

Existential neuroscience: self-esteem moderates neuronal responses to mortality-related stimuli

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According to terror management theory, self-esteem serves as a buffer against existential anxiety. This proposition is well supported empirically, but its neuronal underpinnings are poorly understood. Therefore, in the present neuroimaging study, our aim was to test how self-esteem affects our neural circuitry activation when death-related material is processed. Consistent with previous findings, the bilateral insula responded less to death-related stimuli relative to similarly unpleasant, but death-unrelated sentences, an effect that might reflect a decrease in the sense of oneself in the face of existential threat. In anterior parts of the insula, this 'deactivation' effect was more pronounced for high self-esteem individuals, suggesting that the insula might be of core importance to understanding the anxiety-buffering effect of self-esteem. In addition, low self-esteem participants responded with enhanced activation to death-related over unpleasant stimuli in bilateral ventrolateral prefrontal and medial orbitofrontal cortex, suggesting that regulating death-related thoughts might be more effortful to these individuals. Together, this suggests that the anxiety-buffering effect of self-esteem might be implemented in the brain in the form of both insula-dependent awareness mechanisms and prefrontal cortex-dependent regulation mechanisms.

Keywords: self-esteem; existential; terror management theory; functional magnetic resonance imaging; anxiety buffer

INTRODUCTION

Research indicates that high self-esteem can function as a protection against a series of anxiety-related phenomena. For instance, whereas mental health problems, including anxiety and depression are associated with low self-esteem (Mann *et al.*, 2004; Rosenfield *et al.*, 2005), happiness is associated with high self-esteem (Pelham and Swann, 1989). Self-esteem was shown to improve coping with stressful life events (Hobfoll and Walfisch, 1984; Hobfoll and Liberman, 1987) and to correlate negatively with negative affect and positively with positive affect (Diener, 1984; DeNeve and Cooper, 1998).¹ This article, however, focuses specifically on existential anxiety. Our aim is to understand how self-esteem helps people deal with the fact that death is inevitable. In the last few decades, this question has been extensively addressed in the framework of terror management theory (TMT), a social psychological theory based on the writings of philosopher Ernest Becker (1973). It focuses on an existential dilemma of human kind: on the one hand, humans strive for self-preservation, but on the other hand, their cognitive abilities allow them to realize that they will not live forever, thereby creating a potential for paralyzing terror. TMT argues that in order to cope with this terror, humans have developed a so-called cultural anxiety buffer, consisting of cultural worldviews and self-esteem (Greenberg *et al.*, 1986). In accordance with this idea, experimental evidence suggests that self-esteem indeed helps people cope with death-related anxiety. For instance, Greenberg *et al.* (1992) showed that a self-esteem boost reduced self-reported anxiety in response to videos containing vivid depictions of death. In another study, reminders of mortality only lead to worldview defense in participants with moderate self-esteem, but not in individuals with dispositionally high self-esteem (Harmon-Jones *et al.*, 1997; Study 2). Similarly, boosting self-esteem by positive

feedback on a bogus personality test eliminated peoples' need to defend their cultural worldviews in response to a mortality reminder (Harmon-Jones *et al.*, 1997; Study 1). An even more basic finding is that self-reported death anxiety is negatively related to self-esteem (Davis *et al.*, 1983).² Evidence suggests that in addition to engaging more in worldview defense and experiencing more anxiety, low self-esteem individuals also tend to rely more on other defensive strategies against mortality-related anxiety. For example, in a study by Greenberg *et al.* (1993), low self-esteem individuals tended to deny their vulnerability to an early death in response to mortality salience, whereas high self-esteem participants did not.

The central question of this study is how exactly self-esteem exerts its buffering effect on death-related anxiety. We think that neuroimaging techniques can provide useful evidence here. The results of recent neuroimaging investigations suggest the existence of at least two sets of brain regions that are involved in processing death-related information. First, two functional MRI (fMRI) studies (Han *et al.*, 2010; Shi and Han, 2012) reported that relative to neutral and unpleasant stimulus words, death-related words reliably induced less activation in the bilateral insula. Based on a prominent model of insula functioning that relates this region to interoceptive awareness (Craig, 2002, 2009), the authors proposed that this insula deactivation might reflect a decrease in the sense of oneself. Such a decrease might reduce the negative impact of mortality reminders, thereby alleviating death-related concerns. This phenomenon might be a key to understanding why self-esteem is a protective factor against existential anxiety: high self-esteem individuals might have less of a problem with mortality because they are able to temporarily down-regulate the intensity of their emotional experience or even a more general form of awareness.

A second possibility of how self-esteem might alleviate anxiety is based on work by Quirin *et al.* (2011). These authors contrasted

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¹It is important to note here that some forms of high self-esteem (i.e. those associated with narcissistic and conceited personalities) also have non-desirable consequences (Baumeister *et al.*, 2003).

²We have to note that there have been inconsistencies regarding the question whether high or low self-esteem is related to more defensive behaviors. For instance, in a study by Baldwin and Wesley (1996), high self-esteem individuals displayed stronger ingroup bias in response to mortality primes. High self-esteem was also associated with a higher level of motivation to join the military after MS (Taubman-Ben-Ari and Findler, 2006). The results of a recent investigation (Schmeichel *et al.*, 2009) provides a possible solution for these inconsistencies by demonstrating that low implicit rather than explicit self-esteem predicts defensive behaviors after MS.

visually presented statements from a death anxiety questionnaire (e.g. 'I am afraid of a painful death') with comparable statements about dental pain (e.g. 'I am getting panicked, when I am sitting in the dentist's waiting room') and found increased responses to the death anxiety statements in the amygdala and the anterior cingulate cortex (ACC), both of which are critically involved in emotional processing (Phan *et al.*, 2002). They proposed that the ACC and the amygdala might reflect the experience of threat or distress induced by the death anxiety statements. Thus, a second possibility of how self-esteem counteracts anxiety is through reduced threat-related processing in the amygdala and/or the ACC. Because evidence to date is limited to the brain regions mentioned earlier (i.e. the insula, the ACC and the amygdala), we will focus our attention on these brain regions by using region-of-interest (ROI)-based analyses. However, as other brain regions might play important roles as well, we will also look for effects outside of these regions using whole brain, voxel-based analyses.

