ventral striatum [19], (b) self-referential networks encompassing cortical midline structures and the dorsolateral PFC (DLPFC) [20–27], and eventually – corresponding to the sociocognitive part – (c) regions associated with evaluation by others and theory of mind (ToM; e.g. the superior temporal sulcus/temporoparietal junction, lateral prefrontal and parietal regions) [28, 29]. Until now, studies on self-referential emotions have either addressed only negative valence such as guilt, shame and embarrassment [30–35], or only positive emotions such as pride compared with joy [36]. To the best of our knowledge, no studies have directly compared the neural correlates of positive and negative valence in self-referential emotions. Furthermore, most studies used sentences or short stories which the participants had to imagine in order to induce the respective emotions. Two studies [30, 35] assessed and later re-presented autobiographical situations which contained some aspects of guilt, shame or sadness. In this way, this study took into account that self-referential emotions are often very individual, associated with personal values, events, memories and cognitions.

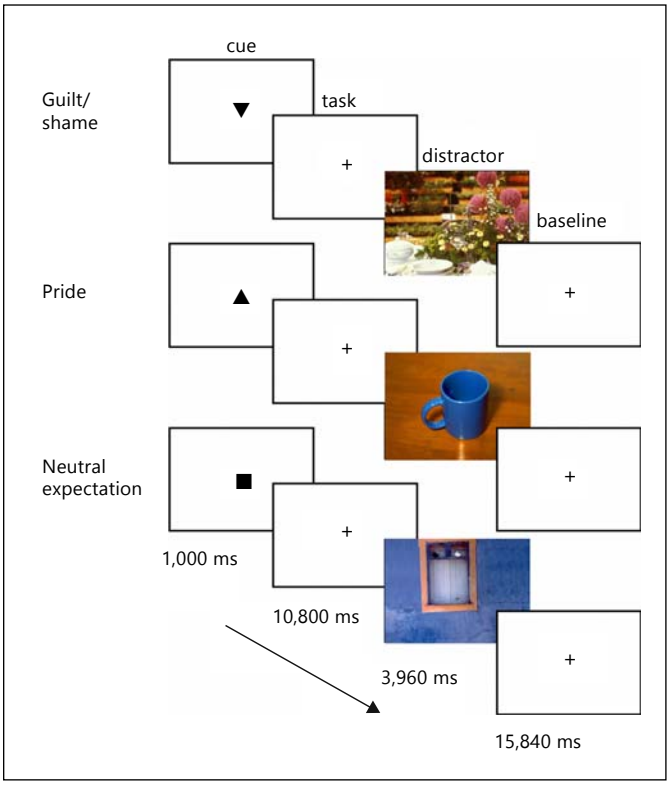


Fig. 1. Experimental task: 3 different conditions were presented, which consisted of the cued remembrance of a prideful or shameful event or a neutral condition with 12 runs each. Neutral pictures served to indicate the end of the periods and as a distractor.

This method is suitable to elicit positive and negative self-referential feelings with relatively high intensity and specificity. The current study aimed at comparing the neural correlates of positive and negative self-referential emotions. Compared with the prior studies [30, 35], we here defined the time frame for the event as the recent past to minimize time- and memory-associated influences. Subjects chose a situation in which they had felt proud and another situation associated with feelings of shame or guilt. During functional magnetic resonance imaging (fMRI), they were instructed to recall and reexperience the situation priorly chosen (fig. 1). We aimed at examin-

ing the valence-specific aspects of self-referential emotions, and in a broad sense compared the neural correlates of such internally triggered self-referential emotions with a neutral condition. We hypothesized brain activation in self-referential brain areas such as the dorsomedial PFC (DMPFC) and DLPFC, and in emotion-associated regions such as the amygdala and insula, when comparing the emotion conditions with neutral ones. Due to the autobiographical memory component, we also hypothesized activation in the hippocampus and posterior cingulate cortex (PCC). We predicted pride to activate brain areas associated with positive emotions, such as the ventral striatum [37, 38] and amygdala [39]. We hypothesized the shame/guilt condition to increase activity in the anterior insula [40, 41] and amygdala [42]. We first analyzed the data in anatomically defined regions of interest (ROI; DMPFC, DLPFC, amygdala, anterior insula and ventral striatum) as well as in the whole brain. The whole-brain analysis was done on an exploratory basis.

Methods

Participants

Twenty-nine healthy subjects (age: 18–50 years; 16 female) were recruited via E-mail advertisements and by word of mouth. All participants were right-handed according to a handedness scale [43]. The participants were preassessed with a semistructured interview based on the ICD-10 to exclude prior and current neurological and psychiatric illnesses and intake of any medication (except for oral contraceptives) or psychotropic substances. Further exclusion criteria were: pregnancy; excessive consumption of alcohol (>7 units/week), cigarettes (>1 pack/day) and caffeine (>5 cups/day); and contraindication to fMRI. The study was approved by the local ethics committee and was conducted in compliance with the Declaration of Helsinki [44]. All participants gave their written informed consent. Immediately after scanning, the participants were systematically asked about their performance on the task in a qualitative postexperimental interview, with specific reference to lack of concentration or sleepiness. One subject reported sleepiness and was therefore excluded from the analysis, and 3 subjects showed several movement artifacts (sudden head movements of >3 mm), such that, in total, 4 subjects had to be excluded. The included subjects confirmed that they were able to follow the instructions. In total, 25 subjects were included in the analysis.

Experimental Design

The subjects underwent fMRI while performing a task comprising 3 conditions in a pseudorandom order: remembrance of an event in which the subject felt ashamed or guilty ('shame' condition); remembrance of an event associated with feelings of pride ('pride' condition); and a neutral waiting condition ('neutral' condition). Prior to scanning, the subjects were instructed to choose 1 situation between 3 weeks and 6 months ago in which they had felt ashamed/guilty or proud, and which they remembered vividly and easily. During fMRI, simple visual cues indicated to the participants to recall and reexperience the respective situations (fig. 1). Compared with previous studies which provided the participants with external, experimenter-chosen stimuli as anchors for remembrance, the method used here was easy for the participants because it included only 1 personally prechosen situation. For the 'neutral' condition, the subjects were instructed to await the upcoming picture. The time frame of 3 weeks to 6 months for the situation to be remembered was chosen according to pretests to reduce effects of differences in 'nearness' and vividness of events and therefore of differing emotional activation between the conditions. The periods for the conditions were initiated by an indicating cue and ended by presenting a distracting neutral picture (fig. 1). The instructing cues (pride ▲, shame/guilt ▼, and neutral ■) were presented for 1 s. Including this cue, the conditions lasted a period of 11,880 ms, equivalent to 6 TR (repetition time for the fMRI volumes). Thereafter, as a stop signal, distracting neutral pictures from the International Affective Picture System [45] were presented for 3,960 ms (2 TR). Then a baseline period of 8 TR followed until the next trial was started. In total, each condition occurred 12 times in a randomized order (total task duration: about 21 min). The symbols were easily understandable, so that no interfering working memory activity had to be used. Intentionally, the task further did not comprise an interfering decisional or motor reaction component. The task was programmed and presented with Presentation™ (Neurobehavioral Systems, Albany, N.Y., USA).

