Neurocognitive processes of linguistic cues related to death

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ABSTRACT

Consciousness of the finiteness of one's personal existence influences human thoughts and behaviors tremendously. However, the neural substrates underlying the processing of death-related information remain unclear. The current study addressed this issue by scanning 20 female adults, using functional magnetic resonance imaging, in a modified Stroop task that required naming colors of death-related, negative-valence, and neutral-valence words. We found that, while both death-related and negative-valence words increased activity in the precuneus/posterior cingulate and lateral frontal cortex relative to neutral-valence words, the neural correlate of the processing of death-related words was characterized by decreased activity in bilateral insula relative to both negative-valence and neutral-valence words. Moreover, the decreased activity in the left insula correlated with subjective ratings of death relevance of death-related words and the decreased activity in the right insula correlated with subjective ratings of arousal induced by death-related words. Our fMRI findings suggest that, while both death-related and negative-valence words are associated with enhanced arousal and emotion regulation, the processing of linguistic cues related to death is associated with modulations of the activity in the insula that mediates neural representation of the sentient self.

1. Introduction

Death is one of the existential problems that constitute basic motivations of human life (Koole, Greenberg, & Pyszczynski, 2006). Consciousness of the finiteness of one's personal existence or the awareness of mortality influences individuals' thoughts and behaviors tremendously (Kastenbaum & Costa, 1977). For example, death-related thoughts and concomitant anxiety tend to modulate human reactions to others who violate or validate one's own cultural worldview (Greenberg, Pyszczynski, Solomon, Simon, & Breus, 1994). Thinking about one's own death leads to endorsement of positive personality descriptions or increased self-esteem (Pyszczynski, Greenberg, Solomon, Arndt, & Schimel, 2004; Schmeichel, Gailliot, Filardo, McGregor, & Gitter, 2009) and enhances forgiveness of violent ingroup and outgroup members (Schimel, Wohl, & Williams, 2006). Recent event-related potential study also showed that reminders of death modulate neural activities underlying perception and evaluation of ingroup members' faces (Henry, Bartholow, & Arndt, 2010). However, although these findings indicate that death-related thoughts affect human social cognition and support the terror management theory (Greenberg, Pyszczynski, & Solomon, 1986), we have known little about the neural substrates associated with the awareness of mortality itself.

This issue can be addressed by recording neural activity underlying the processing of death-related information using brain imaging techniques such as functional magnetic resonance imaging (fMRI). Brain imaging results may reveal the neural mechanisms underlying death-related psychological processes. In addition, brain imaging results may provide neural constraints on psychological models of the awareness of mortality. For example, social psychological studies suggest that death-related thought induces negative emotions such as anxiety (Bassett & Dabbs, 2003; Pyszczynski, Greenberg, & Solomon, 1999) and provokes avoidance of the self-focused state (Arndt, Greenberg, Simon, Pyszczynski, & Solomon, 1998). These death-related psychological processes can be tested by examining if brain areas involved in the processing of negative affect and self-awareness are engaged during the processing of death-related information.

The current work investigated the neurocognitive mechanisms involved in the processing of linguistic cues specifically related to death. We employed fMRI to monitor blood oxygen level dependent (BOLD) responses to three categories of words, i.e., death-related, negative-valence, and neutral-valence words. Subjects were asked to perform a modified Stroop task that required color naming of the words. Similar paradigm has been used in the previous research to examine social cognition about a target concept by measuring behavioral responses to emotion-laden or neutral words (Bassett, Washburn, Vanman, & Dabbs, 2004; Williams, Mathews, & MacLeod, 1996

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information. For example, Whalen, Bush, McNally, Wilhelm, and McInerney (1998) found greater activation in the anterior cingulate (ACC) for negative versus neutral words. Compton, Banich, Mohanty, Milham, and Herrington (2003) also found that, relative to neutral words, emotion words increased activity in the left frontal cortex and bilateral parietal and temporal gyri in the color naming task. In addition, the neural network consisting of bilateral frontal and parietal cortices engaged in the processing of high-arousal versus low-arousal emotion words. A positron-emission tomography research found increased activity in bilateral amygdala during color naming of threat words than during color naming of neutral words (Isenberg et al., 1999). However, as only about one-tenth of the threat words were related to death, the activity in bilateral amygdala observed in Isenberg et al.'s (1999) work was mainly associated with the processing of negative affect rather than the processing of death-related information.

