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Distinct brain activity in processing negative pictures of animals and objects --- the role of human contexts

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Abstract

Previous studies have shown that the amygdala is important in processing not only animate entities but also social information. It remains to be determined to what extent the factors of category and social context interact to modulate the activities of the amygdala and cortical regions. In this study, pictures depicting animals and inanimate objects in negative and neutral levels were presented. The contexts of the pictures differed in whether they included human/human parts. The factors of valence, arousal, familiarity and complexity of pictures were controlled across categories. The results showed that the amygdala activity was modulated by category and contextual information. Under the nonhuman context condition, the amygdala responded more to animals than objects for both negative and neutral pictures. In contrast, under the human context condition, the amygdala showed stronger activity for negative objects than animals. In addition to cortical regions related to object action, functional and effective connectivity analyses showed that the anterior prefrontal cortex interacted with the amygdala more for negative objects (vs. animals) in the human context condition, by a top-down modulation of the anterior prefrontal cortex to the amygdala. These results highlighted the effects of category and human contexts on modulating brain activity in emotional processing.

Keywords

Stimulus category; emotion; context; amygdala; prefrontal cortex

Introduction

In our daily lives we may fear different kinds of things, e.g., snakes, plane crashes, or blood. Some people develop as phobia to excessively fear certain classes of objects or contexts. Among the specific phobias, animal phobia has the highest prevalence (Damsa et al., 2009; Pull, 2008), but its neural mechanisms remain unclear. One influential hypothesis, the preparedness theory, posits that fear of snakes and spiders may be associated with prepared

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networks because ancient humans faced attacks from these animals (Ohman and Mineka, 2001; Seligman, 1970). Compared to ontogenetic fear stimuli (e.g., guns), phylogenetic fear stimuli (e.g., snakes) are more attended to (e.g., New et al., 2007; Ohman et al., 2001a; Ohman et al., 2001b), and lead to stronger physiological responses (e.g., Cook et al., 1986; Hugdahl and Karker, 1981).

Specifically the preparedness theory proposes that the enhanced response to phylogenetic fear stimuli is associated with activity in the amygdala. This result is supported by the evidence that the amygdala is more responsive to animate stimuli compared to inanimate objects, in addition to being extensively involved in processing threatening stimuli. In a previous study the neurons in the right amygdala were more responsive to animal pictures, which was independent of emotional valence and arousal (Mormann et al., 2011). The medial temporal region, including the amygdala, was preferentially responsive to personally relevant images (vs. unfamiliar people) (Viskontas et al., 2009). The animate advantage is also shown in fMRI studies. In one study, Yang et al. (2012a) compared brain activation in American participants for faces, nonhuman animals and inanimate objects in negative, positive and neutral levels. The results demonstrated that activation in the right amygdala was the strongest for human faces, less strong for animals, and weakest for inanimate objects. This pattern was clear for negative and neutral pictures and suggested that the amygdala is more involved in processing animate (vs. inanimate) entities.

Various studies have also revealed that the amygdala is important for processing social information (e.g., Norris et al., 2004; Sakaki et al., 2012; Wheatley et al., 2007. For reviews, see Adolphs, 2010; Frith and Frith, 2012). In the Wheatley et al. (2007) study, subjects viewed moving shapes in two different backgrounds biased towards animate or inanimate interpretations. Because the shapes were the same, the interpretation was determined by the contextual background. The results showed that animate interpretation significantly activated the amygdala, insula, medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) relative to inanimate interpretation. Sakaki et al. (2012) divided pictures into survival-related (e.g., threats, food) and social life-related categories (e.g., trust, friendship) with the two types of pictures matched in their valence and arousal levels. The results showed that the left amygdala and the left mPFC were activated for both survival- and social-related pictures. The amygdala also had addictive effects when pictures were negative and included social contents (i.e., pictures containing human information) (Norris et al., 2004).

Althougth the factors of emotion, category and context are important for amygdala activation, to what extent they interact to influence the activation of the amygdala and other brain regions is unclear. Some studies found comparable emotional responses to living and nonliving entities under some conditions. For example, pointed guns and pointed snakes had comparable resistance to extinction (Hugdahl and Johnsen, 1989) because guns with sounds are more likely to be associated with threatening situations. Indeed, when seeing a gun handled by a human hand, one likely finds the gun more threatening than a gun on the table and as threatening as a snake biting a man. A recent eye-tracking study showed that, although animal pictures attract more attention than inanimate objects (New et al., 2007), they had comparable numbers of gaze fixations and gaze durations when human contexts were included in both types of pictures (Yang et al., 2012b). This result suggested that contextual information is important for understanding how people react to negative inanimate objects. Processing pictures with human contextual information may critically depend on that context and is associated with top-down modulation and executive control of social information (Frith and Frith, 2012). Neural recordings of rats found that the prefrontal cortex encoded contextual information to form rich contextual representations and alter the interpretations or meanings of stimuli (Hyman et al., 2012). Thus, the amygdala and the prefrontal cortex possibly interact to process emotional pictures with human contexts, but more evidence is needed to confirm the prediction.

The question addressed in this study was to explore the extent to which the activities of the amygdala and cortical regions were modulated by contextual information when subjects processed animals and objects in different emotional levels. In a pilot experiment (Supplementary Material), we adopted the design of Yang et al. (2012a); Chinese subjects viewed pictures of facial expressions, animals and manipulable objects in different emotional levels (i.e., negative, neutral and positive). In this study, we further included pictures with human or human body information as contexts for nonhuman animals and inanimate objects in negative and neutral dimensions. To dissociate the factors of emotion and category, we matched valence and arousal levels across categories and controlled for complexity and familiarity levels. We hypothesized that factors of emotion, category and context interact to influence the amygdala activation (e.g., Yang et al., 2002b; Hayman et al., 2012). We predicted that the amygdala activation was stronger for negative (vs. neutral) pictures, and stronger for animals than objects, as shown in previous studies. In addition, the category effect is expected to interact with that of emotion and context. For pictures without human contexts, nonhuman animals elicit stronger activation in the amygdala than inanimate objects. For the pictures with human contexts, the animate advantage in negative dimensions may attenuate or disappear in the amygdala due to top-down processing of the prefrontal cortex.

Materials and Methods

Subjects

Sixty healthy, right-handed subjects (28 males) participated in the study, with the mean age 22.54 ± 2.75 yrs. Of these subjects, 21 participated in emotional rating (10 male), 18 participated in familiarity and complexity rating (7 males), and the other 21 subjects participated in the fMRI experiment (11 males). All subjects were native Chinese speakers, and gave written informed consent in accordance with procedures and protocols approved by the Institutional Review Board of the Department of Psychology, Peking University.