Image Acquisition

Imaging was performed with a 3.0-tesla GE Signa™ HD Scanner (GE Medical Systems, Milwaukee, Wisc., USA; 8-channel head coil). Echo-planar imaging was performed for fMRI (TR/TE: 1,980/32 ms; 22 sequential axial slices, whole brain; slice thickness: 3.5 mm; 1-mm gap; resulting voxel size: 3.125 × 3.125 × 4.5 mm; matrix: 64 × 64; field of view: 200 mm; flip angle: 70°); 676 volumes were obtained per subject, 16 per trial. The first 4 volumes were discarded to allow for T2 equilibration effects. High-resolution 3-D T1-weighted anatomical volumes were acquired (TR/TE: 9.9/2.9 ms; matrix size: 256 × 256; 1 × 1 × 1 mm resolution; axial orientation) for coregistration with the functional data. T2-weighted images in parallel to the echo-planar imaging sequence were acquired to exclude possible T2-sensitive abnormalities. The stimuli were presented via digital video goggles (Resonance Technologies, Northridge, Calif., USA).

Data Analysis

The fMRI data were analyzed using BrainVoyager™ QX 2.3.0 (Brain Innovation, Maastricht, The Netherlands) [46]. Preprocessing of the functional scans included motion correction, slice scan time correction, high-frequency temporal filtering and removal of linear trends, as has been described before [47]. Functional images were superimposed on the 2-D anatomical images and incorporated into 3-D data sets. The individual 3-D data sets were transformed into Talairach space [48], resulting in a voxel size of 3 × 3 × 3 mm, and then spatially smoothed with an 8-mm gaussian kernel for subsequent group analysis. Four predictors representing the 3 conditions and the distractor (shame, pride, neutral, presentation of neutral picture) were used to build the design matrix. Single trials with fMRI signal artifacts of more than 3 times the mean signal change amplitude (e.g. due to head movements) were eliminated. The periods were modeled as epochs using a two-gamma hemo-

Table 1. ROI analysis

	Talairach x/y/z	F(72, 2); p	Shame/guilt > neutral, p[1]	Pride > neutral, p[1]	Pride > shame/guilt, p[1]
Anterior insula – left	–34/13/4	17.27; *<0.001*	*<0.0001*	*<0.0001*	n.s.
Anterior insula – right	34/13/4	4.98; *0.009*	*0.0092*	0.0960	n.s.
DMPFC – left	–6/6/50	27.51; *<0.001*	*<0.0001*	*<0.0001*	n.s.
DMPFC – right	6/6/50	15.74; *<0.001*	*<0.0001*	*<0.0001*	n.s.
DLPFC – left	–42/10/34	6.90; *0.002*	*0.0086*	*0.0041*	n.s.
DLPFC – right	42/10/34	2.55; 0.085	–	–	–
Ventral striatum – left	–9/6/6	7.50; *0.001*	*0.0212*	*0.0011*	n.s.
Ventral striatum – right	9/6/6	6.44; *0.003*	*0.0282*	*0.0032*	n.s.
Amygdala – left	–19/–5/–17	3.25; *0.045*	n.s.	*0.0494*	n.s.
Amygdala – right	19/–5/–17	2.68; 0.075	–	–	0.084

Given is F of the one-factorial ANOVA and p of the respective contrasts. Significant contrasts are marked in italics. Contrasts were calculated using the mean β-weights of the respective ROI. x/y/z = Talairach coordinates of the center of the cubic ROI.

[1] Bonferroni-corrected for multiple comparisons.

dynamic response function adapted to the applied period duration provided by BrainVoyager.

The fMRI data analysis, based on the general linear model, comprised the following steps. First, fixed-effects analyses were calculated separately for each subject for the 3 contrasts, comparing the 3 conditions 'pride versus shame', 'shame versus neutral' and 'pride versus neutral', resulting in summary images. The summary images were subjected to second-level analyses within the anatomically predefined ROI. Bilateral cubic ROI were positioned in the DMPFC, DLPFC, anterior insula, amygdala and ventral striatum according to the respective literature (Talairach coordinates and volumes are given in table 1). According to anatomy, the DMPFC ROI each measured 12 × 12 × 12 mm (resulting volume: 1,728 mm^3) and the DLPFC ROI 15 × 15 × 15 mm (volume: 3,375 mm^3). Both ROI were based on previous studies [20, 49]. For the amygdala, cubic ROI with an edge length of 10 mm (volume: 1,000 mm^3) were centered according to the Talairach Daemon [50]. The ROI in the anterior insula were based on the existing literature (15 × 15 × 15 mm; volume: 3,375 mm^3) [40, 51], as were the ROI in the ventral striatum (10 × 10 × 10 mm; volume: 1,000 mm^3) [52, 53]. From these ROI, the mean β-weights for each subject and each condition were extracted. With the β-weights, we calculated a one-factorial ANOVA with the factors 'task condition' and 'ROI' using SPSS version 20. In those ROI where the overall F test was significant, the contrasts 'pride versus shame', 'shame versus neutral' and 'pride versus neutral' were calculated with Bonferroni correction for multiple comparisons.

In addition, we performed exploratory whole-brain random-effects analyses for each of the 3 contrasts. For the contrast 'pride versus shame', the voxel-wise statistical threshold was set to $p < 0.001$ with a cluster threshold of 5 voxels of 3 × 3 × 3 mm (135 mm^3), as suggested before [54], to avoid too many false negatives. For the more basic contrasts 'pride versus neutral' and 'shame versus neutral' and for the conjoined contrast '(pride vs. neutral) plus (shame vs. neutral)', the threshold was set to $p < 0.0001$ with the same cluster threshold of 135 mm^3. Anatomical regions were identified based on the Talairach atlas [48] and Talairach Daemon [50].

Questionnaires

For general psychometric characterization, the participants completed a Self-Rating Depression Scale (SDS) [55], and for state and trait anxiety, the State-Trait Anxiety Inventory [56]. After the task, all participants were interviewed about their ability to remember and to reexperience the 2 chosen situations. To avoid too intensive intrusion and possible embarrassment, we intentionally did not ask the subjects about the specific content of the situation, but only openly about the time since the event and the specific emotion and circumstances (e.g. type of emotion elicited, pride/shame due to own appraisal or due to others' appraisals and comments). The participants could name more than 1 emotion per condition or event, and could describe self-appraisal or appraisal by others freely and in parallel. All subjects confirmed that they were able to remember and imagine each one event vividly. However, due to technical reasons, the detailed interview results were only available from 18 of the 25 participants included. Questionnaires were analyzed using SPSS version 20; the significance level was set at $p < 0.05$.

Results

Behavioral Results

The included participants (9 male, 16 female) were of a mean age of 31.9 years (standard deviation, SD: 10.2 years; range: 21–50 years). The mean score on the SDS was 35.5 (SD: 7.27), the mean state anxiety score 33.3 (SD: 7.02), and the mean trait anxiety score 31.6 (SD: 6.52). Thus, the participants' ratings corresponded to SDS and state anxiety norms in the general population, only trait anxiety was slightly lower [57, 58].