To test our hypotheses, we designed and conducted an fMRI experiment in which participants were asked to read and rate the emotional valence of visually presented unpleasant death-related sentences, unpleasant death-unrelated sentences and neutral sentences.³ After the experiment, participants completed a self-esteem scale (Rosenberg, 1965). We used the resulting scores to predict death-related brain activation using both *a priori*-defined ROI centered onto insula, amygdala and ACC, and a whole-brain correlation approach. The main comparison of interest, which should reveal the pure effect of death content irrespective of emotional parameters such as valence or arousal, is between death-related and death-unrelated unpleasant sentences. We expected to find neuronal evidence that enables us to discern whether self-esteem alleviates mortality-related existential concerns primarily by reducing interoceptive processes in the insula (Han *et al.*, 2010; Shi and Han, 2012) or by reducing the threatening impact of mortality-related threat by lowering activation in the amygdala and/or the ACC (Quirin *et al.*, 2011).

METHODS

Participants

The study sample consisted of 30 participants (18 female), mean age 21.80 (s.d. = 2.09). All were students at the University of Salzburg. None reported any history of neurological disorders or prior head trauma. All participants gave written informed consent to participate in the study, which ostensibly investigated emotional processing. Participants received course credits and a digital copy of their structural whole-head scan for participation.

Stimuli

In sum, we used 27 German sentences, which described death-related negative, death-unrelated negative or neutral situations. For brevity, we will refer to these stimulus categories as death-related, unpleasant and neutral. In order to keep the three categories as similar as possible with regard to length and lexical features, we designed sentence triplets which differed only with respect to one or several key words. For instance, the neutral sentence 'The worker received new work clothes' was turned into an unpleasant sentence 'The worker received an instant dismissal' and a death-related sentence 'The worker had a fatal work accident'. Pretests were done to determine whether these death-related and death-unrelated negative sentences differed with respect to

arousal, valence and the extent to which they were related to mortality. For this pretest, 19 participants were asked to rate each sentence with respect to emotional arousal (How emotionally arousing is this sentence?), valence (How negative/positive is this sentence?) and death-relatedness (How much does the sentence relate to mortality?). Seven-point scales (1 = not at all, 7 = extremely) were used for arousal, valence and death-relatedness. A bipolar scale ranging from -3 (extremely negative) to +3 (extremely positive) was used for valence ratings. Table 1 shows the mean ratings across participants for each of the three stimulus categories.

An item-based statistical analysis of these ratings confirmed that the sentence categories differed in arousal, $F(2, 24) = 26.11$; $P < 0.001$, with neutral sentences being lower than both death-related and unpleasant sentences (both P s < 0.001). Importantly, death-related and unpleasant sentences did not differ ($P = 0.73$) in arousal. Sentence categories also differed in valence, $F(2, 24) = 17.09$; $P < 0.001$, with valence being more negative for death-related and unpleasant than for neutral sentences (both P s < 0.001). Importantly, death-related and negative sentences did not differ ($P = 0.50$). Thus, any activation difference between the death-related and unpleasant sentences is unlikely to be explained simply by arousal or valence. The sentence categories also differed with regard to death-relatedness, $F(2, 24) = 40.33$; $P < 0.001$. As expected, death-related sentences were rated as more death-related than unpleasant sentences ($P < 0.001$). Unpleasant sentences were also rated as more death-related than neutral sentences ($P < 0.01$). However, the mean difference between death-related and negative sentences (3.16) was twice as large compared with the mean difference between neutral and negative sentences (1.56). Moreover, the death-relatedness ratings of death-related words were close to ceiling.

We also determined whether the sentence categories differed in length, because differences in sentence length might lead to differences in activation. The sentence categories did not differ with respect to number of words per sentence, $F(2, 16) = 0.32$, $P = 0.72$ [death-related sentences: $M(s.d.) = 6.78$ (2.22); unpleasant sentences: $M(s.d.) = 7.00$ (1.80); neutral sentences: $M(s.d.) = 6.67$ (1.94)]. Also, they were not different regarding number of characters (including spaces), $F(2, 16) = 0.45$, $P = 0.64$ [death-related: $M(s.d.) = 44.67$ (10.85); unpleasant: $M(s.d.) = 47.00$ (10.23); neutral: $M(s.d.) = 46.00$ (11.90)]. Thus, any differences between the sentence categories are unlikely to be explained simply by length.