Stimuli

The stimuli setup was the same as Yang et al. (2012b). Three within-subject factors were included in the study with a 2×2×2 structure: context (with or without human contexts), emotion (negative, neutral) and category (nonhuman animals, inanimate objects). The factorial combination of the three factors made up eight experimental conditions. The stimuli in the fMRI experiment consisted of 240 colorful, nameable experimental pictures (30 per condition) with a resolution of 640*480 pixels. Each of the 30 concepts was depicted as different pictures in contexts with and without human (or human parts). Low-level visual features, stimulus saliency, picture size, position of focal object and context were also analyzed and matched across categories (Yang et al., 2012b). Both small and large sizes of animals and inanimate objects were included to match their actual size. The orientation of the pictures was also matched across categories.

fMRI procedure

Pictures were clustered into blocks by context, emotion and category, with each of the 2×2×2 conditions having 2 blocks. In each block, there were 19 pictures (15 different items and 4 repeats). Each picture was presented for 1 s, followed by a fixation for 500ms, which yielded a duration of 28.5 s for each block. Subjects were asked to pay attention to all the stimuli, and to perform a repetition detection task. The 16 picture blocks and 16 scrambled blocks were pseudo-randomly assigned to 4 runs; the picture conditions, concepts and backgrounds were balanced across runs. The picture and scrambled blocks were interleaved in each run. Because four additional TRs (two before the first block and two after the last block) were inserted for each run, each run lasted 240 sec, and the entire experiment lasted about 30 min. The orders of the blocks and runs were counterbalanced across subjects.

MRI acquisition

MRI data were collected on a Siemens Trio 3T scanner (Magnetom Trio). Functional data were collected using a gradient echo, echo-planar imaging (EPI) sequence (TR = 3s, TE = 40ms, flip angle = 90°, FOV = 24cm, matrix = 96×96, slice = 34 and resolution = 2.5×2.5×3 mm^3), and anatomical data were acquired using a high-resolution MP-RAGE sequence (TR = 7.6ms, flip angle = 6°, FOV = 22cm, matrix = 224×224, resolution = 1×1×1.2 mm^3) after functional scanning.

MRI statistical analysis

AFNI was used for pre-processing imaging data and statistical analysis (http://afni.nimh.nih.gov). The first three EPI volumes in each run were discarded due to the issue of magnetization equilibrium. The remaining volumes were registered, smoothed with an RMS width of 3mm, and scaled to a mean of 100. Multiple regression analysis was performed to calculate the response to each condition compared with the scrambled baseline. The model included eight regressors of interest, each of which was created by the convolution of a gamma variate for each condition, six regressors of non-interest (motion parameters), and second-order polynomials for slow drift. Anatomical images and the volumes of effect estimates from the regression analysis were then warped into the standard stereotaxic space of the Talairach and Tournoux (1988) atlas.

For group analysis, a voxel-wise four-way repeated-measures ANOVA was performed with context, emotion and category as three within-subjects factors and subjects as between-subjects factor (voxel-wise $p < 0.01$, two-tailed). Monte Carlo simulations were used to correct for multiple comparisons at a corrected p-value of 0.05 in cortical regions (number of voxels = 13, volume = 244 mm^3) and the amygdala (SVC, number of voxels = 4, volume = 75 mm^3). The amygdala for each subject was manually drawn and averaged as the anatomical mask to confine the activation located within the amygdala. To further determine the relations between the amygdala and prefrontal cortex, the psychophysiological interaction analysis (PPI, Friston et al., 1997), the ROI analysis, and the dynamic causal modeling (DCM, Friston et al., 2003; SPM8, http://www.fil.ion.ucl.ac.uk) were performed. For the PPI analysis, the seed regions were created as a 5 mm-radius sphere centered on the peak voxel. Then the average time series from the seed region was extracted from the dataset with baseline, slow drift and head motion removed. A correlational map for each subject was produced between the time course from the seeds and rest of the brain. To combine results across subjects, the correlation coefficients were converted to z scores and analyzed using a one-sample t-test ($p < 0.05$, corrected, two-tailed). For the ROI analysis, we selected regions of the amygdala and the anterior prefrontal cortex that were activated in each category contrast, extracted the time series of that condition from each subject and averaged the series across subjects.

For the DCM, we used SPM8 to perform the preprocessing and deconvolution, then selected the peak location of the prefrontal cortex (−45, 32, 7) and the amygdala (27, −1, −20) from the group level contrast and created the ROIs as a 4 mm-radius sphere for each peak. The first eigenvariate across those voxels was extracted. The DCM models were analyzed for negative objects and animals under the human context condition separately. With the assumptions that there were intrinsic bidirectional connections between the aPFC to the amygdala (Volman et al., 2013) and category modulation for the bidirectional connections, we estimated the parameters for each model and divided the possible models into three families for negative animals and objects separately (Supplementary Material, Figure S3). These models and families were common in their self-connection and intrinsic connections of the aPFC and the amygdala. The models differed in category modulation to the connection of aPFC --> amygdala or amygdala --> aPFC, and the families differed in where the input came from. According to the results of the Bayesian model selection (BMS) in a random-effects approach, we identified the family that was most likely to have generated the data across subjects. Then, we performed the Bayesian model averaging (BMA) on the winning family for each subject (Penny et al., 2010). This procedure computed weighted means of each model parameter in the winning family, in which the weighting was determined by the posterior probability of each model. In addition, we performed the BMA on each model within the winning family for each subject. The mean parameters were averaged across subjects and t-test was performed to estimate the modulatory effect ($p < 0.05$, two-tailed).

Results

Rating results

Analyses of the rating data confirmed that the object categories were equated for valence and arousal (Table 1). Pictures in animals and objects were rated in comparable scores ($F(1,20) = 0.09$, $p = 0.76$ for valence, and $F(1,20) = 3.44$, $p = 0.08$ for arousal). As designed, negative pictures were more negative and more arousal than neutral pictures ($F(1,20) = 230.73$, $p < 0.001$, and $F(1,20) = 99.26$, $p < 0.001$). The interactions related to category were not significant (all p values > 0.05). For the familiarity rating, subjects evaluated how often they saw or thought of the focal object (i.e., an animal or object) in their daily life (1 = least familiar; 7 = most familiar). The results showed that category effect was not significant ($F(1,17) = 1.66$, $p = 0.22$). Neutral pictures were more familiar than negative pictures ($F(1,17) = 17.65$, $p < 0.001$), and pictures without human contexts were more familiar than those with human contexts ($F(1,17) = 12.09$, $p < 0.003$). There were no significant category-related effects (p’s > 0.20). For the complexity rating, subjects rated the degree of details in a picture and the degree of changes on its contours (1 = least complex; 7 = most complex). Animal pictures were more complex than objects ($F(1,17) = 39.15$, $p < 0.001$). Negative pictures were more complex than neutral pictures ($F(1,17) = 4.89$, $p < 0.05$). The interactions related to category were not significant (p’s > 0.30).

Behavioral results

During scanning, subjects were highly accurate when performing the repetition detection task (0.94 ± 0.06). Analyses of the accuracy and reaction time data failed to reveal any effects of category, emotion, or their interaction (all F’s < 1.0, p’s > 0.20).

ANOVA results

Main effects of emotion and context—Many brain regions showed significant effects of emotion and context (Table 2). Among them, there was stronger activation in the bilateral amygdala (−21, −9, −9, $t(20) = 6.42$, $p < 0.001$ on the left and 21, −4, −9, $t(20) = 5.25$, $p < 0.001$ on the right) for negative pictures than neutral pictures (Figure 2A). For the context difference, the bilateral amygdala (−19, −11, −6, $t(20) = 6.01$, $p < 0.001$ on the left and 21, −6, −6, $t(20) = 6.67$, $p < 0.001$ on the right) was also more responsive to pictures with human contexts than those without human contexts. This result was consistent with previous findings that the amygdala is involved in processing both emotional and social information (Adolphs, 2010; Frith and Frith, 2012; Zald, 2003).