The mean time passed since the remembered event was reported to be 6.2 ± 6.6 weeks (±SD) in the positive

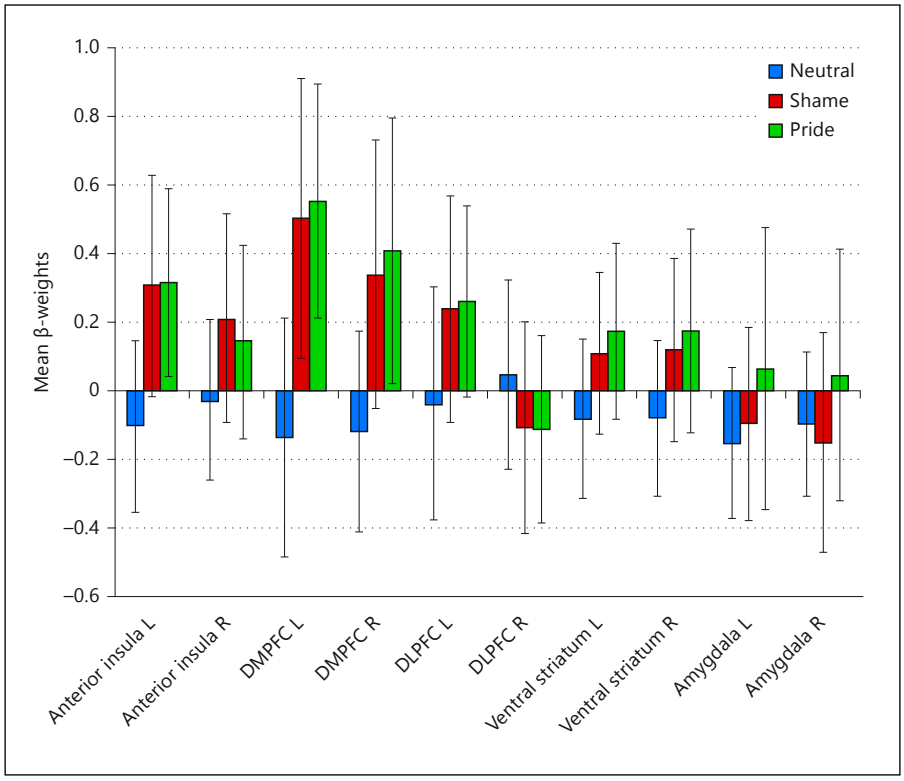


Fig. 2. Bar chart depicting the mean β-weights of the ROI analysis (±SD). Location and size of the ROI are given in table 1. L = Left; R = right.

and 7.7 ± 9.9 weeks in the negative condition (paired Student's t test: t = 0.526, p = 0.606, not significant). In the positive condition, 97% of the participants reported pride as the elicited emotion, 63% joy. In the negative condition, 92% of the participants reported shame, 37% guilt and 63% feelings of failure. In 87% of the participants, the positive situation was associated with self-evaluation ('I did well according to my own values'), in 40% with praise by others. In the negative condition, the situation was mostly associated with negative evaluation by others (76%) and to a lesser degree with negative self-evaluation (58%). Between the conditions, the degree of self-evaluation was significantly higher in the positive condition than in the negative condition (t = 2.357, p = 0.030), whereas the negative condition was significantly more associated with evaluations by others compared with the positive condition (t = 3.071, p = 0.007).

Brain Activity Associated with Pride and Shame in Selected ROI

Pride and shame/guilt compared with the neutral condition showed comparable activation bilaterally in the DMPFC, bilaterally in the ventral striatum, and in the left anterior insula and left DLPFC (table 1). The left amygdala was significantly activated only by the contrast 'pride vs. neutral', whereas the right anterior insula was active with the contrast 'shame/guilt vs. neutral', with only a trend in the 'pride vs. neutral' contrast. With correction for multiple comparisons, we found no significant activation in the right DLPFC. When comparing pride and shame/guilt directly, the ANOVA revealed no significant difference. There was only a trend for a difference in the right amygdala, which was otherwise not significantly differently activated (fig. 2).

Brain Activation in Whole-Brain Analysis

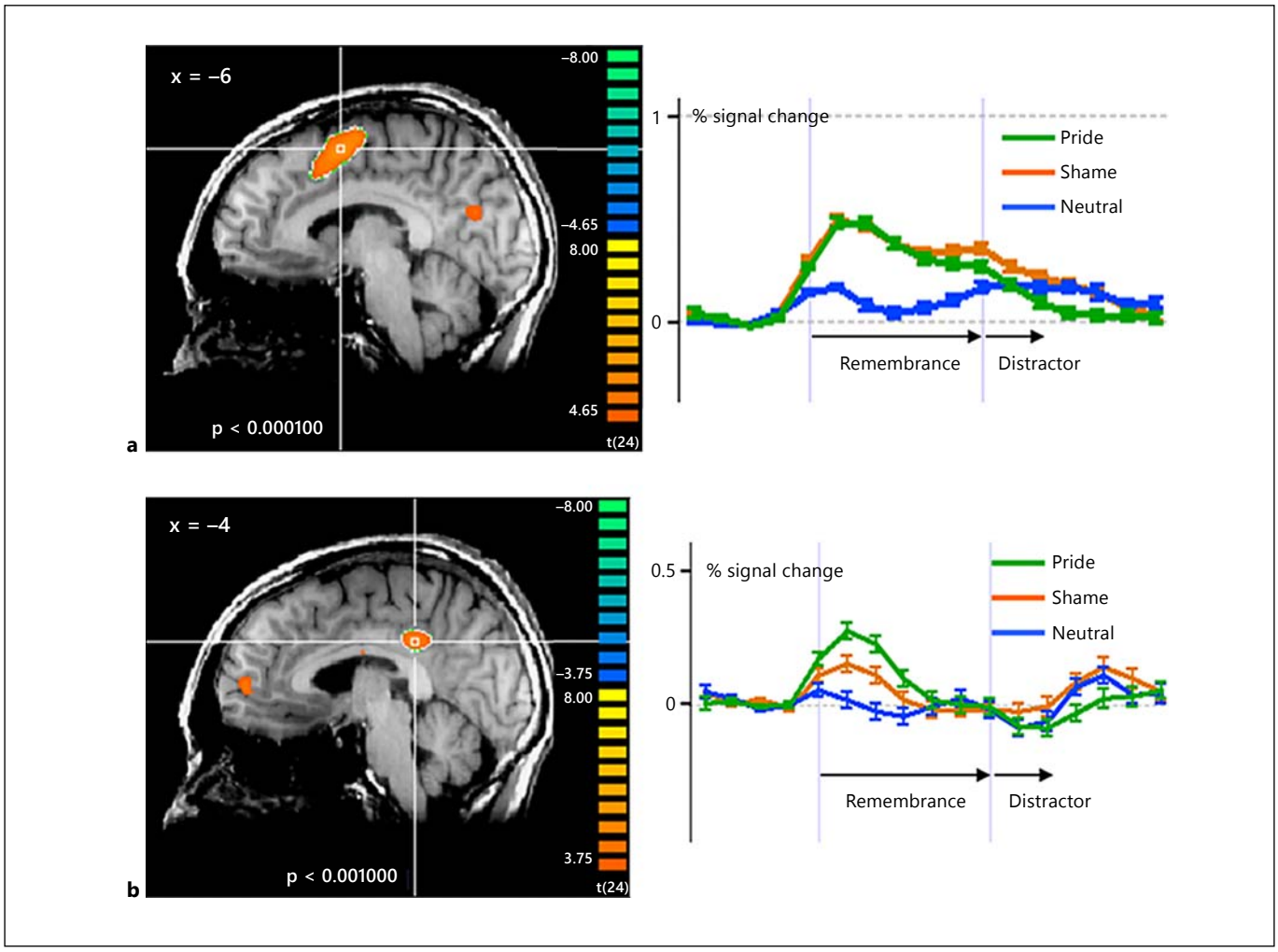
The comparison of pride with shame/guilt in the whole-brain analysis (table 2) was associated with increased activation cortically in the left superior frontal gyrus (FG) and the left medial FG within the ventromedial PFC, as well as with activation in the middle and PCC (fig. 3b) and the inferior temporal and parietal gyrus, and subcortically in the left caudate body and lateral thalamus. Shame/guilt activated no brain region significantly stronger than pride (table 2).