We employed the modified Stroop task to investigate neural correlates of the processing of death-related words when subjects made judgments of colors of the words. A block design, in which death-related, negative-valence, and neutral-valence words were presented in different sessions, was used in current study in order to obtain strong sustained BOLD signals (Huettel, Song, & McCarthy, 2009) related to the processing of death-related words. As the Stroop task typically taps automatic semantic processes, BOLD signals specifically associated with death-related words uncover neural substrates underlying the process of death-related information. As women consciously fear death more than men do (Russac, Gatliff, Reece, & Spottswood, 2007) and men react more strongly than women do after mortality is made salient (Greenberg et al., 1994), there may be sex differences in neural substrates of the processing of death-related information. In addition, men and women differ in volumes of brain structures involved in emotional processing such as the temporo-limbic and frontal brain (Gur, Gunning-Dixon, Bilker, & Gur, 2002). To avoid the potential confound of sex differences in brain imaging results, the current study recruited only female subjects.

We tested two hypotheses about the neurocognitive processes involved in the processing of death-related linguistic cues. First, as death-related thought is accompanied by negative emotions such as anxiety (Bassett & Dabbs, 2003; Pyszczynski et al., 1999), the neural activity involved in the processing of death-related words may overlap partially with that of negative-valence words in association with enhanced attention/arousal (Compton et al., 2003) and emotional/memory-related processes (Maddock, Garrett, & Buonocore, 2003; Whalen et al., 1998) in the lateral frontal cortex and the precuneus/posterior cingulate. If this hypothesis is correct, one would expect similar activations to death-related and negative-valence words in the brain regions that are associated with emotion and arousal. This was tested by examining modulations of neural activities that were observed to both death-related and negative-valence words relative to the baseline of naming the color of neutral-valence words.

Second, as the human body functions as an agency of the self (Young, 1984), death implies permanent termination of biological functions of the body and inevitable foundering of the self (Seale, 1998). Behavioral studies suggest that death-related thought initiates self-related processes such as loss of one's own life and degeneration of one's own body after death (Widera-Wysoczańska, 1999) and provokes avoidance of the self-focused state (Arndt et al., 1998). Neuroimaging studies have shown that the posterior insula represents sensory stimulation to human bodies from various modalities (Craig, 2002). The mid-insula is associated with feeling of agency or awareness of body control (Farrer & Frith, 2002; Farrer, Franck, Georgieff, Frith, & Decety, 2003). The anterior insula engages during experiencing varieties of emotional feelings (Craig, 2009) and shows increased activity to stimuli with high ver-

sus low personal relevance (Enzi, de Greck, Prösch, Tempelmann, & Northoff, 2009). Damage of the insula results in selective loss of self-conscious behaviors and emotional awareness (Sturm, Rosen, Allison, Miller, & Levenson, 2006). As these findings suggest a key role of the insula in representations of the sentient self (Craig, 2009), we hypothesized that the processing of death-related words may be associated with modulations of the activity in the insula that underpins the sense of oneself as a sentient being. This was assessed by examining whether the insular activity decreases to death-related words compared to negative-valence and neutral-valence words. We also analyzed correlations between neural activity and subjective ratings of death relevance and emotional arousal related to death-related words to further evaluate the functional role of the neural activities in association with the processing of death-related words.