Main effect of category—There was significant category effect on the left (−21, −4, −6, t(20) = 3.78, $p < 0.002$) and right (26, 6, −9, t(20) = 4.34, $p < 0.001$ and 19. −1, −16, t(20) = 3.03, $p < 0.01$) amygdala even when the activation was constrained by the anatomical amygdala mask. The animal pictures elicited stronger activation in the amygdala than object pictures (Figure 2B). Similar findings were shown in Yang et al. (2012a) and our pilot study with Chinese participants (Supplementary Material, Figure S1). Note that the effects of category, emotion and context were overlapped in the amygdala (Figure S2). The category effect was smaller than and included in emotional and contextual effects, and the effects of emotion and context were partly overlapped.

Category-related differences were also found in animate and inanimate networks, including posterior regions of ventral and lateral temporal lobes and in regions of the parietal and frontal cortices (Figure 3A). Nonhuman animals elicited stronger activation than inanimate objects in the bilateral lateral fusiform gyrus, right superior temporal sulcus (STS), occipital cortex, posterior cingulated cortex (PCC), insula and the right thalamus. In contrast, inanimate objects elicited stronger activation in the left medial fusiform gyrus, left middle temporal gyrus (MTG), left parietal cortex, bilateral anterior prefrontal cortex (aPFC) and the middle prefrontal cortex.

Interactions among factors—A noteworthy result is that the amygdala activation was modulated by the interaction of the three factors (Table 3, Figure 2C). There were significant interactions in the amygdala for category by emotion (−31, −6, −11, F(1,20) = 18.75, $p < 0.001$), category by context (−26, −1, −13, F(1,20) = 14.04, $p < 0.001$), emotion by context (−21, −6, −4, F(1,20) = 14.58, $p < 0.001$), and the 3-way interaction (−19, 1, −16, F(1,20) = 6.01, $p < 0.05$). For the interaction of emotion by context, the emotional effect in the amygdala was obvious for pictures with human contexts (vs. without human context). The emotion effect was significant in the right for animals and mainly in the left for objects, suggesting that the left and right amygdala may be involved in processing different aspects of information (Glascher et al., 2003; Hariri et al., 2002).

The interaction was also manifested in the category effect (Figure 4A). For the interaction of emotion by category, the category effect was significant in the right (19, −1, −14, t(20) = 3.05, $p < 0.01$) for the negative pictures and in the left (−31, −6, −14, t(20) = 5.05, $p < 0.001$) for the neutral pictures, both showing animate advantage. The amygdala showed increased activation (animals > objects) (left: −26, 1, −21, t(20) = 2.51, $p < 0.03$; right: 21, 4, −21, t(20) = 3.05, $p < 0.01$) when the contexts did not include human information, but showed opposite patterns (animals < objects) (left: −29, −11, −11, t(20) = 3.05, $p < 0.01$; right: 21, 1, −14, t(20) = 3.61, $p < 0.002$) for the human-context pictures.

The simple category effects showed similar results (Figure 4B). When the context did not include human information, nonhuman animals elicited stronger activation than inanimate objects for both the negative (19, −1, −14, t(20) = 3.24, $p < 0.005$) and neutral conditions (−19, −6, −14, t(20) = 3.94, $p < 0.001$). However, when the context included human information, the animate advantage only occurred for neutral pictures (−19, −4, −9, t(20) = 2.65, $p < 0.02$). For negative pictures with human contexts, the amygdala elicited stronger activation for inanimate objects than nonhuman animals (26, −1, −24, t(20) = 2.83, $p < 0.02$).

The animate and inanimate networks were manifested in both negative and neutral pictures. In particular, for pictures with human contexts (Figures 3B, 3C), negative animals elicited stronger activation in the right STS (46, −66, 21, t(20) = 3.92, $p < 0.001$), PCC (−11, −39, 44, t(20) = 5.06, $p < 0.001$), precuneus (−14, −59, 56, t(20) = 4.67, $p < 0.001$) and the inferior PFC (59, 6, 29, t(20) = 5.62, $p < 0.001$) than negative objects, and negative objects elicited stronger activation in the left MTG (−49, −44, −6, t(20) = 4.42, $p < 0.001$), left premotor cortex (PMC, −39, 1, 29, t(20) = 5.05, $p < 0.001$) and left parietal cortex (−39, −34, 39, t(20) = 3.71, $p < 0.002$ and −41, −44, 46, t(20) = 3.37, $p < 0.005$) than negative animals. In addition to these regions, the aPFC (−46, 46, 1, t(20) = 5.51, $p < 0.001$ on the left and 39, 46, −9, t(20) = 5.35, $p < 0.001$ on the right) also showed stronger activation for negative objects than animals.

In addition to the cortical regions that are widely reported in the literature (Martin, 2007), we found that the bilateral aPFC (−39, 46, −4, t(20) = −3.37, $p < 0.005$) showed significant activation for objects vs. animals (Table 2). However, for simple contrasts, the aPFC manifested different patterns (Figure 5A). The aPFC was more strongly activated for negative inanimate objects (vs. animals) when the negative pictures included human contexts, but it was more strongly activated for nonhuman animals vs. objects in the other three contrasts.

Previous studies have found that the mPFC is highly associated with emotional processing and regulation (Ochsner and Gross, 2005; Quirk and Beer, 2006; Roy et al., 2012). Our study showed similar results, and more specifically, the mPFC activity was significant for negative pictures (vs. neutral) (−5, 44, −4, t(20) = 3.53, $p < 0.005$) and pictures with human contexts (vs. those without human contexts) (5, 46, −11, t(20) = 3.45, $p < 0.005$). There was also stronger activation in the mPFC for animals vs. objects (−4, 51, −1, t(20) = 4.36, $p < 0.001$) and the bilateral aPFC for objects vs. animals. However, in regard to the category effect in human condition, there was only significant activation in the bilateral aPFC for negative objects (vs. animals).

PPI and ROI Results—To determine the network differences for negative objects (weapons) and negative animals, we performed the PPI analysis to find regions that were significantly correlated with the left aPFC (−46, 46, 1, t(20) = −5.51, $p < 0.001$), which were selected as seed regions from the category contrast of negative pictures in the human-context condition (objects vs. animals). The results showed that the activity of the right amygdala was positively correlated with the activity of the left aPFC in the human-context condition (Figure 5B). It suggested that when human contexts are included in the context, the left aPFC is more activated for negative objects and modulates the amygdala activation by top-down processing.

We also performed the correlation analysis between ROI regions of the amygdala and aPFC. The results showed that for negative pictures with human contexts, the left aPFC was significantly correlated with activation in the right amygdala ($r = 0.48$, $p < 0.04$) (Figure 5C). For neutral pictures with human contexts, the left aPFC (−31, 56, −1, t(20) = −6.10, $p < 0.001$) was significantly correlated with activation in the left amygdala ($r = 0.46$, $p < 0.04$). There were no significant correlations between the aPFC and amygdala for pictures without human contexts ($r < 0.15$, p’s > 0.5). These results suggested that the prefrontal cortex modulates the amygdala activation with respect to whether the context includes a human factor.