Comparing pride with the neutral condition (table 3) was associated with increased activity in the left superior and medial FG as part of the MPFC (fig. 3a), in the left

Table 2. Activated regions in whole-brain analysis of contrast 'pride versus shame/guilt'

Anatomic regions	Talairach coordinates x/y/z	Cluster size, mm^3	t_{max}	p_{max}
Pride vs. shame/guilt				
Superior FG – left (BA 6)	–19/16/60	212	4.490	0.000152
Medial FG – left (BA 10)	–4/55/6	473	4.747	0.000079
Cingulate gyrus – left/right (BA 31)	–4/–35/30	2,067	6.533	0.000001
PCC – right (BA 30)	29/–29/33	358	4.499	0.000148
Inferior temporal gyrus – left (BA 37)	–55/–44/–18	357	4.701	0.000089
Inferior parietal lobe – left (BA 39)	–34/–68/30	985	4.738	0.000081
Caudate body – left	–10/–11/24	779	4.860	0.000059
Lateral thalamus – left	–22/–20/–3	1,312	4.599	0.000115
Shame/guilt vs. pride	no significant regions	–	–	–

Given are the Talairach coordinates of peak activation; $p < 0.001$; cluster threshold: 135 mm^3. BA = Brodmann area.



Color version available online

Fig. 3. Color bars (colors online only) represent t values. Right column: average time course of activation (with standard errors). Gray vertical lines: marking task periods. The Talairach x-coordinates indicate the location of the sagittal section. **a** Activation in the medial PFC in the contrast 'pride vs. neutral' ($p < 0.0001$). The contrast 'shame vs. neutral' resulted in a nearly identical activation at the same statistical threshold. **b** Activation in the PCC in the contrast 'pride vs. shame' ($p < 0.001$).

Table 3. Activation in whole-brain analysis of contrasts of self-referential emotions versus neutral

Anatomic region	Talairach coordinates x/y/z	Cluster size, mm^3	t_{max}	p_{max}
Pride vs. neutral				
Medial/superior FG – left (BA 6)	–10/–5/57	6,552	7.912	<0.000001
Middle FG/precentral gyrus – left (DLPFC; BA 6)	–40/–8/57	2,790	6.639	0.000001
Inferior FG/insula – left (BA 13)	–40/7/9	1,800	5.711	0.000007
PCC – left (BA 30)	–19/–53/12	1,973	5.900	0.000004
Precuneus – left (BA 31)	–10/–68/21	829	5.577	0.00001
Extended amygdala/BNST – left	–16/–2/–3	197	5.553	0.00001
Lateral thalamus/caudate body	–28/–20/27	1,663	5.200	0.000025
Neutral vs. pride	no significant regions			
Shame/guide vs. neutral				
Medial FG/anterior cingulate – left (BA 6)	–7/1/54	4,168	6.781	0.000001
Superior FG – left (BA 10)	–19/49/21	184	5.219	0.000024
Middle FG/precentral gyrus – left (DLPFC; BA 6)	–37/–5/54	696	5.477	0.000012
Inferior FG/insula – left (BA 45, 13)	–58/19/9	5,905	6.352	0.000001
Insula – right (BA 13)	47/13/6	1,397	6.092	0.000003
PCC – left (BA 30)	–19/–50/9	2,775	5.277	0.000021
Lingual gyrus – left (BA 19)	–10/–56/–15	1,247	5.599	0.000009
Lentiform nucleus – left/ventral striatum	–19/4/0	214	5.528	0.000011
Lentiform nucleus – left/caudate head	–22/1/21	136	5.067	0.000035
Neutral vs. shame/guilt				
Supramarginal gyrus – right (BA 40)	44/–38/36	512	5.205	0.000025
Superior parietal lobule – right (BA 7)	29/–65/42	233	5.567	0.00001
Conjunction analysis (shame/guilt vs. neutral) and (pride vs. neutral)				
Medial FG/anterior cingulate cortex – left (BA 6/32)	–7/4/51	6,209	6.587	0.000001
PCC – left (BA 30)	–13/–59/9	2,306	5.352	0.000015
Insula – left (BA 13)	–43/10/12	2,234	6.032	0.000003
Precentral gyrus – left (BA 6)	–37/–8/57	275	5.113	0.000028

Given are the Talairach coordinates of peak activation; $p < 0.0001$; cluster threshold: 135 mm^3. BA = Brodmann area; BNST = bed nucleus of stria terminalis; DLPFC = dorsolateral prefrontal cortex; FG = frontal gyrus; PCC = posterior cingulate cortex.

middle FG and precentral gyrus within the DLPFC, in the left insula and inferior FG as part of the ventrolateral PFC, in the left PCC, and subcortically in the left bed nucleus of the stria terminalis as part of the extended amygdala and in the left lateral thalamus extending to the caudate body.

Shame/guilt compared with neutral (table 3) was similarly associated with activity in the left medial FG (fig. 3a) extending to the anterior cingulate cortex and with activity in the superior and middle FG as well as the precentral gyrus, all belonging to the DLPFC. Furthermore, the insula and inferior FG were more active bilaterally with shame/guilt, as well as, additionally, the left PCC and lingual gyrus, and subcortically the ventral striatum and caput of the caudate, both belonging to the lentiform nucleus. In this contrast, we detected a decreased activation in the right supramarginal gyrus and in the right superior parietal lobule with shame/guilt compared with neutral. The conjoined contrast identifying those brain regions activated by both self-referential conditions versus neutral (table 3) resulted in increased activation in the MPFC and left PCC and in the left insula and left premotor cortex.