Task and procedure

The stimulus sentences were presented visually onto a screen at the end of the scanner bore which participants viewed from inside the scanner using a mirror attached to the head coil. For stimulus presentation, we used the software Presentation (Presentation Version 14.2, Neurobehavioral Systems Inc., Albany, CA). Stimuli were presented in yellow letters on a uniformly black background. Each sentence was

Table 1 Mean ratings of arousal, valence and death-relatedness of each sentence category

	Neutral		Unpleasant		Death-related	
	<i>M</i>	s.d.	<i>M</i>	s.d.	<i>M</i>	s.d.
Arousal (in-scanner) ^a	1.4	0.20	2.65	0.31	2.74	0.50
Arousal (pretest) ^b	2.09	0.85	4.57	0.84	4.71	0.91
Valence (pretest) ^c	0.05	0.61	-1.57	0.60	-1.37	0.71
Death-relatedness (pretest) ^b	1.9	1.06	3.46	1.63	6.62	0.27

^aFour-point scale (1 = not at all, 4 = very much). ^bSeven-point scale (1 = not at all, 7 = very much). ^cBipolar scale ranging from -3 to +3 (-3 = very unpleasant, 3 = very pleasant).

³We have put a strong emphasis on using death-related and unpleasant stimuli that do not differ with respect to emotionality. De-confounding death-relatedness and emotionality is an absolute necessity for isolating the effects of death-relatedness, because there are well-documented effects of stimulus arousal and valence on brain activation (e.g. see Phan *et al.*, 2002; Posner *et al.*, 2008). To this end, we selected stimuli that met the necessary criteria and in addition, asked participants to make in-scanner arousal judgments upon each presented sentence to assure that no confound with emotionality was present.

presented for 3 s, with an inter-stimulus interval (ISI) of 2 s. During the ISI, a fixation cross appeared on the screen. None of the participants had any trouble reading the statements in time. Sentence presentation was blocked, with each block comprising three sentences of one category (i.e. AAABBBCCC). Each of the 27 sentences was presented three times in three successive runs. In each of these runs, one of three different pseudo-randomized stimulus sequences was used. The order of the sequences was counterbalanced across participants.

Upon entering the lab, participants were welcomed and informed about the experimental procedure and familiarized with the in-scanner task prior to scanning, which ostensibly investigated emotional processing. During scanning, participants were instructed to rate how arousing they found each of the situations described in the sentences (1 = not at all, 4 = very much) using an MRI-compatible response pad. After the in-scanner task, a whole-head structural scan was acquired, which took approximately 7 min. The Rosenberg (1965) self-esteem scale was administered after scanning.⁴ A 5-point scale (1 = completely disagree, 5 = completely agree) was used. Internal consistency was satisfying ($\alpha = 0.81$). Scores were determined by summing up the responses to all 10 items, after reverse-coding five negatively worded items. The sample had an average self-esteem score of 40.22 (s.d. = 5.77).

Imaging parameters

For magnetic resonance imaging, we used a 3 T Siemens Tim Trio scanner together with a 32-channel head coil. For the functional runs, we used a T2*-weighted gradient echo EPI sequence sensitive to blood oxygen level dependent contrast. Data were collected in three sessions, each comprising 92 T2*-weighted whole-brain images (36 slices, slice thickness 3 mm, 210 mm FoV, TR = 2200 ms, TE = 30 ms, flip angle = 70°). Parallel imaging was used (GRAPPA level = 2). Slice orientation was tilted by 30° in order to minimize signal loss in orbitofrontal cortex (Deichmann et al., 2003). Six dummy scans were performed prior to each run and discarded before data analysis. Whole-head high-resolution structural scans were collected using a T1-weighted MPRAGE sequence (FoV: 256 mm, slice thickness 1.20 mm, TR = 2300 ms, flip angle 9°), resolution: 1 × 1 × 1.2 mm.

Data analysis

fMRI data were analyzed using SPM8 (Wellcome Department of Cognitive Neurology, London, UK), operating in a MATLAB environment (MATLAB Version 7.6.0.324; The MathWorks Inc., Natick, MA). First, head movements were estimated across the time course of the experiment. After unwarping and slice-timing, the functional images of each participant were co-registered to the corresponding structural image. The structural scan was then normalized to the ICBM 152 brain template (Montreal Neurological Institute) using a 12-parameter affine transformation. The resulting normalization parameters were applied to both the functional and the structural scans. Functional images were resampled to 3 mm isotropic voxels and smoothed with an 8 mm Gaussian kernel.

⁴Reminders of mortality were found to elicit self-esteem striving (Ben-Ari et al., 1999; Hirschberger et al., 2002; Arndt et al., 2003). To determine whether the in-scanner task (which contained reminders of mortality) might have raised peoples' self-esteem to a level that is unusual for a student population, we administered the Rosenberg self-esteem scale to an unrelated sample of 20 (12 female, 8 male) Salzburg University students (mean age 21.21 years, s.d. = 2.39). One participant (male) did not fill in one item of the Rosenberg scale and was therefore excluded, resulting in a sample of 19 participants. Self-esteem means did not differ between scanner (scanner: $M = 40.22$, s.d. = 5.77; non-scanner sample: $M = 40.15$, s.d. = 4.72; $t(47) = -0.03$, $P = 0.97$). This cannot guarantee that the in-scanner procedure did not affect self-esteem. However, it suggests that self-esteem levels were not unusually high or low after scanning.

Voxel-based fMRI analysis

For the voxel-based statistical analyses, we used a two-stage mixed effects model. At the first level, for each participant, each stimulus sentence was modeled as a discrete event (rather than specifying each sentence triplet as a block). This provides a more accurate model of the hemodynamic response (Mechelli et al., 2003). Death-related, unpleasant and neutral sentences were modeled using separate regressors. The model was convolved with a hemodynamic response function and its temporal derivative. Movement parameters obtained during head movement estimation (three for translation, three for rotation) were also included as covariates of no interest. The functional time series were high-pass filtered (128 s cut-off) and corrected for autocorrelation using an AR(1) model (Friston et al., 2002). At the second level, we first investigated differences between the three conditions using a repeated measures ANOVA. Specifically, we chose a flexible factorial design in SPM8 with one factor coding stimulus identity (death, unpleasant or neutral, assuming dependencies between levels and equal variance among levels) and a subject factor that accounts for between-subject variance (assuming independence between levels and equal variance). Subsequently, we used *t*-contrasts to investigate between-condition activation differences.