DCM Results—Based on the PPI and ROI results, the connection between the aPFC and the amygdala was modulated by stimulus category. The DCM results further suggested a connection from the aPFC to the amygdala. Figure S3 showed that the most suitable models were those in Family C, in which the input projection was connected to the aPFC, suggesting a possible top-down modulation originated from the aPFC. In addition, negative objects had strong influence on modulating the top-down connections. The modulatory strength of the aPFC --> amygdala connection was significant for negative objects (t(20) = 2.67, $p < 0.02$), but not for negative animals (t(20) = 1.23, $p = 0.23$) (Table 4). In contrast, stimulus category had small modulatory effects on the amygdala --> aPFC. The modulatory strength of the amygdala --> aPFC connection was not significant for negative objects (t(20) = 0.42, p = 0.68) or negative animals (t(20) = 1.55, p = 0.64). The results for each model within the winning family also showed that there was significant modulatory effect of negative objects for the aPFC --> amygdala connection (Supplementary results, Table S1).

Discussion

The objective of this study was to explore the extent to which the amygdala activation was modulated by category and contextual information when subjects processed animals and objects in different emotional levels. We had three main findings. First, the amygdala responded more to animals than objects when the contexts did not include human information. Second, the amygdala activity was modulated by contextual information of the pictures. When pictures included human contexts, the amygdala activation was stronger for negative objects than animals. Third, in addition to regions related to object action, the aPFC was more activated for negative objects (vs. animals) with human contexts, and modulate the amygdala activation. The results suggested that contextual information and category interact to influence the amygdala and cortical activations in emotional processing.

Category effect in the amygdala with non-human contexts

The results showed that, when the context did not include human information, the amygdala was more responsive to animals than objects. This was consistent with previous studies that used neural recordings and fMRI techniques. Some neurons in the amygdala preferred animal pictures (Mormann et al., 2011), and others preferred human faces (Viskontas et al., 2009). The amygdala is activated in processing visual information about animate geometric shapes (Castelli et al., 2000, Martin and Weisberg, 2003), biological motions (Bonda et al., 1996) and animate pictures (Yang et al., 2012a).

One of the common characteristics of faces and animals is their animacy. Both categories can be agents that initiate goal-directed self-movements (Rakison and Dubois, 2001), and both can interact with humans for social interactions, whereas man-made objects can only be acted on by agent manipulations. Because faces and animals can initiate threatening actions, paying more attention to them (Lipp et al., 2004; New et al., 2007; Yang et al., 2012b) and identifying animate entities/agents are important for human survival (Heberlein and Adolphs, 2004, New et al., 2007). Similar mechanisms may apply to neutral animate stimuli because they are potentially threatening to humans. For example, the social meaning of neutral faces is ambiguous, and faces may even be untrustworthy, which evokes stronger amygdala activation (Fitzgerald et al, 2005; Wright and Liu, 2006). Neutral animals are less threatening than fearful animals, but they still have higher potential to be predators than tools (Purkis and Lipp, 2007). Taken together, the amygdala may have a broader role in detecting and appraising any potential biological sign of threat (Adolphs, 2010; Davis and Whalen, 2001; Sander, 2003; Whalen, 1998).

An interesting part of the results was that the Chinese subjects manifested different characteristics than did their American counterparts. The animate advantage in the amygdala between animals and objects was smaller than that in Yang et al. (2012a), although not compared directly. This result occurred because negative objects showed strong activation in the amygdala, and positive objects (toys) did not show enhanced activation in the amygdala (vs. other objects) (Supplementary Results). Studies have suggested that the two populations adopt different strategies to process scenes. Chinese participants were more likely to attend to the context and background of the pictures, whereas Americans paid more attention to the objects (Chua et al., 2005). Our rating results confirmed that Chinese subjects thought more of social interaction when they viewed the negative objects (Supplementary Results), suggesting a mechanism of automatic generating social inferences when viewing objects. In general it was consistent with the results that contextual information with humans significantly increased the amygdala activation for negative objects. It also suggested that cultural factor should be considered in emotional processing, especially when pictorial stimuli were used.

Category effect in the amygdala with human contexts

The novel finding of our study was that there was stronger activation in the right amygdala for negative objects than animals with human contexts and positive connectivity from the left aPFC to the right amygdala in this condition. The results were obtained when various factors were controlled, and the levels of valence, arousal and familiarity for negative animals and objects with humans included in the contexts were comparable. Although animals were generally more complex than objects, there were no significant interactions among factors, which was different from the pattern in the amygdala response. It suggested that the increased amygdala activation for negative objects vs. animals with human contexts is not due to the difference in affective and perceptual features across categories. But rather, the fMRI result may reflect the interaction between the object and its context in processing pictures.

When human-related information is included in the picture, subjects can use the context to make inferences about the intentions of conspecifics (Adolphs, 2010; Frith and Frith, 2012) and how serious the situations are to them. In modern society, human beings face many disasters related to threatening inanimate objects (e.g., car accidents and wars) that more frequently occur than events related to threatening animals (e.g., snakes biting people). Previous studies also found comparable emotional responses to living and nonliving things under some conditions (e.g., Blanchette, 2006; Brosch and Sharma, 2005; Hugdahl and Johnsen, 1989; Yang et al., 2012b). Our results showed that the increased response to threatening objects is associated with the amygdala activation. Neuroimaging studies have suggested that the amygdala is important for processing social information (e.g., Martin and Weisberg, 2003; Norris et al., 2004; Sakaki et al., 2012; Wheatley et al., 2007). It suggested that, although animate advantage is a general rule for the amygdala response, the amygdala responds more to negative pictures with human context in deliberating their salient meanings to human beings.

We also found that the amygdala activation was significantly correlated with the aPFC activation for negative pictures with human contexts. In addition, the DCM attempts to infer the dynamics of the underlying neuronal systems from the observed fMRI signal (Friston et al., 2003), and the results showed that there were strong aPFC --> amygdala connection. The aPFC is located in the anterior part of the prefrontal cortex and has strong connections with other parts of the prefrontal cortex (e.g., dorsal and medial PFC) and other brain regions. While the mPFC is highly associated with emotional processing and regulation (Bishop, 2007; Ochsner and Gross, 2005; Quirk and Beer, 2006; Roy et al., 2012), the aPFC is involved in semantic encoding and memory retrieval process (Simons and Spiers, 2003). Our study showed that there was significant activation in the bilateral aPFC for objects (vs. animals) and negative pictures with human contexts. The amygdala-prefrontal circuitry has been shown to be responsible for attentional capture to threatening stimuli and interpretation of emotionally ambigious stimuli. Stronger activation in the prefrontal cortex led to reduced activation in the amygdala (e.g., Bishop, 2007; Quick & Beer, 2006; Wager et al., 2008). On the other hand, the PFC subregions, especially the ventral and anterior parts, are involved in generating emotional responses (Etkin et al., 2011) and increasing emotional responses (Ochsner et al., 2005). The PFC is also responsible for processing contextual information (Hyman et al., 2012). It is possible that the PFC activity is task-based and different subregions of the PFC play different roles in emotional processing. We hypothesized that the role of the aPFC is to integrate information from affective features with social cues and to evaluate its social meaning based on long-term memory. The stronger activation of the aPFC for negative objects (vs. animals) indicated the significance of social situation for processing scenes of negative objects. The aPFC is therefore associated with top-down modulation and executive control of social information that is processed in the amygdala.