Discussion

The aim of our study was to investigate the neuronal correlates of the positive and negative self-referential emotions pride and shame/guilt with particular regard to valence when specifically evoked by the remembrance of individual autobiographical events. Both conditions activated brain regions involved in self-referential processing such as the MPFC and PCC [20, 59], as well as emotion-

related brain regions such as the insula, amygdala and ventral striatum [13, 60].

When comparing pride and shame/guilt directly, in the whole-brain analysis pride was associated with stronger brain activity than shame/guilt, particularly in brain regions involved in emotion processing, such as the left amygdala. Activation of the left ventral striatum, which is known to be implicated in the processing of hedonic stimuli [61, 62] and in reward processing [63, 64], could be a correlate of positive emotions and perhaps even pleasure which is associated with the remembrance of a prideful event. However, we found no difference between pride and shame/guilt in the ventral striatum. Activation of the ventral striatum with aversive stimuli [61], with disgust and fear [65] and with pain [66] has been shown before, and there is an ongoing debate on a function of the nucleus accumbens as a behaviorally activating system which motivates the individual to either approach or withdraw from an object [67]. Therefore, our findings are in line with the presumption that the ventral striatum is involved in the identification of salience and the production of affective or motivational states [68] beyond reward. In parallel to the ventral striatum, pride involved the left amygdala more strongly than did shame/guilt. The amygdala is central for the processing of emotional information [19, 68–71]. Amygdala activation has been associated with negative emotion, particularly with fear and also with sadness and disgust [15, 65, 72], but also with pleasant emotional and reward-related stimuli [15, 39, 73]. Furthermore, studies rather point to a correlation of amygdala activity with arousal than with valence [16, 70]. In contrast with other studies [74], here the amygdala was not more active in the negative than in the positive condition, but rather conversely. This difference could be explained by the nature of emotional stimulation, which in our study was created by the subjects themselves and by their engagement and ability to remember and relive the respective events. According to a known self-positivity bias [18], healthy participants encode and remember positive self-referential information better than negative information. This could have caused more pride-associated activation in emotion-processing brain regions such as the amygdala and ventral striatum.

The pattern of activation in the bilateral anterior insula supports the suggestion that pride and shame/guilt involved brain regions similarly to basic emotional stimuli [75]. The left insula was active in both conditions, whereas the right insula was less active with pride, although a significant difference between pride and shame/guilt was lacking. The insula is known to be involved in the generation of affective states in response to emotive stimuli of both negative and positive valence [68, 76, 77], as well as of pain [68, 78]. Previous studies have also shown insular activation during the experience of guilt and shame [30, 35] and associated the insula more strongly with negative emotional valence and, particularly, anxiety [79, 80]. Taken together, the parallel involvement of the insular cortex in both self-referential emotions with a mild overweight in the negative condition in our study could reflect emotional arousal. In summary, pride and shame/guilt were activated in our study networks similarly to basic emotions.

In our study, the self-referential aspect of pride and shame was reflected by the strong bilateral activation in the DMPFC, anatomically defined, and in the whole-brain analyses. The DMPFC is part of the cortical midline structures, which are supposed to be core structures of self-referential processing [20]. We found no differential activation in the DMPFC with pride and with shame/guilt. This could correlate with the similar degree of self-reference of these conditions. However, the study by Takahashi et al. [36] on pride found no involvement of the MPFC, whereas 4 other studies did [30–32, 34]. All of these authors interpreted the function of the MPFC primarily as a neural substrate of social cognition or ToM. This interpretation could be justified by some aspects of the specific tasks (such as to imagine being in the described situation, which means to put oneself into the position of someone). However, the 'stimuli' in the current study were completely self-generated and based on individual memories, whereas any interference due to external stimuli or external monitoring – and particularly marked ToM aspects – were excluded. This supports more the self-referential, relatively valence-independent function of the DMPFC than ToM, social transgression and judgement aspects (although we did not control for the involvement of the DMPFC in ToM). This is backed up by a study on the neural basis of human social values [33] which found higher activation within the ventral MPFC during self-agency conditions such as pride and guilt compared with other-agency conditions such as gratitude and anger – however, without a strong effect of valence in the MPFC. The same reasons could explain why the current study lacks activation in the characteristic regions involved in social cognition or ToM, such as the posterior superior temporal sulcus and temporal poles [81–83].

The PCC activation during pride and shame in our study could be explained by the aspect of autobiographical remembrance of our task. The PCC is involved in en-

coding and retrieving autobiographical memory [20, 84, 85]. A previous study on guilt-specific processing using autobiographical memory found similar PCC activation as in the current study [30]. When comparing pride and shame/guilt, the PCC here was more active in the positive condition. This could be explained again by a general proneness to positive self-relevant stimuli and memories in healthy individuals (positivity bias) [18], even if the participants showed no marked difference in perceived vividness of the positive and negative memories. In the two self-referential conditions, the explorative whole-brain analysis revealed activation in brain regions associated with visual imagery, such as the lingual gyrus and precuneus, and in areas associated with verbal processing, such as the left inferior FG. These findings are consistent with the supposition of visual and verbal imagination during the remembrance task [86]. One might perhaps have expected to find activation in the hippocampal region during remembrance of the events. Only half of the studies addressing neural circuits of self-referential emotions found activation in the hippocampal region [31–33], and even in these studies, hippocampal activation was not consistent (in none of these studies was guilt associated with hippocampal activation, only embarrassment or shame or pride was). The other studies [30, 34–36] detected no hippocampal activation in self-referential emotional conditions. Regarding models of autobiographical memory, a recent meta-analysis of studies on self-referential memory processes detected no significant hippocampal activation [87]. Furthermore, the hippocampus might be more sensitive to concrete contextual aspects versus scenic emotional memories [88], and to remote versus recent events [89].

In the DLPFC ROI and whole-brain analysis, we found only an activation of the left DLPFC during the two self-referential conditions, which in the whole-brain analysis was stronger with pride than with shame/guilt. The DLPFC is involved in a number of neuropsychological functions such as executive functions (planning, execution of actions) [90], reasoning, action inhibition, working memory and attention [91–94], which involve not only separate but also overlapping parts of the DLPFC. One meta-analysis associated the MPFC more strongly with emotional processes, whereas the DLPFC was more active with cognitive tasks [95]. Emotion regulation processes also involve the DLPFC with a right-lateralized preponderance [96, 97]. Furthermore, studies on depressed patients predominantly detected hypoactivity of the left and hyperactivity of the right DLPFC [98–101]. In healthy subjects, an imbalance between right and left DLPFC, with a left-lateralized association with positive valence and a right-lateralized association with negative valence, has been postulated [102, 103]. However, our study revealed no such valence-specific lateralization of DLPFC activity. One prior study on self-referential emotions described bilateral activation of superior and middle FG corresponding to the DLPFC with shame-related processing [32], whereas Wagner et al. [30] found lower activation of the right DLPFC with guilt and shame compared with the non-self-referential sadness condition ([30], supplementary material). The other studies on self-referential emotions described no prominent activation of the DLPFC [31, 33, 34, 36]. One explanation for the involvement of the DLPFC in the current study could rely on cognitive processes (remembrance vs. simple expectation in the neutral condition).