2. Materials and methods

2.1. Subjects

Twenty female undergraduate and graduate students (18–25 years of age, mean age ± SD = 21.80 ± 2.28) participated in this study. All were right-handed according to the Edinburgh questionnaire measurements and had normal or corrected-to-normal vision. All reported no neurological or psychiatric history. Subjects gave informed consent prior to the study. This study was approved by a local ethics committee.

2.2. Stimuli and procedure

Three categories of Chinese words (each consisting of two Chinese characters)

to measure individuals' degree of anxiety about death. The DAS (coefficient $\alpha = 0.75$, Saggino & Kline, 1996) consists of 15 true-false items which are scored 0 or 1 such that a high score indicates a high degree of death anxiety. Templer and Ruff (1971) provided the normal range of total DAS scores from 4.5 to 7.0 with standard deviations of about 3.0. The EAQ is a self-report measure of existential anxiety, consisting 13 true-false items (coefficient $\alpha = 0.71$, test–retest reliability $r = 0.72$, Weems, Costa, Dehon, & Berman, 2004).

2.3. fMRI data acquisition and analysis

Scanning was performed on a GE 3-T scanner with a standard head coil. Thirty-two transverse slices of functional images covering the whole brain were acquired using a gradient echo-planar pulse sequence ($64 \times 64 \times 32$ matrix with a spatial resolution of $3.75 \times 3.75 \times 4$ mm, repetition time (TR) = 3000 ms, echo time (TE) = 30 ms, field of view (FOV) = 24 cm $\times$ 24 cm, flip angle = 90°). Anatomical images were obtained using a 3D FSPGR T1 sequence ($256 \times 256 \times 128$ matrix with a spatial resolution of $0.938 \times 0.938 \times 1.4$ mm, TR = 7.4 ms, inversion time (TI) = 450 ms, TE = 3.0 ms, flip angle = 20°).

SPM2 (the Wellcome Trust Centre for Neuroimaging, London, United Kingdom) was used for imaging data preprocessing and analysis. The functional images were realigned to the first scan to correct for head motion between scans. The anatomical image was co-registered with the mean functional image produced during the process of realignment. All images were normalized to a 2 mm $\times$ 2 mm $\times$ 2 mm Montreal Neurological Institute (MNI) template. Functional images were spatially smoothed using a Gaussian filter with the full-width/half-maximum parameter (FWHM) set to 8 mm. The image data were modeled using a canonical hemodynamic response function (HRF). Effects at each voxel were estimated and regionally specific effects were compared using linear contrasts in individual participants using a fixed effect analysis. Contrasts between death-related and neutral-valence words defined neural activities related to the processing of death-related linguistic cues. Contrasts between negative-valence and neutral-valence words examined neural activity related to the process of negative word valence. Random effect analyses were then conducted based on statistical parameter maps from each individual participant to allow population inference. Areas of significant activation were identified using threshold of $p < 0.001$ (uncorrected) and a spatial extent threshold of $k = 50$. Signal intensity of parameter estimates were calculated from regions of interests (ROIs) defined as spheres of 5 mm radius around the peak voxel of specific activated brain areas identified in the random effect analysis using MarsBaR 0.38 (http://marsbar.sourceforge.net). One subject was excluded from the analysis of subjective ratings because of her extreme scores (over three SDs from the mean).

3. Results

3.1. Behavioral results

Response accuracy to the color naming task during the scanning procedure was high (over 94%). Reaction times (RTs) for correct responses to each word category were calculated. RTs calculated from six scans were slightly shorter to negative-valence words than to death-related words (492 ± 78 ms vs. 501 ± 83 ms, $t(19) = 2.168$, $p < 0.05$). As responses to emotional stimuli may habituate over time (McKenna & Sharma, 1995), we also calculated RTs in the first two scans and found slower responses to neutral-valence words (498 ± 82 ms) than to negative-valence words (474 ± 73 ms, $t(19) = 3.374$, $p < 0.01$) and to death-related words (483 ± 73 ms, $t(19) = 2.056$, $p = 0.054$).