Category representation for negative pictures in cortical regions

Converging evidence from neuropsychological and functional brain imaging investigations suggest that different object categories, such as animate, biological objects (e.g., four-legged animals) and man-made manipulable objects (e.g., tools) are represented in distinct neural networks in the brain (Mahon and Caramazza, 2009; Martin, 2007). The network for different categories was consistent with the analysis of the main effect of category in the study. Then the following question should be addressed. In the human context condition, are negative animals and objects represented differently in the cortical region? Our results showed that the two types of pictures were indeed represented in the animate and inanimate networks. Negative animals elicited stronger activation in the right STS, PCC, precuneus and inferior PF than negative objects. Both the PCC and STS are involved in the social network and were activated in previous studies (e.g., Norris et al., 2004; Sakaki et al., 2012; Wheatley et al., 2007). The STS is important for inferred intentions of social cues (Nummenmaa and Calder, 2009), and the PCC is related to interpreting the meaning of other people's actions (Adolps, 2010). In addition to the left aPFC, negative objects elicited stronger activation in the left MTG, left PMC and left parietal cortex than negative animals. These regions are associated with action representation (Chao and Martin, 2000; Martin, 2007; Yang et al., 2012a) and are consistently reported in many studies. The fear of negative animals and objects thus relies on different cortical mechanisms, regardless of their contexts.

Theoretical Implications and fear processing

The amygdala is a complex collection of 13 nuclei in primates. Numerous studies have shown its important role in processing emotionally and socially relevant information. There are some theories that account for the amygdala activation. For example, the amygdala may be more responsible for processing negative stimuli (Amaral, 2003), emotional stimuli (Zald, 2003), phylogenetic fear stimuli (Ohman and Mineka, 2001), vigilance and ambiguity resolution (Davis and Whalen, 2001), or salient and relevance detection (Adolphs, 2010; Sander, 2003). In general, these theories are not necessarily contradictory to each other. The core role of the amygdala may be responsible for detecting and evaluating the meaning and consequences of a relevant external event, especially when uncertain and ambiguous interpretation occurs (Adolphs, 2010). Because biological or animate stimuli are more related to human beings and initiate threatening actions, they are more attended to than other types of stimuli in activating the amygdala. The amygdala is therefore a part of the animate network. However, negative objects in a human-related context also contain the information of potential threats and danger to humans (Coelho and Purkis, 2009). Thus, responding to these objects with appropriate action is important. The amygdala may be preferentially activated in this situation, partly through the modulation of the prefrontal cortex.

The theoretical significance of our study was that it highlighted the interaction of category and contextual information in modulating amygdala activation in emotional processing. Particularly, in regard to fearful stimuli, evolutionary features (i.e., phylogenetic and ontogenetic fear) undoubtedly modulate the amygdala activation, but its activation level is also modulated by a stimulus's contextual information. Clarifying the role of the amygdala is important for understanding the neural mechanisms of various emotional disorders, such as animal phobias and posttraumatic stress disorder (PTSD). PTSD is characteristic of the overwhelming terror resulting from certain trauma, especially in people who underwent life-threatening events (McNally, 2006). This result explains why animal phobia has the highest prevalence among specific phobias (Damsa et al., 2009; Pull, 2008). In addition, PTSD patients are not possibly afraid of object itself, but the scene that object is located in a certain situation. The fear of ontogenetic stimuli may rely on human contexts.

Limitation

Our study has some limitations. First, the rating results were obtained from subjects who were not scanned although the two groups of subjects were matched in their age and gender. Second, the difference between negative and neutral pictures could arise from both valence and arousal. In general negative animals and objects are more aroused than neutral pictures, so by our design it is hard to tease apart the two effects, although this co-effect should not influence the category effect because the valence and arousal levels were optimally matched across categories. Further studies could control the arousal rating as covariate in the analysis when the same group of subjects were rated and scanned. Third, although aPFC --> amygdala connection was identified as significant in the DCM, caution should be taken due to the limitations of the design. For example, functional data with a shorter (vs. longer) TR and continuous acquisition (vs. interleaved) are recommended for DCM (Stephan et al., 2010), but our data were acquired with relatively long TR (3 s) and interleaved slice sequence. Fourth, a picture includes human parts only reflects parts of social interaction. In this study, because we used animal and object pictures as stimuli, we selected pictures that human interacted with animals and inanimate objects (e.g., a hand grasps a gun). It would be interesting to use dynamic motion pictures as stimuli in future studies to induce more realistic social situation related to animals and objects.

Conclusion

In conclusion, our study showed that animate pictures elicited stronger activation in the amygdala than did inanimate objects whether the pictures were negative or neutral. However, when human information was included in the context, negative objects elicited stronger activation in the right amygdala than negative animals, and the amygdala activation was modulated by the activation in the left aPFC for negative objects. The results highlighted the role of stimulus category and contextual information in modulating the amygdala and cortical activation in emotional processing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Stimulus example. Cited from Yang et al. (2012b).

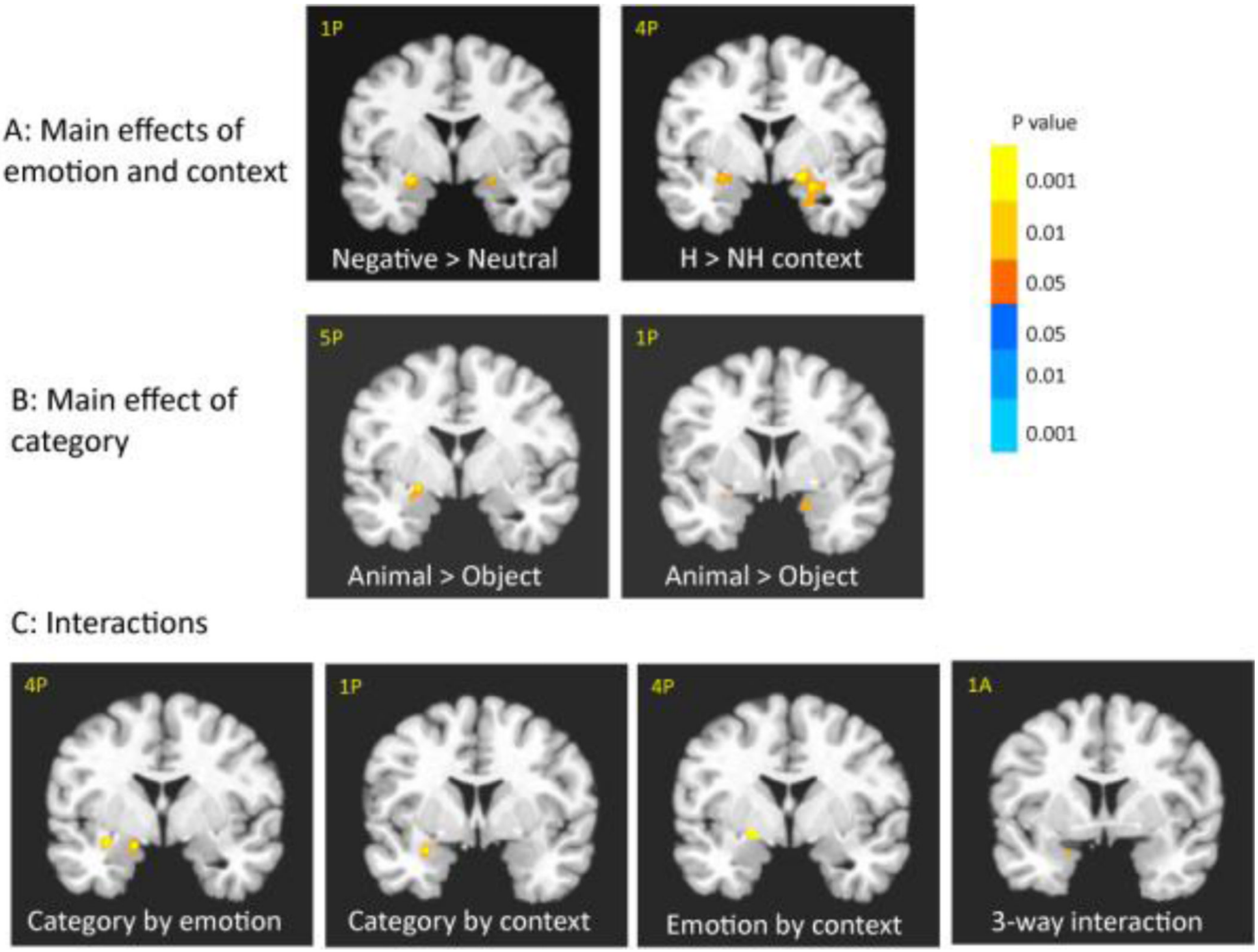

Figure 2.