In order to test our hypotheses on correlations with self-esteem, we generated death > unpleasant contrast maps based on each participants' first level design and subjected these to a second-level whole-brain regression analysis to predict activation based on participants' mean-centered self-esteem scores. In order to see whether the correlations involving self-esteem are specific to death > unpleasant, we repeated this procedure with contrast maps reflecting death > neutral and unpleasant > neutral activation. Throughout all the second-level analyses, our criterion for significance was an initial voxel-wise threshold of $P < 0.001$ together with a cluster-level correction for multiple comparisons (false discovery rate, $q < 0.05$).

ROI-based fMRI analysis

In order to provide a more sensitive and regionally specific test of our hypotheses that self-esteem is related to stronger insula deactivation (Han et al., 2010; Shi and Han, 2012) and/or weaker ACC/amygdala activation during death-related stimulus processing, we extracted and analyzed data from spherical 6 mm-radius ROI centered on coordinates reported by Han et al. (2010), Shi and Han (2012) and Quirin et al. (2011). Table 3 provides a complete list of these regions. Unfortunately, data at right amygdala coordinates of Quirin et al. ($x = 8$, $y = 0$, $z = -20$) were unavailable in 10 of our participants due to signal dropouts. In order to determine amygdala activation nevertheless, we chose to extract data at coordinates from a recent meta-analysis on the amygdala (Sergey et al., 2008; see Table 3 for coordinates). At these coordinates, no dropouts were present in any of our participants. To see whether and how these regions were differentially sensitive to death-related, unpleasant and neutral sentences, we performed one repeated measures ANOVA and *post hoc* tests, where appropriate, for each ROI.

RESULTS

Behavioral results

We first determined whether the in-scanner response times (RTs) differed as a function of sentence category. Mean RTs were computed for each participant across all sentences of each sentence category and subjected to a repeated measures ANOVA with sentence category (death-related, unpleasant, neutral) as factor. There were no missing responses. RTs differed between sentence categories, $F(2, 58) = 11.08$, $P < 0.001$. Responses to death-related sentences ($M = 3448.79$ ms, s.d. = 564.33 ms) were slower ($P < 0.001$) than those of neutral

sentences ($M = 3314.31$ ms, $s.d. = 605.21$ ms). Unpleasant sentences ($M = 3477.11$ ms, $s.d. = 582.91$ ms) also required longer RTs than those of neutral sentences ($P = 0.001$). Death-related and unpleasant sentences, however, did not differ ($P = 0.47$). Thus, both death-related and unpleasant sentences led to prolonged reaction times.

Next, we determined whether participants assigned different ratings of emotional arousal to the sentence categories (see Table 1 for means). A repeated measures ANOVA showed a main effect of sentence category, $F(2, 58) = 212.49$, $P < 0.001$. Both death-related ($M = 2.74$, $s.d. = 0.50$) and unpleasant sentences ($M = 2.65$, $s.d. = 0.31$) received higher arousal ratings than those of neutral sentences ($M = 1.40$, $s.d. = 0.20$; both P s < 0.001). Death-related and unpleasant sentences, however, did not differ ($P = 0.19$). Together, this confirms that we were successful in composing death-related and death-unrelated unpleasant sentences with comparable emotional impact, while keeping both 'emotional' sentence categories more arousing than the neutral sentence category.

FMRI results

Differences between conditions: voxel-based analysis

We first investigated which brain regions responded to death-related over neutral and unpleasant over neutral sentences (see Table 2 for a list of regions). Both contrasts revealed large clusters that encompassed the left precentral gyrus and extended medially into postcentral gyrus and precuneus and laterally into left angular gyrus. Both contrasts also revealed clusters in sensorimotor regions (SMA) and right-hemispheric cerebellar areas. Both contrasts also revealed left prefrontal clusters. In the right striatum, lingual gyrus and the left insula, only unpleasant sentences elicited activation. Subsequently, we contrasted death-related with unpleasant sentences. Although no region exhibited greater activation to death-related sentences, we discovered that unpleasant sentences led to more activation in bilateral lingual gyri and clusters at the border between posterior aspects of left superior temporal cortex and the left posterior insula (see Table 2, Figure 1).

Differences between conditions: ROI analysis

Among the coordinates reported by Quirin *et al.* (2011), only the right caudate nucleus was differentially sensitive to the three sentence categories. It was more active for death-related over neutral and for unpleasant over neutral sentences, but activation did not differ between death-related and unpleasant sentences, suggesting no special role of death reminders in this region (see Table 3). The amygdala and ACC ROIs were not differentially activated by the sentence categories. Together, the brain areas that exhibited death vs dental pain effects in the study of Quirin *et al.* did not respond to death-related over unpleasant stimuli in the present experiment.

Both left and right insula ROIs from the study of Han *et al.* (2010) were less active when participants read death-related sentences, compared with when they read unpleasant sentences. Both insula regions also responded to unpleasant over neutral sentences. No difference emerged between death-related and neutral sentences (see Table 3, Figure 1). Thus, we were able to replicate previous findings that death-related stimuli activated the insula less than unpleasant stimuli (Han *et al.*, 2010; Shi and Han, 2012). However, whereas Han *et al.* observed a gradual decrease of insula activation from neutral over unpleasant to death-related words, such a pattern was not observed here. In our study, unpleasant sentences activated the insula more strongly than both death-related and neutral stimuli, but neutral and death-related sentences did not differ (see Table 3, Figure 1).