Analysis of behavioral performances obtained after the scanning procedure showed that rating scores of death relevance of death-related words were higher than those of negative-valence words (9.12 ± 0.63 vs. 1.55 ± 1.32, $t(19) = 25.47$, $p < 0.001$), which in turn were higher than those of neutral-valence words (0.43 ± 0.44, $t(19) = 4.226$, $p < 0.005$). Similarly, rating scores of negative emotion induced by death-related words were greater than those of negative-valence words (6.62 ± 2.41 vs. 4.19 ± 1.68, $t(19) = 4.427$, $p < 0.001$), which were subsequently higher than those of neutral-valence words (0.46 ± 0.44, $t(19) = 9.621$, $p < 0.001$). The rating scores of the Death Anxiety Scale and Existential Anxiety Questionnaire were 6.37 ± 3.11 and 7.53 ± 3.06, respectively.

3.2. fMRI results

fMRI data analysis first contrasted death-related words with neutral-valence words and showed increased activations in the

Table 1
Brain areas showing increased and decreased activity associated with death-related and negative-valence words.

Region	Voxel no.	X	Y	Z	Z value
Death-related vs. neutral-valence words					
Medial prefrontal cortex	512	−4	48	36	4.85
Posterior cingulate cortex	541	−6	−58	38	4.12
Left superior parietal cortex	358	−32	−66	40	4.10
Right inferior parietal cortex	353	40	−64	28	3.44
Right middle frontal cortex	574	44	16	38	3.83
Left middle frontal cortex	150	−48	24	20	3.59
Negative-valence vs. neutral-valence words					
Anterior cingulate cortex	104	−6	42	22	3.38
	75	−8	60	18	3.55
Precuneus	213	−12	−74	14	4.34
Posterior cingulate cortex	222	−8	−58	46	3.32
Right superior frontal cortex	531	30	24	46	3.81
Right middle frontal cortex	227	24	48	30	3.28
Right superior temporal sulcus	241	42	−30	12	3.26
Neutral-valence vs. death-related words					
Left insular cortex	238	−40	−4	2	3.46
Right insular cortex	216	48	−8	10	3.69
Negative-valence vs. death-related words					
Mid-cingulate cortex	470	0	14	28	4.19
Left insular cortex	310	−40	−14	12	3.80
Right insular cortex	76	42	−8	8	3.23

Note: X/Y/Z are MNI coordinates.

medial prefrontal cortex, posterior cingulate cortex, bilateral parietal cortex, and bilateral middle frontal gyrus (Fig. 1a and Table 1). Relative to neutral-valence words, negative-valence words induced activations in the ACC, precuneus/posterior cingulate cortex, right superior and middle frontal gyrus, and right superior temporal sulcus (Fig. 1b and Table 1). These results suggest overlap between the neural substrates underlying the processing of death-related thoughts and negative feelings.

Interestingly, we found that, relative to neutral-valence words, death-related words also resulted in decreased activity in the left and right insula. Negative-valence words, however, did not show decreased activity in any brain areas compared to neutral-valence words. The contrasts of death-related and negative-valence words were also calculated to confirm brain activations specific to the processing of death-related words. Relative to negative-valence words, death-related words did not show increased activity in any brain areas. However, death-related words yielded decreased activity in bilateral insula and the mid-cingulate cortex compared to negative-valence words (Fig. 1c). These results uncovered neural activity specific to the processing of death-related words.