Main effects and interactions in the amygdala. There were significant main effects of emotion, context (A) and category in the amygdala (B). The amygdala also showed significant interactions of category by emotion, category by context, emotion by context and 3-way interactions (C).

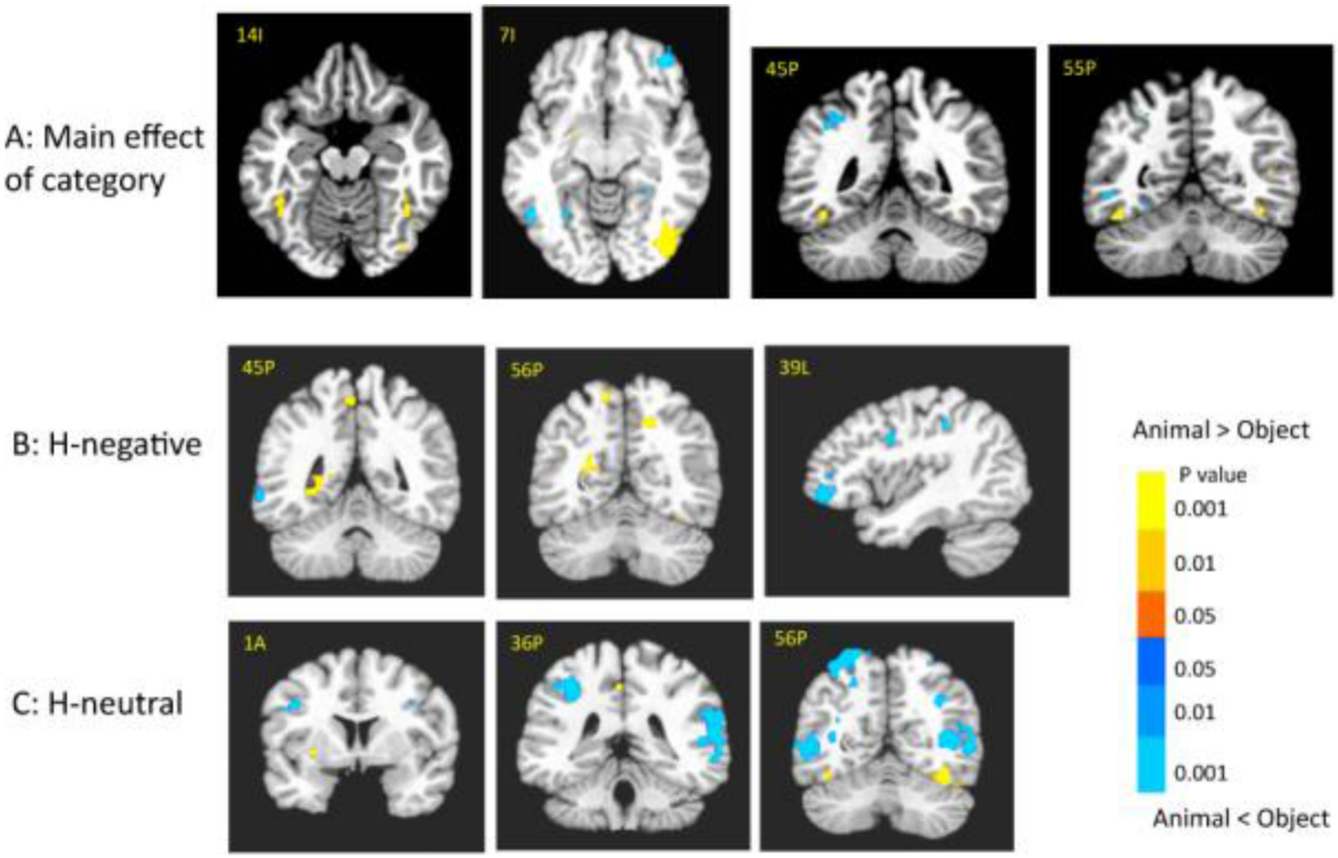

Figure 3.

Category effect in cortical regions. The animate network and inanimate network were shown in distinct cortical regions for the main effect (A) and for negative (B) and neutral (C) pictures with human contexts.