Next, we focused on data extracted based on coordinates taken from Shi and Han (2012). In the posterior insula ROIs, we obtained the same pattern of results as with the insula coordinates from Han *et al.*

Table 2 Significant activations obtained with between-condition contrasts and whole-brain correlations with self-esteem. Only clusters that survived correction for multiple comparisons are reported

		Cluster-level		Voxel-level		MNI coordinates				
		<i>n</i> voxels	<i>P</i> (FDR)	<i>T</i>	<i>Z</i>	<i>x</i>	<i>y</i>	<i>z</i>		
Death > neutral										
L	Precentral	1965	<0.001	6.38	5.53	−30	−4	58		
L	Angular			5.71	5.07	−42	−67	31		
L	Precuneus			5.71	5.07	−3	−64	34		
L	Posterior cingulate			5.50	4.92	−9	−52	28		
L	Precuneus			5.44	4.87	−12	−64	58		
L	Postcentral	325	<0.001	4.51	4.16	−42	−34	58		
R	SMA			5.03	4.56	6	11	64		
R	Cerebellum			359	<0.001	4.67	4.28	12	−85	−35
L	Middle Frontal			79	0.02	4.17	3.88	−30	56	10
Neutral > death										
—										
Unpleasant > neutral										
L	Precentral	2791	<0.001	5.79	5.12	−33	−4	58		
L	Posterior cingulate			5.73	5.08	−3	−52	28		
L	Postcentral					−60	−19	31		
R	Postcentral	405	<0.001	5.48	4.46	63	−10	37		
L	Angular	66	0.03	4.90	4.46	−39	−61	25		
L	SMA	180	0.001	4.86	4.44	−6	11	52		
R	Striatum	109	0.007	4.67	4.29	21	5	16		
R	Cerebellum	73	0.005	4.60	4.23	12	−82	−38		
R	Lingual	247	<0.001	4.52	4.17	12	−61	−11		
R	Precentral	104	0.007	4.43	4.09	27	−7	55		
L	Superior frontal	57	0.04	4.39	4.06	−15	56	31		
L	Insula	112	0.007	4.37	4.05	−33	23	19		
Neutral > unpleasant										
—										
Death > unpleasant										
—										
Unpleasant > death										
L	Calcarine	449	<0.001	5.34	4.80	−9	−85	1		
R	Calcarine			4.50	4.15	9	−79	4		
L	Supramarginal	264	<0.001	4.76	4.36	−54	−28	25		
L	Middle temporal			4.49	4.14	−48	−43	7		
L	Superior temporal			4.06	3.79	−57	−10	10		
Positive correlations between unpleasant > death and self-esteem										
L	VLPFC	234	<.001	5.47	4.47	−39	41	10		
L	VLPFC			5.36	4.41	−27	44	−2		
L	LOFC			5.07	4.24	−30	29	−14		
L	AI/Putamen			4.79	4.06	−27	17	4		
L	VMPFC			3.86	3.43	−12	59	1		
R	VLPFC	215	<0.001	5.48	4.48	45	44	13		
R	LOFC			4.02	3.54	18	38	−8		

AI, anterior insula.

(2010): both left and right posterior insula exhibited unpleasant > neutral and unpleasant > death activation, but no differences between death-related and unpleasant sentences were present (see Table 3). The anterior ROIs revealed a slightly different pattern of results: although the right anterior insula did not change its activation as a function of sentence category, there was a significant effect of sentence category in the left anterior insula ROI. This effect was carried mainly by stronger activation to unpleasant over neutral sentences. Responses to unpleasant sentences were marginally stronger than those of death-related sentences (see Table 3, Figure 1).

Together, the ROI analysis yielded the following pattern of results: among the regions of Han *et al.* (2010), both left and right ROIs showed the expected effect, that is, reduced activation to death-related compared with unpleasant sentences. Looking at data extracted from ROIs based on the study of Shi and Han (2012), which offered a more fine-grained anterior–posterior division, only the posterior insula