Regarding the discussion on the differentiation of shame and guilt, the participants in the current study reported shame more often than guilt; only 1 participant reported no shame. Therefore, these results cannot contribute to this discussion. In addition to the hypotheses given above, the self-focus associated with shame could account for the lack of activation in other-referential temporoparietal and lateral orbitofrontal brain regions in our study.

The open and noncontrolled instruction in our study could be regarded as a limitation, because we could not explicitly control whether the participants indeed remembered situations associated with pride and shame or guilt as they were instructed. However, we regard just this as a major strength of our design, i.e. that we did not interfere with the individual memories and personal feelings. Such interference can and will occur for instance with real-time monitoring of mood or emotions. By using this design, it was possible to let the participants immerse themselves in very personal and individual memories and the associated unpleasant emotions, even if we as experimenters could not control this completely. However, we interviewed the participants rather explicitly (nevertheless avoiding disclosure of the content of the memory itself) about the vividness and type of the elicited emotion, and whether the situation contained more evaluation from other people or from themselves. We found no clear difference between the two conditions with regard to self-reported vividness in this interview. However, due to the subjective nature of the events, we did not conduct a quantitative analysis of this aspect. Anyway, it might have influenced the neural representation of these conditions.

Another limitation of the current study is that we enclosed no non-self-referential emotional conditions

which could have served as direct controls for valence and for disentangling valence from self-reference. This could perhaps be done in future studies. This limitation applies particularly to the neutral condition, which, compared with the two self-referential conditions, was much less complex and controlled, in particular not for memory-associated processes in the self-referential conditions. One specific focus of the current study was the evocation of pride and shame by remembrance of two individual situations, which is a new approach to examining individual self-referential processes. Respective stimuli associated with individual remembrance, but without the self-referential aspect, are difficult to develop. We therefore accepted the lack of specific control conditions for the sake of introducing and testing the principle of self-referential, memory-associated emotions.

This study could be the basis for examining these self-referential emotions in patients in which these emotions are less controllable and more influential on everyday life, such as patients suffering from a depressive or (hypo) manic mood episode, in continuation of the pioneering study by Green et al. [104]. Such studies could help in identifying the neurobiological differences between well-contained and rather helpful self-referential emotions in healthy subjects and their sometimes overwhelming and destructive counterparts in mental disorders, and perhaps in developing strategies assisting in the treatment of these disorders.

Acknowledgements

This study was supported by a grant from the Swiss National Science Foundation (No. 320030-133009).

References

1 Zinck A: Self-referential emotions. Conscious Cogn 2008;17:496–505.
2 Tangney JP, Tracy JL: Self-conscious emotions; in Leary MR, Tangney JP (eds): Handbook of Self and Identity. New York, Guilford, 2012, vol 1, pp 446–478.
3 Eisenberg N: Emotion, regulation, and moral development. Ann Rev Psychol 2000;51:665–697.
4 Ekman P: Basic emotions; in Dalgleish T, Power T (eds): Handbook of Cognition and Emotion. New York, Wiley, 1999, pp 45–60.
5 Tracy JL, Randles D: Four models of basic emotions: a review of Ekman and Cordaro, Izard, Levenson, and Panksepp and Watt. Emot Rev 2011;3:397–405.
6 Izard CE: Basic emotions, natural kinds, emotion schemas, and a new paradigm. Perspect Psychol Sci 2007;2:260–280.
7 Power M, Dalgleish T: Cognition and Emotion: From Order to Disorder, ed 2. New York, Psychology Press, 2008.
8 Lewis M: The self in self-conscious emotions. Ann NY Acad Sci 1997;818:118–142.
9 Tracy JL, Matsumoto D: The spontaneous expression of pride and shame: evidence for biologically innate nonverbal displays. Proc Natl Acad Sci USA 2008;105:11655–11660.
10 Darwin C: The Expression of the Emotions in Man and Animals. Chicago, Chicago UP, 1872.
11 Tracy JL, Robins RW: Show your pride: evidence for a discrete emotion expression. Psychol Sci 2004;15:194–197.
12 Sabatinelli D, Fortune EE, Li Q, Siddiqui A, Krafft C, Oliver WT, Beck S, Jeffries J: Emotional perception: meta-analyses of face and natural scene processing. Neuroimage 2011; 54:2524–2533.
13 Dalgleish T: The emotional brain. Nat Rev Neurosci 2004;5:583–589.
14 Fusar-Poli P, Placentino A, Carletti F, Landi P, Allen P, Surguladze S, Benedetti F, Abbamonte M, Gasparotti R, Barale F, Perez J, McGuire P, Politi P: Functional atlas of emotional faces [sic!] processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. J Psychiatry Neurosci 2009;34:418–432.
15 Lindquist KA, Wager TD, Kober H, Bliss-Moreau E, Barrett LF: The brain basis of emotion: a meta-analytic review. Behav Brain Sci 2012;35:121–143.
16 Lewis PA, Critchley HD, Rotshtein P, Dolan RJ: Neural correlates of processing valence and arousal in affective words. Cereb Cortex 2007;17:742–748.
17 Sergerie K, Chochol C, Armony JL: The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. Neurosci Biobehav Rev 2008;32:811–830.
18 Leary MR: Motivational and emotional aspects of the self. Ann Rev Psychol 2007;58: 317–344.
19 Ochsner KN, Silvers JA, Buhle JT: Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. Ann NY Acad Sci 2012;1251:E1–E24.
20 Northoff G, Heinzel A, de Greck M, Bermpohl F, Dobrowolny H, Panksepp J: Self-referential processing in our brain: a meta-analysis of imaging studies on the self. Neuroimage 2006;31:440–457.
21 Moran JM, Macrae CN, Heatherton TF, Wyland CL, Kelley WM: Neuroanatomical evidence for distinct cognitive and affective components of self. J Cogn Neurosci 2006;18: 1586–1594.
22 Northoff G, Bermpohl F: Cortical midline structures and the self. Trends Cogn Sci 2004; 8:102–107.
23 Herwig U, Kaffenberger T, Schell C, Jäncke L, Brühl A: Neural activity associated with self-reflection. BMC Neurosci 2012;13:52.
24 van der Meer L, Costafreda S, Aleman A, David AS: Self-reflection and the brain: a theoretical review and meta-analysis of neuroimaging studies with implications for schizophrenia. Neurosci Biobehav Rev 2010;34: 935–946.
25 Qin P, Northoff G: How is our self related to midline regions and the default-mode network? Neuroimage 2011;57:1221–1233.
26 Sperduti M, Delaveau P, Fossati P, Nadel J: Different brain structures related to self- and external-agency attribution: a brief review and meta-analysis. Brain Struct Funct 2011; 216:151–157.
27 Platek SM, Wathne K, Tierney NG, Thomson JW: Neural correlates of self-face recognition: an effect-location meta-analysis. Brain Res 2008;1232:173–184.
28 Forbes CE, Grafman J: The role of the human prefrontal cortex in social cognition and moral judgment. Annu Rev Neurosci 2010;33: 299–324.
29 Lieberman MD: Social cognitive neuroscience: a review of core processes. Ann Rev Psychol 2007;58:259–289.
30 Wagner U, N'Diaye K, Ethofer T, Vuilleumier P: Guilt-specific processing in the prefrontal cortex. Cereb Cortex 2011;21:2461–2470.