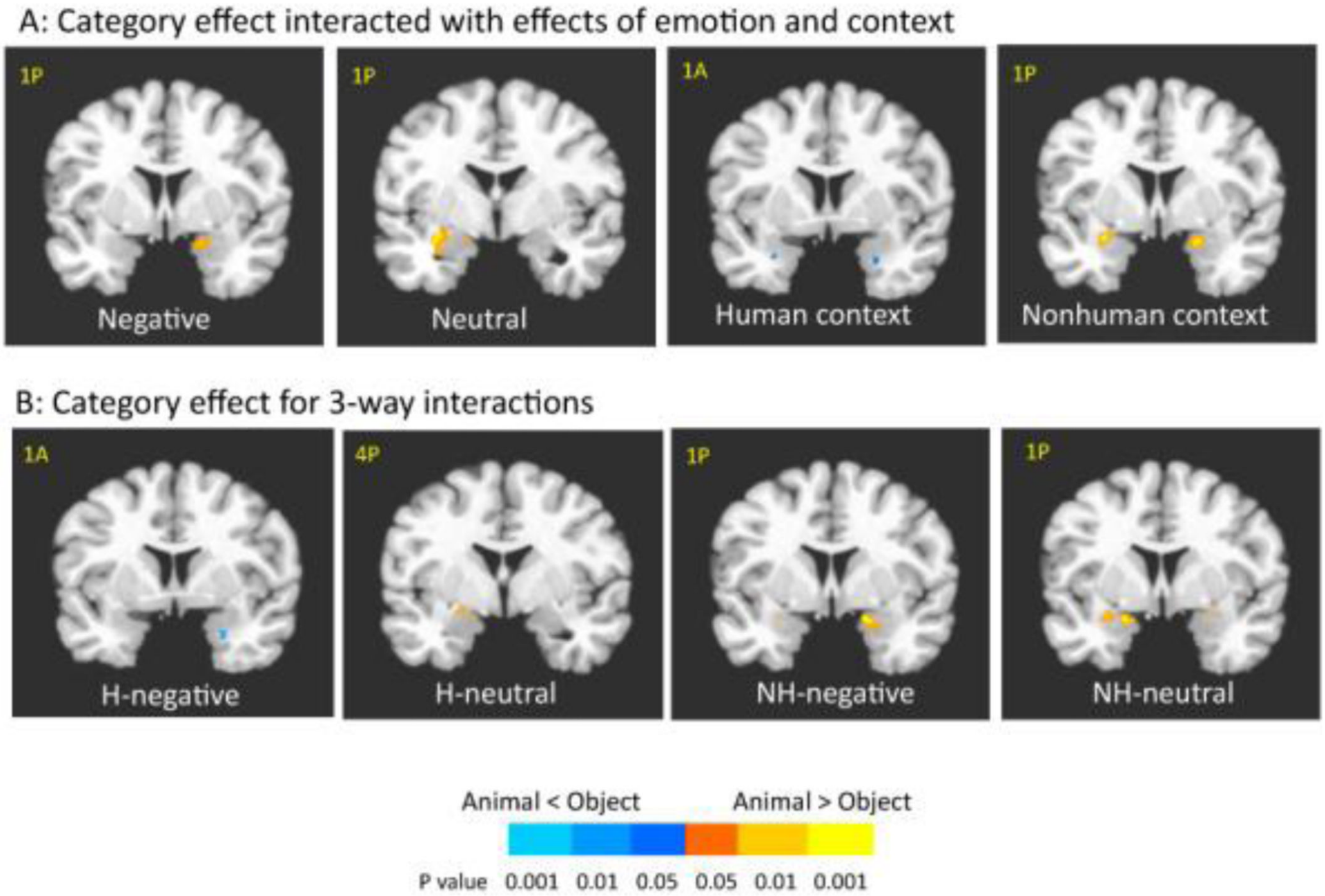

Figure 4.

Category effect in the amygdala for the interactions. The amygdala were activated differentially for negative and neutral pictures, pictures with and without human context (A). For the simple effect, category effects in the amygdala were shown in human-negative (H-negative), human-neutral (H-neutral), nonhuman-negative (NH-negative), and nonhuman-neutral (NH-neutral) conditions (B). Note that different from other condition, in the H-negative condition, the animals showed decreased activation than objects in the amygdala.

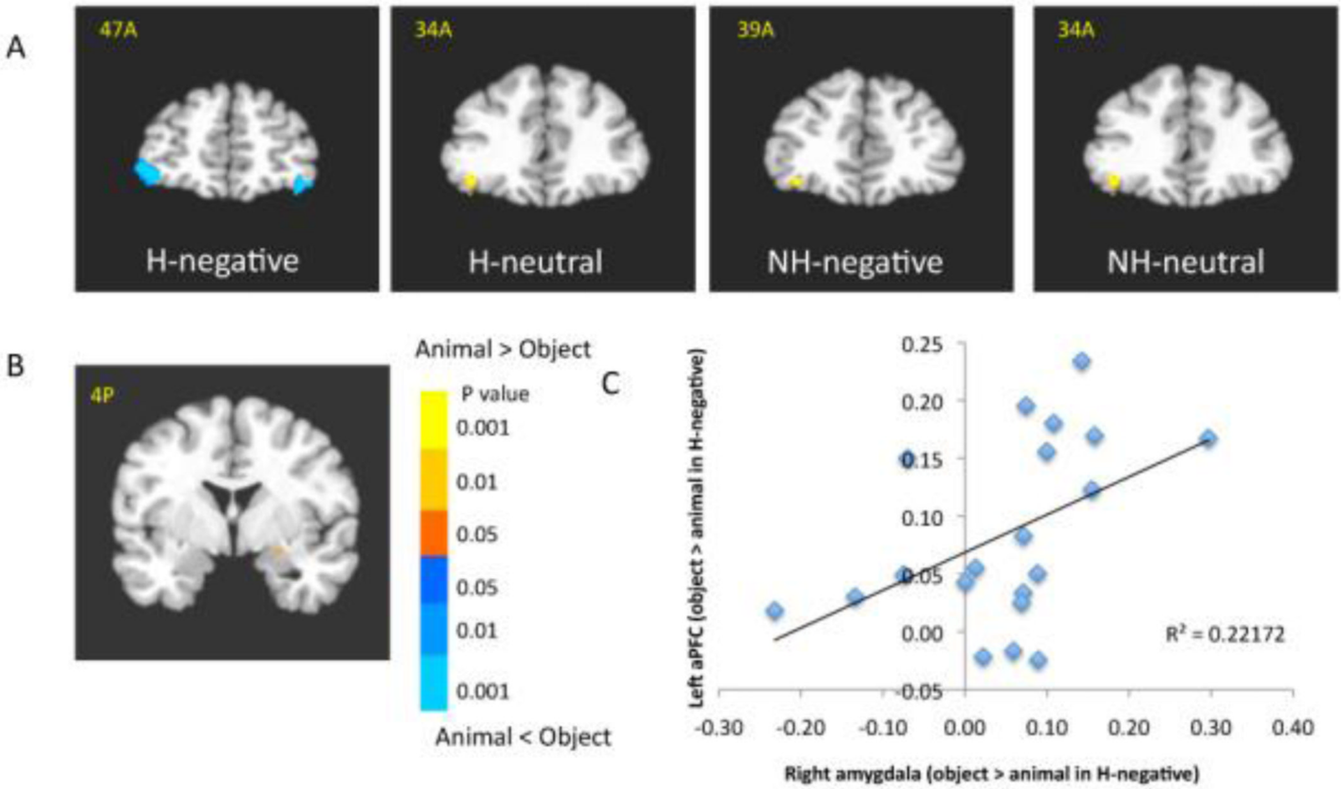

Figure 5.

The aPFC activation. The aPFC showed stronger activation for negative objects than animals in the human context condition but not in other conditions (A). In addition, the activity of the left aPFC (object > animal) was positively correlated with the activity of the right amygdala in the human-negative condition, from the PPI analysis (B) and the ROI analysis (C).

Table 1

Rating results in different conditions.

		Human context				Nonhuman context			
		Negative		**Neutral**		**Negative**		**Neutral**	
		Animal	Object	Animal	Object	Animal	Object	Animal	Object
Valence	Mean	3.08	2.95	4.84	4.75	3.65	3.82	5.10	4.94
	SD	0.79	0.53	1.02	0.41	1.01	0.79	1.19	0.37
Arousal	Mean	6.61	6.43	4.51	4.22	5.89	5.56	4.02	3.82
	SD	1.20	1.35	1.24	1.39	1.19	1.18	1.31	1.48
Familiarity	Mean	3.43	3.71	4.15	4.39	3.59	3.72	4.29	4.55
	SD	1.41	1.33	1.51	0.74	1.39	1.29	1.54	0.75
Complexity	Mean	4.95	3.76	4.82	3.81	5.04	3.86	4.84	3.69
	SD	0.87	0.88	0.89	0.86	0.86	0.97	0.85	0.87

Table 2

Main effects of category, emotion and context.