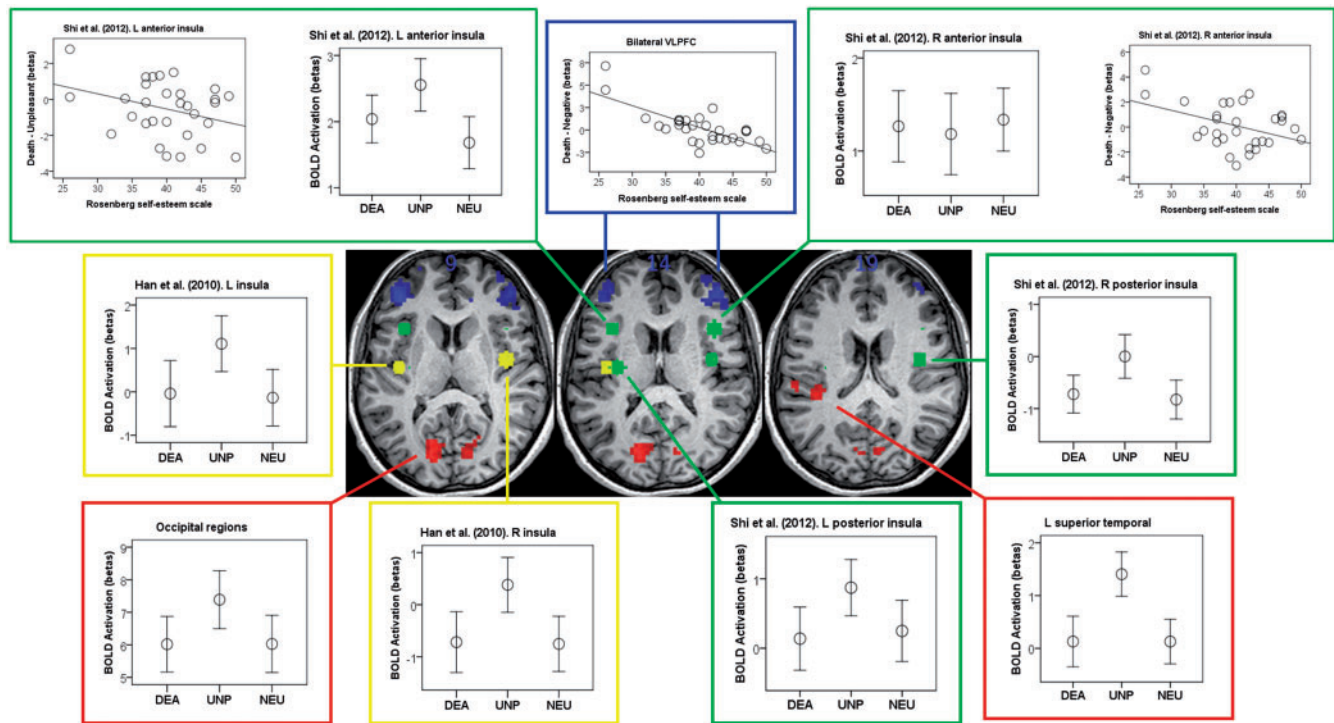


Fig. 1 A summary of the key findings. Red clusters display unpleasant > death-related activation in occipital and left superior temporal regions. Blue clusters indicate regions that exhibited an inverse relationship between self-esteem and death-related > unpleasant activation, as revealed by the voxel-based analysis. An ROI analysis using insula coordinates from Han et al. (2010; outlined in yellow) confirmed that the insula responded with less activation to death-related compared with unpleasant sentences. Among the insula ROIs extracted at coordinates reported by Shi and Han (2012; outlined in green), left and right posterior parts of the insula also responded with decreased activation to death-related sentences. At anterior locations, no unpleasant > death effects were present; in the right insula, however, activity was sensitive to individual differences in personal self-esteem, with high self-esteem participants reporting greater while reading death-related sentences.

Table 3 Summary of the ROI analysis investigating differences between the neutral, unpleasant and death-related stimulus conditions

	MNI				Step 1 (main effect of category)		Step 2 (differences between specific sentence categories)	
	x	y	z	F (P)	Death > neutral	Unpleasant > neutral	Death > unpleasant	Unpleasant > death
<i>Quirin et al. (2011)</i>								
L ACC	-2	38	-2	0.57 (0.56)	0.828	0.360	0.410	
R caudate nucleus	-16	-20	16	3.37 (0.04)	0.05	0.02	0.67	
L amygdala	22	-4	-15	0.19 (0.82)	0.551	0.959	0.601	
R amygdala	-21	-5	-16	0.01 (0.98)	0.892	0.972	0.871	
<i>Han et al. (2010)</i>								
Mid-cingulate	0	14	28	2.99 (0.05)	0.125	0.038	0.328	
L insula	-40	-14	12	5.80 (<0.01)	0.80	<0.01		0.02
R insula	42	-8	8	5.23 (<0.01)	0.81	<0.01		0.01
<i>Shi and Han (2012)</i>								
L anterior insula	-36	16	12	6.30 (<0.01)	0.07	<0.01		0.06
L posterior insula	-32	-14	14	4.20 (0.02)	0.66	0.02		0.02
R anterior insula	42	16	14	0.11 (0.89)	0.806	0.673		0.792
R posterior insula	40	-8	18	4.77 (0.01)	0.71	<0.01		0.02

In step 1, we determined whether activation in the respective ROIs taken from existing fMRI studies on death-related processing was sensitive to sentence category in the present experiment. If this was the case, we tested for differences between the three conditions (step 2). ROIs in which we were able to identify significant differences between death-related and unpleasant stimuli are printed in boldface. Due to signal drop-out at the Amygdala coordinates reported by Quirin et al. (2011), coordinates for this ROI were instead taken from a meta-analysis (Sergerie et al., 2008).

exhibited less activation to death-related sentences as compared with unpleasant ones.

Effect of self-esteem on brain activation: ROI analysis

This part of the data analysis sought to determine whether differential sensitivity to death-related vs unpleasant sentences in any of the ROIs under investigation can be explained by differences in self-esteem. Table 4 provides an overview over these correlative findings. In the right anterior insula ROI taken from Shi and Han (2012), a negative

correlation was present (see Table 4 and Figure 1). This effect was present only in the right anterior insula, but not at posterior insula coordinates or in the left anterior insula. Also, there was no significant relationship found at the insula coordinates reported by Han et al. (2010). Apart from the right anterior insula, no significant correlations between self-esteem and death > unpleasant activation were present in any other ROI under investigation.