To examine whether the neural activity associated with death-related words can predict subjective thoughts of death, we calculated the correlation between subjective rating scores and contrast values of signal intensity of parameter estimates to death-related versus neutral-valence words. We found that the contrast values of death-related versus neutral-valence words in the left insula negatively correlated with the rating scores of death relevance of death-related words ($r = -0.615$, $p = 0.005$, Fig. 2a), suggesting that the greater the left insular activity decreased, the higher subjects rated death relevance of death-related words. The contrast values of death-related versus neutral-valence words in the right insula correlated with the rating scores of negative emotion induced by death-related words ($r = -0.536$, $p = 0.018$, Fig. 2b), suggesting that the greater the right insular activity decreased, the stronger negative emotion death-related words generated in subjects. However, increased activity in the left and right parietal cortex positively correlated with rating scores of negative emotions to death-related words ($r = 0.623$ and 0.479, $p = 0.004$ and 0.038, Fig. 2c and d). No correlation was observed between neural activity associated with death-related words and rating scores of the Death Anxiety and Existential Anxiety Scales. Similar analysis did
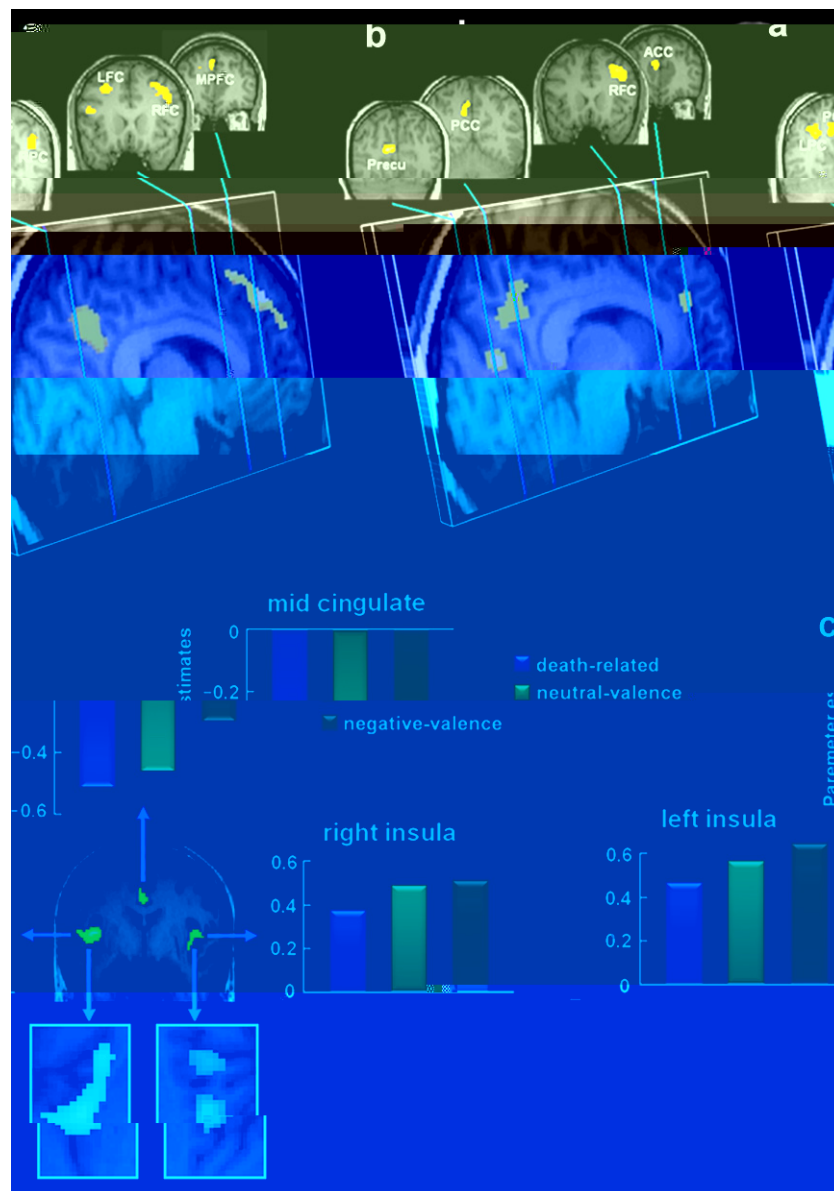
Fig. 1. (a) Illustration of increased activity to death-related than to neutral-valence words. (b) Illustration of increased activity to negative-valence than to neutral-valence words. (c) Illustration of decreased activity to death-related compared to negative-valence and neutral-valence words. LPC: left parietal cortex; RPC: right parietal cortex; PCC: posterior cingulate cortex; LFC: left frontal cortex; RFC: right frontal cortex; MPFC: medial prefrontal cortex; Precu: precuneus; ACC: anterior cingulate cortex.