31 Takahashi H, Yahata N, Koeda M, Matsuda T, Asai K, Okubo Y: Brain activation associated with evaluative processes of guilt and embarrassment: an fMRI study. Neuroimage 2004; 23:967–974.
32 Michl P, Meindl T, Meister F, Born C, Engel RR, Reiser M, Hennig-Fast K: Neurobiological underpinnings of shame and guilt: a pilot fMRI study. Soc Cogn Affect Neurosci, Epub ahead of print.
33 Zahn R, Moll J, Paiva M, Garrido G, Krueger F, Huey ED, Grafman J: The neural basis of human social values: evidence from functional MRI. Cereb Cortex 2009;19:276–283.
34 Finger EC, Marsh AA, Kamel N, Mitchell DGV, Blair JR: Caught in the act: the impact of audience on the neural response to morally and socially inappropriate behavior. Neuroimage 2006;33:414–421.
35 Shin LM, Dougherty DD, Orr SP, Pitman RK, Lasko M, Macklin ML, Alpert NM, Fischman AJ, Rauch SL: Activation of anterior paralimbic structures during guilt-related script-driven imagery. Biol Psychiatry 2000;48:43–50.
36 Takahashi H, Matsuura M, Koeda M, Yahata N, Suhara T, Kato M, Okubo Y: Brain activations during judgments of positive self-conscious emotion and positive basic emotion: pride and joy. Cereb Cortex 2008;18:898–903.
37 Knutson B, Cooper JC: Functional magnetic resonance imaging of reward prediction. Curr Opin Neurol 2005;18:411–417.
38 O'Doherty JP: Reward representations and reward-related learning in the human brain: insights from neuroimaging. Curr Opin Neurobiol 2004;14:769–776.
39 Burgdorf J, Panksepp J: The neurobiology of positive emotions. Neurosci Biobehav Rev 2006;30:173–187.
40 Craig AD: How do you feel – now? The anterior insula and human awareness. Nat Rev Neurosci 2009;10:59–70.
41 Nitschke JB, Sarinopoulos I, Mackiewicz KL, Schaefer HS, Davidson RJ: Functional neuroanatomy of aversion and its anticipation. Neuroimage 2006;29:106–116.
42 Aldhafeeri FM, Mackenzie I, Kay T, Alghamdi J, Sluming V: Regional brain responses to pleasant and unpleasant IAPS pictures: different networks. Neurosci Lett 2012;512:94–98.
43 Annett M: A classification of hand preference by association analysis. Br J Psychol 1970;61: 303–321.
44 World Medical Association: World Medical Association Declaration of HELSINKI: ethical principles for medical research involving human subjects. Ferney-Voltaire, World Medical Association, 2008.
45 Lang PJ, Bradley MM, Cuthbert BN: International Affective Picture System (IAPS): affective ratings of pictures and instruction manual. Technical Report A-6. Gainesville, Center for Research in Psychophysiology, University of Florida, 2005.
46 Goebel R, Esposito F, Formisano E: Analysis of functional image analysis contest (FIAC) data with BrainVoyager QX: from single-subject to cortically aligned group general linear model analysis and self-organizing group independent component analysis. Hum Brain Mapp 2006;27:392–401.
47 Herwig U, Baumgartner T, Kaffenberger T, Brühl A, Kottlow M, Schreiter-Gasser U, Abler B, Jäncke L, Rufer M: Modulation of anticipatory emotion and perception processing by cognitive control. Neuroimage 2007;37: 652–662.
48 Talairach J, Tournoux P: Co-Planar Stereotaxic Atlas of the Human Brain: Three-Dimensional Proportional System. New York, Thieme Medical, 1988.
49 Herwig U, Kaffenberger T, Jäncke L, Brühl AB: Self-related awareness and emotion regulation. Neuroimage 2010;50:734–741.
50 Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, Kochunov PV, Nickerson D, Mikiten SA, Fox PT: Automated Talairach atlas labels for functional brain mapping. Hum Brain Mapp 2000;10:120–131.
51 Paulus MP, Stein MB: Interoception in anxiety and depression. Brain Struct Funct 2010; 214:451–463.
52 McClure SM, York MK, Montague PR: The neural substrates of reward processing in humans: the modern role of fMRI. Neuroscientist 2004;10:260–268.
53 Heimer L, van Hoesen GW: The limbic lobe and its output channels: implications for emotional functions and adaptive behavior. Neurosci Biobehav Rev 2006;30:126–147.
54 Lieberman MD, Cunningham WA: Type I and type II error concerns in fMRI research: re-balancing the scale. Soc Cogn Affect Neurosci 2009;4:423–428.
55 Zung WW: A self-rating depression scale. Arch Gen Psychiatry 1965;12:63–70.
56 Laux L, Glanzmann P, Schaffner P, Spielberger CD: Das State-Trait-Angstinventar. Weinheim, Beltz, 1981.
57 Crawford J, Cayley C, Lovibond PF, Wilson PH, Hartley CA: Percentile norms and accompanying interval estimates from an Australian general adult population sample for self-report mood scales (BAI, BDI, CRSD, CES-D, DASS, DASS-21, STAI-X, STAI-Y, SRDS, and SRAS). Aust Psychol 2011;46:3–14.
58 Spielberger CD, Gorsuch RL, Lushene RE: STAI Manual for the State-Trait Anxiety Inventory. Palo Alto, Consulting Psychologist Press, 1970.
59 Whitfield-Gabrieli S, Moran JM, Nieto-Castanon A, Triantafyllou C, Saxe R, Gabrieli JD: Associations and dissociations between default and self-reference networks in the human brain. Neuroimage 2012;55:225–232.
60 Lindquist KA, Barrett LF: A functional architecture of the human brain: emerging insights from the science of emotion. Trends Cogn Sci 2012;16:533–540.
61 Jensen J, McIntosh AR, Crawley AP, Mikulis DJ, Remington G, Kapur S: Direct activation of the ventral striatum in anticipation of aversive stimuli. Neuron 2003;40:1251–1257.
62 Cardinal RN, Everitt BJ: Neural and psychological mechanisms underlying appetitive learning: links to drug addiction. Curr Opin Neurobiol 2004;14:156–162.
63 Knutson B, Fong GW, Adams CM, Varner JL, Hommer D: Dissociation of reward anticipation and outcome with event-related fMRI. Neuroreport 2001;12:3683–3687.
64 Peters J, Büchel C: Neural representations of subjective reward value. Behav Brain Res 2010;213:135–141.
65 Klucken T, Schweckendiek J, Koppe G, Merz CJ, Kagerer S, Walter B, Sammer G, Vaitl D, Stark R: Neural correlates of disgust- and fear-conditioned responses. Neuroscience 2012; 201:209–218.
66 Gear RW, Levine JD: Nucleus accumbens facilitates nociception. Exp Neurol 2011;229: 502–506.
67 Salamone JD, Correa M: The mysterious motivational functions of mesolimbic dopamine. Neuron 2012;76:470–485.
68 Phillips ML, Drevets WC, Rauch SL, Lane R: Neurobiology of emotion perception I: the neural basis of normal emotion perception. Biol Psychiatry 2003;54:504–514.
69 LeDoux JE: Emotion circuits in the brain. Annu Rev Neurosci 2000;23:155–184.
70 Pessoa L, Adolphs R: Emotion processing and the amygdala: from a 'low road' to 'many roads' of evaluating biological significance. Nat Rev Neurosci 2010;11:773–783.
71 Fossati P: Neural correlates of emotion processing: from emotional to social brain. Eur Neuropsychopharmacol 2012;22(suppl 3): S487–S491.
72 Davis M, Rainnie D, Cassell M: Neurotransmission in the rat amygdala related to fear and anxiety. Trends Neurosci 1994;17:208–214.
73 Baxter MG, Murray EA: The amygdala and reward. Nat Rev Neurosci 2002;3:563–573.
74 Habel U, Klein M, Kellermann T, Shah NJ, Schneider F: Same or different? Neural correlates of happy and sad mood in healthy males. Neuroimage 2005;26:206–214.
75 Menon V, Uddin L: Saliency, switching, attention and control: a network model of insula function. Brain Struct Funct 2010;214: 655–667.
76 Britton JC, Taylor SF, Sudheimer KD, Liberzon I: Facial expressions and complex IAPS pictures: common and differential networks. Neuroimage 2006;31:906–919.
77 Viinikainen M, Jääskeläinen 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.
78 Casey KL, Minoshima S, Morrow TJ, Koeppe RA: Comparison of human cerebral activation pattern during cutaneous warmth, heat pain, and deep cold pain. J Neurophysiol 1996;76:571–581.