To see whether self-esteem specifically affected activation in the death > unpleasant contrast, we repeated the analysis with the

Table 4 A summary of the results from the ROI analysis investigating correlations between self-esteem and differential activation in the neutral, unpleasant and death-related stimulus conditions

	MNI			Death > unpleasant		Unpleasant > neutral		Death > neutral	
	x	y	z	r	p	r	p	r	p
<i>Quirin et al. (2011)</i>									
L ACC	-2	38	-2	-0.32	0.09	0.32	0.09	0.03	0.87
R caudate nucleus	-16	-20	-16	-0.28	0.14	0.13	0.50	-0.14	0.45
L amygdala	22	-4	-15	-0.18	0.33	0.28	0.14	0.10	0.60
R amygdala	-21	-5	-16	-0.34	0.06	0.36	0.05	0.05	0.79
<i>Han et al. (2010)</i>									
Mid-cingulate	0	14	28	-0.27	0.15	0.00	0.99	-0.27	0.14
L insula	-40	-14	12	-0.15	0.43	-0.04	0.82	-0.20	0.29
R insula	42	-8	8	-0.03	0.88	0.12	0.51	0.07	0.72
<i>Shi and Han (2012)</i>									
L anterior insula	-36	16	12	-0.31	0.09	0.23	0.23	-0.13	0.50
L posterior insula	-32	-14	14	-0.09	0.65	0.08	0.67	-0.02	0.91
R anterior insula	42	16	14	-0.44	0.02	0.31	0.09	-0.07	0.73
R posterior insula	40	-8	18	0.03	0.86	0.04	0.84	0.07	0.70

Significant ($P < 0.05$) correlations are printed in boldface. Due to signal drop-out at the amygdala coordinates reported by *Quirin et al. (2011)*, coordinates for this ROI were instead taken from a meta-analysis (*Sergerie et al., 2008*). Regions in which self-esteem significantly predicted death > unpleasant activation are printed in boldface.

unpleasant > neutral and death > neutral contrasts. These correlations revealed only one significant finding: in the right amygdala, high self-esteem was associated with stronger unpleasant > neutral activation (see Table 4). To summarize, among all insula coordinates under investigation, only the right anterior insula was less active for death-related compared with unpleasant sentences in people who reported higher personal self-esteem.

Effect of self-esteem on brain activation: voxel-based analysis

Finally, in order to see whether there are other regions apart from those addressed in the ROI analysis that respond to mortality-related stimuli as a function of self-esteem, we performed a whole-brain regression in SPM that regressed activation differences between death-related and unpleasant sentence processing (with positive values indicating more activation to death-related sentences) on self-esteem. Negative effects of self-esteem (i.e. stronger activation to death-related sentences in people with lower self-esteem) were obtained in bilateral ventrolateral prefrontal cortex (VLPFC), left ventromedial prefrontal cortex (VMPFC), bilateral lateral orbitofrontal cortex (LOFC) and the left anterior insula (see Table 2 and Figure 1). We did not find any significant positive correlations between self-esteem and activation for death-related over unpleasant sentences (see Supplementary Table S1). To determine whether self-esteem specifically predicted brain activation associated with death-related vs unpleasant activation, we ran two additional whole-brain regressions. In these additional tests, we regressed unpleasant vs neutral and the death-related vs neutral contrasts on self-esteem. None of the clusters obtained after the initial voxel-wise threshold of $P < 0.001$ exceeded the FDR-corrected P -value required for significance (see Supplementary Table S1 for a complete list of clusters). In fact, the P -values ranged from 0.49 to 0.73, indicating that these correlations were not even close to significant. We therefore conclude that using the voxel-based correlation approach, low self-esteem specifically predicted enhanced responses to death-related over unpleasant sentences in bilateral VLPFC and LOFC, left VMPC, and the left anterior insula.

DISCUSSION

In this study, our goal was to address the question how exactly self-esteem might buffer existential anxiety. We found that the middle and

posterior insula regions were less active when our participants were processing death-related sentences, compared with when they were processing unpleasant sentences that were not death-related, a phenomenon that has been shown previously and interpreted as reflecting a decreased feeling of 'self' in the face of existential threat (*Han et al., 2010; Shi and Han, 2012*). Although this pattern of effects was not seen in anterior parts of the insula, the activation patterns in these anterior parts seemed to depend on self-esteem. First, an ROI analysis indicated that high self-esteem individuals deactivated the right anterior insula more strongly during death-related sentence reading. Second, a whole-brain regression identified a cluster of voxels exhibiting a correlation in the same direction in the left anterior insula. Although these results do not directly improve our understanding of how the insula contributes to existential threat processing, they suggest that self-esteem seems to play an important role for how strongly this brain region responds (i.e. deactivates) to death-related stimuli.

How exactly might the insula buffer existential anxiety? It has been proposed that the insula plays a central role in the generation of subjective awareness: by integrating information from environmental, homeostatic, motivational, social, hedonic and cognitive sources into a 'global emotional moment', it might be the region in the brain that gives rise to the representation of a sentient self (*Craig, 2002, 2009*). Applying this reasoning to the present results, self-esteem might be related to a stronger deactivation of the global emotional moment in the face of existential threat. It is possible that such a state of reduced awareness could enable people to feel less exposed to the worrisome nature of death-related thoughts. Such an interpretation would be compatible with observations that after mortality salience, people tend to avoid self-awareness (*Arndt et al., 1998*). The fact that the insula deactivation in response to death reminders has been demonstrated both in the present middle European as well as in Chinese samples (*Han et al., 2010; Shi and Han, 2012*) suggests that it is not a culture-bound phenomenon. However, regarding the exact pattern of activation in the insula, we noticed one surprising difference between our results and those of *Han et al. (2010)*: although these authors observed a gradual decrease of insula activation from neutral over unpleasant to death-related words, our unpleasant sentences activated the insula more strongly than neutral ones, but neutral and death-related sentences did not differ.