not show any significant correlation between subjective ratings and neural activity associated with negative-valence words.

4. Discussion

The present study explored regional brain activity associated with death-related and negative-valence words in a modified Stroop task that allowed to distinguish between the processing of semantic meanings of words related versus unrelated to death. The results of subjective ratings after the scanning procedure suggest that both death-related and negative-valence words produced negative emotion in subjects. In parallel with the subjective reports, our fMRI data showed that, relative to neutral-valence words, both death-related and negative-valence words elicited increased activity in emotion related brain areas such as the precuneus and posterior cingulate. Similar increased activations in these brain areas were observed in previous studied to emotionally valenced than neutral words (Maddock et al., 2003; Malhi, Lagopoulos, Sachdev, Ivanovski, & Shnier, 2005).

Previous studies suggest that the posterior midline cortical structures are involved in different aspects of emotional processing. For example, the precuneus is associated with attribution of emotion to the self or others (Ochsner, Knierim, Ludlow, Hanelin, & Ramachandran, 2004) and the posterior cingulate engages in modulations of memory by emotionally arousing stimuli (Maddock, 1999; Maddock et al., 2003). Similarly, death-related and negative-valence words used in our study were associated with stronger negative emotion compared to neutral-valence words, as shown in the results of subjective ratings. It is likely that, even though each word was presented with a short duration, being exposed continuously to death-related and negative-valence words in a session of 30 s induced negative emotion in subjects. This possibly in turn required regulation of negative emotion associated with death-related or negative-valence words. Indeed, both death-related and negative-valence words generated increased activity in the lateral prefrontal cortex that has been demonstrated to play a key role in emotion regulation (Ochsner & Gross, 2005; Ochsner, Ray, Cooper, Robertson, & Chopra, 2004). The direct contrast of death-related
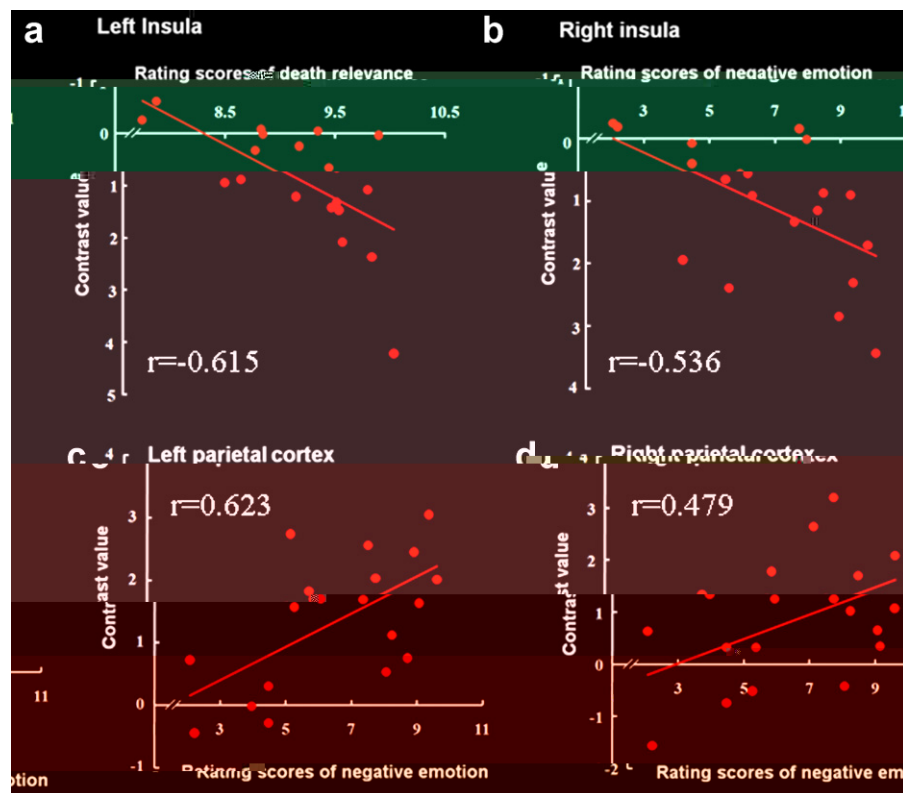
Fig. 2. Illustration of correlations between contrast values of death-related vs. neutral-valence words in the insula and subjective rating scores of death relevance of words (a) and of negative emotion induced by death-related words (b). (c) and (d) show correlations between left and right parietal activity and subjective rating scores of negative emotion induced by death-related words.