Area		Region	t-value	x	y	z
Category effect						
Animal > Object						
frontal	L	PCC	6.57	−6	−44	44
frontal	L	Fusiform gyrus	4.51	−44	−51	−19
frontal	R	PCC	3.52	14	−46	61
frontal	L	Insula	4.24	−39	14	16
frontal	L	Cingulated cortex	3.47	−6	−11	41
temporal	R	Fusiform gyrus/STS	8.49	41	−69	−1
occipital	L	Occipital cortex	5.78	−41	−74	−16
occipital	R	Occipital cortex	5.00	29	−84	−4
subcortical	R	Thalamus	3.85	4	−14	9
subcortical	L	Hippocampus/amygdala	3.63	−21	−16	−14
Animal < Object						
frontal	R	aPFC	−3.73	41	46	−9
frontal	L	Middle prefrontal cortex	−2.81	−26	−51	−14
frontal	R	Middle prefrontal cortex	−3.57	26	−41	−6
frontal	L	aPFC	−3.37	−39	46	−4
parietal	L	Intraparietal cortex	−5.17	−44	−36	41
parietal	R	Parietal cortex	−3.36	29	−69	49
temporal	L	Middle temporal cortex	−5.43	−49	−56	−6
Emotional effect						
Negative > Neutral						
frontal	L	aPFC	4.98	−39	26	−9
frontal	R	Postcentral cortex	5.41	54	−21	29
frontal	R	Middle prefrontal cortex	5.00	44	−1	44
frontal	L	middle frontal	4.24	−44	29	19
frontal	L	Cingulated cortex	4.85	−9	−31	39
frontal	L	Premotor cortex	5.19	−41	−6	39
frontal	R	Premotor cortex	4.00	31	21	−39

Area		Region	t-value	x	y	z
frontal	R	inferior frontal cortex	3.89	46	29	−1
parietal	R	Precuneus	4.71	24	−49	46
parietal	R	Precuneus	6.01	34	−36	49
subcortical	LR	Amygdala	5.87	−24	−6	−9
subcortical	R	Amygdala	5.37	21	−1	−9
subcortical	R	Amygdala	4.91	29	−1	−24
subcortical	R	Thalamus	3.95	11	−16	−1
Negative < Neutral						
frontal	R	aPFC	−5.09	36	49	−6
frontal	R	Middle frontal cortex	−5.20	41	41	19
frontal	R	Super. Frontal cortex	−4.39	24	21	49
parietal	R	Parietal cortex	−5.90	41	−56	34
parietal	L	Parietal cortex	−4.19	−36	−61	39
temporal	R	Middle temporal cortex	−5.21	54	−21	−16
Contextual effect						
H > NH context						
frontal	R	Middle frontal cortex	9.92	44	21	21
frontal	L	Middle frontal cortex	7.00	−41	16	29
frontal	R	Medial frontal cortex	3.79	9	51	26
frontal	L	aPFC	4.01	−4	36	−14
frontal	L	Medial frontal cortex	3.39	−4	49	41
parietal	L	Parietal cortex	7.52	−56	−26	24
subcortical	R	lingual/subcortical region	7.42	21	−54	1
subcortical	R	Amygdala	6.30	21	−6	−6
subcortical	L	Amygdala	5.77	−19	−9	−6
subcortical	L	Amygdala	6.54	−24	4	−16
subcortical	R	Parahippocampal cortex	4.17	41	−16	−21
subcortical	L	Thalamus	3.17	−14	−74	−34
temporal	R	Super. Temporal cortex	6.06	56	1	−16
temporal	L	Anterior temporal cortex	4.15	−39	−1	−29
	LR	Occipital/temporal cortex	11.44	44	−61	6

Area		Region	t-value	x	y	z
H < NH context						
occipital	R	Lingual gyrus	−5.21	21	−91	−6
occipital	R	Lingual gyrus	−4.29	6	−86	−1
parietal	R	Supermarginal gyrus	−2.75	41	−51	36

Table 3

Interaction effects among category, affect and context

Area		Region	F-value	x	y	z
Category by affect						
frontal	L	Super. frontal cortex	18.16	−16	51	16
frontal	R	Orbital PFC	16.76	19	61	1
frontal	L	Orbital PFC	21.91	−26	56	4
frontal	R	Precentral cortex	24.59	56	4	34
frontal	R	Precentral cortex	17.55	56	−4	6
frontal	L	Medial frontal cortex	31.76	−6	6	51
frontal	L	Super. frontal cortex	30.13	−14	44	36
frontal	L	aPFC	19.54	−6	54	14
frontal	L	ACC	16.80	−14	39	4
occipital	R	Occipital cortex	18.53	4	−79	26
temporal	L	Anterior temporal cortex	19.99	−51	4	−19
temporal	L	Super. Temporal cortex	19.04	−39	−59	19
temporal	L	Anterior temporal cortex	17.50	−49	14	−19
subcortical	L	Amygdala	18.75	−31	−6	−11
subcortical	L	Amygdala	14.04	−14	−4	−11
Category by context						
occipital	R	Middle occipital cortex	22.94	44	−69	−4
parietal	L	Precuneus	21.53	−11	−64	39
parietal	L	Precuneus	20.09	11	−56	39
temporal	L	Fusiform gyrus/PHG	19.45	−24	−41	1
temporal	R	Fusiform gyrus	19.62	39	−44	−14
temporal	L	Fusiform gyrus	16.58	−44	−39	−21
subcortical	L	Midbrain	14.82	−11	−16	−29
subcortical	R	Hippocampus	16.51	36	−36	−4
subcortical	L	Hippocampus	13.86	−16	−39	6
subcortical	L	Perirhinal cortex	19.64	−26	−21	−19
subcortical	L	Amygdala	14.04	−26	−1	−13
Affect by context						

Area		Region	F-value	x	y	z
frontal	L	Inferior frontal cortex	60.74	−51	14	21
frontal	R	Inferior frontal cortex	34.86	39	21	24
frontal	L	aPFC	23.43	−16	49	19
frontal	R	aPFC	36.67	31	29	−11
frontal	L	aPFC	12.27	−29	29	−9
frontal	L	Medial frontal cortex	26.48	−1	34	39
frontal	L	Super. frontal cortex	14.75	−21	11	54
frontal	L	Precentral cortex	20.71	−34	−6	49
frontal	L	Insula	12.99	−26	21	14
occipital	R	Occipital cortex	22.29	26	−76	−16
occipital	L	Occipital cortex	12.86	−16	−76	−21
occipital	R	cuneus	12.91	1	−69	11
parietal	R	Precuneus	13.15	26	−54	34
temporal	L	Fusiform gyrus	45.55	−21	−86	−14
temporal	L	Super. Temporal cortex	23.65	−34	−76	21
temporal	R	Fusiform gyrus	22.38	44	−61	−14
temporal	R	Fusiform gyrus/PHG	27.50	21	−36	−9
temporal	R	Anterior temporal cortex	24.39	36	4	−26
temporal	L	Super. Temporal cortex	27.35	−46	−26	−1
subcortical	L	Midbrain	33.49	−4	−24	−19
subcortical	L	Thalamus	20.12	−11	−11	6
subcortical	L	PHG	14.62	−24	−66	−31
subcortical	L	Amygdala	14.58	−21	−6	−4
3-way interaction						
frontal	L	aPFC	21.85	−34	41	−9
frontal	R	Inferior frontal cortex	22.85	54	21	21
frontal	R	Inferior frontal cortex	17.15	41	14	39
parietal	L	Superior parietal cortex	18.47	−19	−54	64
parietal	L	Precuneus	21.35	−14	−36	49
subcortical	L	Amygdala	6.01	−19	1	−16

Table 4

DCM parameters showing the estimated mean (SD) for the winning Family C in Hertz

	NH-negative objects	**H-negative animals**
aPFC to amyg	0.14 (0.15)	0.08 (0.14)
Amyg to aPFC	0.02 (0.02)	0.03 (0.02)
C on aPFC to amyg	0.10 (0.18)	0.06 (0.22)
C on amyg to aPFC	−0.02 (0.24)	0.04 (0.10)

Note: C for conditions means the modulatory effect.