In addition to the insula, self-esteem also predicted activation in ventrolateral and ventromedial prefrontal cortex as well as lateral orbitofrontal cortex: low self-esteem participants recruited these brain regions to a greater extent when reading death-related sentences, compared with reading unpleasant sentences. We propose that these results can be interpreted in terms of emotion regulation: various regions within prefrontal cortex, including medial prefrontal cortex (Phan *et al.*, 2004; Ohira *et al.*, 2006; Urry *et al.*, 2006), lateral prefrontal cortex (Phan *et al.*, 2004; Hooker and Knight, 2006; Kalisch *et al.*, 2006; Ohira *et al.*, 2006) and orbitofrontal cortex (Hooker and Knight, 2006; Ohira *et al.*, 2006; Mak *et al.*, 2009; Kanske *et al.*, 2011) were found to be activated when people were asked to regulate emotions. Thus, participants with lower self-esteem might have put more effort into regulating negative emotional states or suppressing negative emotions when reading death-related sentences. Of course, this interpretation must remain speculative for now because it is problematic to infer cognitive processes from neuroimaging results (Poldrack, 2006). Nevertheless, we think that this finding deserves the attention of future studies. For instance, in order to further test whether prefrontal brain regions are necessary for regulating death-related anxiety in low self-esteem individuals, one could use transcranial magnetic stimulation (TMS) to apply temporal lesions to prefrontal areas. If low self-esteem individuals require the use of certain prefrontal areas for effectively suppressing death-related thoughts and feelings, prefrontal TMS might worsen mood, increase the accessibility of death-related thoughts and increase worldview defense (Arndt *et al.*, 1997).

A new and rather unexpected finding of this study was that superior and middle temporal as well as bilateral lingual gyri were less active when people read death-related sentences (compared with unpleasant sentences). These activation foci were neighbors of primary visual and auditory regions. Therefore, these reductions in activity could potentially indicate reduced auditory and visual processing of the death-related sentences. Such an interpretation is compatible with the results of eye-tracking experiments that observed changes in looking strategies when participants were primed with the inevitability of mortality (Hirschberger *et al.*, 2010). Specifically, these authors reported that mortality primes reduced gaze duration toward pictures of physical injury, which are in fact reminders of the fragility of one's existence. It would, of course, be premature to state that these threat-induced changes in gaze behavior and the threat-induced changes in activity observed here are related. Nonetheless, it would be interesting to study the interplay between these phenomena using combined eye-tracking and fMRI methodology (Richlan *et al.*, 2013).

Given the powerful behavioral effects (i.e. cultural worldview defense) in response to mortality reminders (Pyszczynski *et al.*, 2004; Burke *et al.*, 2010), we were surprised to find no single region that exhibited death > unpleasant effects. One possible reason for this is the blocked nature of stimulus presentation in this study. Shi and Han (2012) reported that short-lived, phasic responses to death reminders indeed produce activation in a network of brain regions associated with attention, but insula deactivation towards death reminders was seen only during longer-lasting, sustained periods of death-related stimulus processing. The notion that transient exposure to death primes involves increased attention is supported by a recent event-related potential study from our lab (Klackl *et al.*, 2013), which found that death-related words elicit an especially large late positive potential, an indicator of natural selective attention (Bradley, 2009). What characterizes these transient and sustained responses to death-related material and their roles for subsequent defensive behavior (Burke *et al.*, 2010) or vulnerability-denying distortions (Greenberg *et al.*, 1993) remain to be tested in future studies.

Although we were able to replicate existing findings related to insula deactivation in response to mortality-related stimuli (Han *et al.*, 2010;

Shi and Han, 2012), we were not able to replicate the findings of Quirin *et al.* that death-related stimuli led to greater activation of the ACC, the amygdala and the caudate nucleus. This latter study contrasted visually presented statements from Boyar's (1964) fear of death scale with comparable statements about dental pain. Although we can only speculate about the underlying cause of these divergences, one possible reason relates to task differences: although their task was designed in a way that addressed the emotional aspects of participants' personal existential concerns, we used more subtle death reminders for this study. Furthermore, their stimulus statements were formulated in a first-person perspective, whereas the sentences of this study were formulated in a third-person perspective and the studies of Han *et al.* and Shi *et al.* used single words. Another explanation for the differing results might be differences in the experimental tasks used: only in-scanner task of Quirin *et al.* required participants to explicitly think about their 'own' death. These differences are reminiscent of the observations of Greenberg *et al.* (1992) who found that intense reminders of mortality, such as the footage of an autopsy, indeed elicited anxiety, but more subtle reminders of death did not. We hope that these divergences will inspire future studies on the many ways of how our brains deal with existential threat.

CONCLUSION

TMT tries to explain how humans manage to avoid an ever-present potential for existential anxiety and proposes self-esteem as the main resource to achieve this goal. The results of our investigation indicate that people who report higher self-esteem are more prone to respond to death-related sentences with decreased activation of the anterior insula, which might indicate coping with mortality by reducing self-related awareness. Furthermore, low self-esteem individuals activated a network of prefrontal regions when processing death-related sentences, which might indicate that these people rely to a greater extent on emotion regulation in the face of threat.

Our results indicate that the newly established tradition of 'existential neuroscience' can profit from taking interindividual differences (i.e. self-esteem) into account. This might be true not only for self-esteem but also for other variables that play an important role in the context of coping with mortality, such as religiousness (Jonas and Fischer, 2006; Inzlicht *et al.*, 2011a,b). We propose that understanding how these and other resources influence the neural aspects of responding to existential threat can and will refine our psychological understanding of existential threat management.

SUPPLEMENTARY DATA

Supplementary data are available at SCAN online.

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