and negative-valence words did not show significant activation in the precuneus and posterior cingulate, suggesting comparable neural activity in these brains in association with the processing of death-related and negative-valence words. Similar precuneus and posterior cingulate activations in association with death-related and negative-valence words lend support to our first hypothesis that the neural activity involved in the processing of death-related words may overlap partially with that of negative-valence words. However, it should be noted that negative emotion linked to death-related words were confined mainly to fear and sadness whereas negative-valence words used in the current study might address a variety of negative emotions such as fear, sadness, and anger. The negative affect associated with death-related and negative-valence words might be different although the direct comparison did not differentiate between these two types of words in the precuneus and posterior cingulate. This can be addressed in future work by using negative-valence words that are mainly associated with fear and sadness.

Our fMRI results suggest that the neurocognitive processes of death-related words were different from those of negative-valence words in several aspects. The contrast of negative-valence versus neutral-valence words identified increased activity in the ACC, which was located in the affective division of the cingulate where increased activity has been frequently observed in association with the processing of emotional stimuli (Bush, Luu, & Posner, 2000) including negative-valence words (Whalen et al., 1998). Negative-valence words also yielded activation in the right superior temporal sulcus—a brain area that responds to emotional stimuli in both visual (e.g., emotional face, Narumoto, Okada, Sadato, Fukui, & Yonekura, 2001) and auditory (e.g., emotional intonation, Wildgruber, Riecker, Hertrich, Erb, & Grodd, 2005) modalities. The ACC and right superior temporal activities observed here are consistent with the previous findings and implicate the involvement of

negative emotional processing of negative-valence words even in the color naming task. However, the ACC and right superior temporal activities were not observed with death-related words. Instead, death-related words produced increased activities in the medial prefrontal cortex and bilateral parietal cortex. These activities possibly contribute to subjective evaluation of negative emotion linked to death-related words as we found correlations between subjective ratings of one's own emotional responses to death-related words and the corresponding increased parietal activity. However, the activity in the medial prefrontal cortex and bilateral parietal cortex may not be specific to death-related words as previous fMRI studies using the emotional Stroop task also observed the medial prefrontal and bilateral parietal activations in the contrast of high-arousal versus low-arousal emotion words (Compton et al., 2003; Maddock et al., 2003).