79 Baur V, Hänggi J, Langer N, Jäncke L: Resting-state functional and structural connectivity within an insula-amygdala route specifically index state and trait anxiety. Biol Psychiatry 2013;73:85–92.
80 Stein MB, Simmons AN, Feinstein JS, Paulus MP: Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. Am J Psychiatry 2007;164:318–327.
81 Calarge C, Andreasen NC, O'Leary DS: Visualizing how one brain understands another: a PET study of theory of mind. Am J Psychiatry 2003;160:1954–1964.
82 Frith U, Frith CD: Development and neurophysiology of mentalizing. Philos Trans R Soc Lond B Biol Sci 2003;358:459–473.
83 Gallagher HL, Frith CD: Functional imaging of 'theory of mind'. Trends Cogn Sci 2003;7:77–83.
84 Burianova H, McIntosh AR, Grady CL: A common functional brain network for autobiographical, episodic, and semantic memory retrieval. Neuroimage 2010;49:865–874.
85 Svoboda E, McKinnon MC, Levine B: The functional neuroanatomy of autobiographical memory: a meta-analysis. Neuropsychologia 2006;44:2189–2208.
86 Huijbers W, Pennartz CMA, Rubin DC, Daselaar SM: Imagery and retrieval of auditory and visual information: neural correlates of successful and unsuccessful performance. Neuropsychologia 2011;49:1730–1740.
87 Araujo HF, Kaplan J, Damasio A: Cortical midline structures and autobiographical-self processes: an activation-likelihood estimation meta-analysis. Front Hum Neurosci 2013;7:548.
88 Denkova E, Dolcos S, Dolcos F: The effect of retrieval focus and emotional valence on the medial temporal lobe activity during autobiographical recollection. Front Behav Neurosci 2013;7:109.
89 Bonnici HM, Chadwick MJ, Lutti A, Hassabis D, Weiskopf N, Maguire EA: Detecting representations of recent and remote autobiographical memories in vmPFC and hippocampus. J Neurosci 2012;32:16982–16991.
90 Aleman A, van't Wout M: Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex disrupts digit span task performance. Neuropsychobiology 2008;57:44–48.
91 Cieslik EC, Zilles K, Caspers S, Roski C, Kellermann TS, Jakobs O, Langner R, Laird AR, Fox PT, Eickhoff SB: Is there 'One' DLPFC in cognitive action control? Evidence for heterogeneity from co-activation-based parcellation. Cereb Cortex 2013;23:2677–2689.
92 Fuster JM: Executive frontal functions. Exp Brain Res 2000;133:66–70.
93 MacDonald AW 3rd, Cohen JD, Stenger VA, Carter CS: Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 2000;288:1835–1838.
94 Petrides M: Lateral prefrontal cortex: architectonic and functional organization. Philos Trans R Soc Lond B Biol Sci 2005;360:781–795.
95 Steele JD, Lawrie SM: Segregation of cognitive and emotional function in the prefrontal cortex: a stereotactic meta-analysis. Neuroimage 2004;21:868–875.
96 Kalisch R: The functional neuroanatomy of reappraisal: time matters. Neurosci Biobehav Rev 2009;33:1215–1226.
97 Golkar A, Lonsdorf TB, Olsson A, Lindstrom KM, Berrebi J, Fransson P, Schalling M, Ingvar M, Öhman A: Distinct contributions of the dorsolateral prefrontal and orbitofrontal cortex during emotion regulation. PLoS One 2012;7:e48107.
98 Okada G, Okamoto Y, Morinobu S, Yamawaki S, Yokota N: Attenuated left prefrontal activation during a verbal fluency task in patients with depression. Neuropsychobiology 2003;47:21–26.
99 Herrington JD, Heller W, Mohanty A, Engels AS, Banich MT, Webb AG, Miller GA: Localization of asymmetric brain function in emotion and depression. Psychophysiology 2010;47:442–454.
100 Grimm S, Beck J, Schuepbach D, Hell D, Boesiger P, Bermpohl F, Niehaus L, Boeker H, Northoff G: Imbalance between left and right dorsolateral prefrontal cortex in major depression is linked to negative emotional judgment: an fMRI study in severe major depressive disorder. Biol Psychiatry 2008;63:369–376.
101 Groenewold NA, Opmeer EM, de Jonge P, Aleman A, Costafreda SG: Emotional valence modulates brain functional abnormalities in depression: evidence from a meta-analysis of fMRI studies. Neurosci Biobehav Rev 2013;37:152–163.
102 Davidson RJ, Shackman AJ, Maxwell JS: Asymmetries in face and brain related to emotion. Trends Cogn Sci 2004;8:389–391.
103 Murphy F, Nimmo-Smith I, Lawrence A: Functional neuroanatomy of emotions: a meta-analysis. Cogn Affect Behav Neurosci 2003;3:207–233.
104 Green S, Lambon Ralph MA, Moll J, Deakin JFW, Zahn R: Guilt-selective functional disconnection of anterior temporal and subgenual cortices in major depressive disorder. Arch Gen Psychiatry 2012;69:1014–1021.