Most important, our fMRI results showed evidence for a unique neurocognitive process of death-related words. The results of subjective ratings indicate that subjects clearly classified death-related words and negative-valence/neutral-valence words into different categories in terms of death relevance. In line with the subjective categorization, the insular activity in both hemispheres differentiated between death-related words and negative-valence/neutral-valence words by showing decreased activity to death-related words. The decreased insular activity cannot be accounted for by enhanced arousal associated with negative emotion induced by death-related words because prior neuroimaging studies have repeatedly demonstrated increased, rather than decreased, insular activity in association with negative emotions (Johnstone, van Reekum, Oakes, & Davidson, 2006; Wicker, Keysers, Plailly, Royet, & Gallese, 2003). Similarly, negative-valence words tended to increase insular activity compared to neutral-valence words in the present experiment. As the anatomical posterior-to-mid-to-anterior structure of the insular cortex

functions to integrate the primary interoceptive representations and the ultimate representation of all of one's feelings that constitute the sentient self (Craig, 2009), the decreased activity in the insula linked to death-related words supports the idea that the processing of linguistic cues related to death is associated with the modulation of the sense of oneself as a sentient being. Consistent with this, the magnitude of the decreased activity in the left insular correlated with the rating scores of death relevance of death-related words. The greater the decreased insular activity, the stronger the subjective feeling of death relevance associated with death-related words. However, the decreased insular activity did not correlate with the rating scores of Death Anxiety Scale (Templer, 1970) and Existential Anxiety Questionnaire (Berman et al., 2006). Therefore, it is likely that decreased insular activity reflected online processing engaged in death-related thought rather than sustained existential anxiety. The decreased activity in the right insula associated with death-related words correlated with subjective ratings of one's own emotional responses to death-related words rather than with subjective ratings of death relevance of the words. This implies different functional roles of the right and left insula in the processing of death-related information with the left insula more associated with cognitive aspects and the right insula more associated with the emotional aspects of death-related thought.

Unexpectedly, relative to negative-valence words, death-related words also induced decreased activity in the mid-cingulate that usually shows increased activations during the process to monitor cognitive competition and complex motor control (Bush et al., 2000). A possible account of the decreased mid-cingulate is that death-related thought induced by death-related words also inhibited general processes to monitor cognitive conflict. Alternatively, the differential mid-cingulate activity might reflect greater demand for monitoring the conflict between negative-valence stimuli and positive attitude about oneself. It has been long assumed that human beings have a basic desire to feel good about themselves (James, 1890/1950) and studies of social psychology have shown evidence that most human adults possesses a positive view of the self (Greenwald, 1980). In most cases the positive attitude about oneself is unavailable to self-report or occurs in an implicit mode (Greenwald & Banaji, 1995; Jones, Pelham, Mirenberg, & Hetts, 2002; Ma & Han, 2010). The negative affect induced by negative-valence words may conflict with the implicit positive attitude about the self and results in increased cingulate activity to monitor such conflict.

The behavioral data recorded during the scanning procedure showed faster responses to death-related and negative-valence words relative to neutral-valence words. Previous research showed mixed behavioral results of emotional Stroop tasks that required color naming of emotion-laden and neutral words presented in a random order. Some studies observed slower responses to negative-valence than neutral-valence words whereas others failed to find such difference (Williams et al., 1996). Others reported slower responses to color naming of death-related words than death-unrelated words (Feifel & Branomb, 1973). Slow responses to emotion-laden or death-related words in the Stroop task have been attributed to attention bias to negative-valence or death-related words (Williams et al., 1996). The block design used in our study did not require attentional shift between words from different categories and thus reduced the interference effect in the Stroop task. Instead, sustained hypervigilance induced by the block design facilitated responses when subjects were repeatedly presented with death-related or negative-valence words in one session.

In sum, our neuroimaging findings indicate that, while the processes of both death-related and negative-valence words are characterized by enhanced activity in the precuneus/posterior cingulate and lateral prefrontal cortex that are associated with arousal and emotion regulation, the process of linguistic cues related to death is correlated with decreased insular activity, reflecting the weakened sense of the sentient self during the processing of death-related information. The neurocognitive process specific to death-related thought may provide a mechanism that mediates death anxiety and social behaviors. It should be noted that, as the current study recruited only female subjects, it is unclear whether the same neurocognitive processes observed in the current work can be apply to male subjects, which can be investigated in future work.

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