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Automatic and Intentional Brain Responses during Evaluation of Face Approachability: Correlations with Trait Anxiety

Shigeru Toki[a] Yasumasa Okamoto[a] Keiichi Onoda[c] Akiko Kinoshita[a] Kazuhiro Shishida[a] Akihiko Machino[a] Takuji Fukumoto[a] Hidehisa Yamashita[a] Hiroshi Yoshida[b] Shigeto Yamawaki[a]

[a]Department of Psychiatry and Neurosciences, Graduate School of Biomedical Sciences, Hiroshima University, and [b]Department of Social and Clinical Psychology, Faculty of Contemporary Culture, Hijiyama University, Hiroshima, and [c]Department of Neurology, Shimane University, Shimane, Japan

Key Words

Amygdala · Trait anxiety · Approachability judgment · Functional magnetic resonance imaging

Abstract

Background: The judgment of the approachability of others based on their facial appearance often precedes social interaction. Whether we ultimately approach or avoid others may depend on such judgments. ***Method:*** We used functional magnetic resonance imaging to determine the neural basis for such approachability judgments and the relationship between these judgments and trait anxiety. Participants viewed ambiguous (i.e. neutral) or relatively unambiguous (i.e. angry, happy) faces, assessing either the approachability or the sex of the person depicted. ***Results:*** Neutral faces elicited more inconsistent responses within participants only during approachability judgment, suggesting ambiguous property as signals. The contrast pertaining to the interaction between task and face valence demonstrated activation in several areas, such that the left amygdala and medial, middle and inferior frontal gyri were responsive to angry faces when subjects were asked to recognize the sex (implicit task) and to neutral faces when required to discern the approachability (explicit task). Moreover, the blood oxygenation level-dependent change within the left amygdala in response to neutral faces during the judgment of approachability was positively correlated with participant trait anxiety. ***Conclusions:*** These findings extend a proposed model of social cognition by highlighting the functional engagement of the amygdala in approachability judgments, which underlie an individual's sensitivity to ambiguous sources of probable threat.

Introduction

The faces of others provide a rich source of information about the individuals in question, including identity, emotionality, gender, age, trustworthiness and approachability [1–3]. We use this complex information both automatically and intentionally in our daily social lives. It seems likely that many people often judge the approachability of another individual based on his/her facial expression before communication is initiated. However, the neural processes underlying such judgment remain poorly understood, as do the relationships between the neural substrate and various psychological variables. Previous studies have investigated the neural basis of approachabil-

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Shigeto Yamawaki
Department of Psychiatry and Neurosciences
Graduate School of Biomedical Sciences, Hiroshima University
1-2-3, Kasumi, Minami-ku, Hiroshima 734-8551 (Japan)
E-Mail yamawaki@hiroshima-u.ac.jp

ity judgments from the perspective of trustworthiness [1, 4, 5]. Evolutionally speaking, approachability judgments of faces involve primitive aspects of social functioning related to defensive responses for predators or conspecifics in mammals [1, 6]. The main purpose of our study was to investigate the neural basis underlying the relationship between approachability judgment and an individual's threat sensitivity. Following the classic theory of anxiety, we define threat sensitivity as the tendency to recognize either an ambiguous or a potential threat; in humans, this tendency is considered to be related to anxiety [7, 8].

Todorov and Engell [9] reported that a differential amygdala response to trustworthiness represents a response to differences in valence rather than trustworthiness per se. In addition, it has been observed that exaggerating the facial features that make a neutral face trustworthy produces expressions of happiness, whereas exaggerating the facial features that make a face look untrustworthy produces expressions of anger [10]. Several studies have demonstrated that negatively valenced faces such as angry ones are rated as less approachable and trustworthy [4, 10–13]. Moreover, one study has shown that angry faces trigger automatic avoidance responses [14]. Recently, Blasi et al. [15] reported the preferential amygdala reactivity to the avoidant judgment of neutral faces, suggesting the existence of neural activity for judging approachability beyond that for merely perceiving facial expression. Based on the importance of angry and happy faces as a stimulus of two poles, and the close relationship between facial expression and the judgment of approachability, angry, happy and neutral faces have been used as stimuli, in order to clarify the neural mechanisms underlying the approach-avoidance response.

The evaluation of potential threat appears to be central to the process of making an unapproachability decision [16, 17]. Recognition of facial expressions and assessing the level of potential threat based on facial recognition appear to constitute important aspects of an approachability judgment. Although the relationship between amygdala response to fearful faces and anxiety level has been investigated in healthy participants [18–22], no study has focused on the potential relationship between the participant's neural response during approachability judgments and his or her threat sensitivity. Interestingly, in previous studies, a significant relationship between neural response to fearful faces and anxiety scores emerged during a psychological task that did not require attention to or conscious awareness of the faces [18–22].

Following the approach used in previous studies [22–29], we used Spielberger's State-Trait Anxiety Inventory Trait (STAI-T) form [30]. The STAI is one of the most widely used measures of anxious emotional and cognitive reactions. STAI-T originally aimed to evaluate trait anxiety (TA), that is, the disposition to respond with anxiety to situations perceived as threatening. We used it to help us explore the relationship between the neural response during approachability judgments and the individual's threat sensitivity.

Processing of facial emotion can be implicit, occurring when participants make judgments about facial attributes that are unrelated to emotion [31, 32]. To establish whether approachability judgments might be similarly processed, we used a task in which participants viewed faces while making either an explicit judgment about whether an individual was approachable or a sex discrimination judgment. Thirty healthy adults completed an event-related functional magnetic resonance imaging (fMRI) study during which they were required to make approachability judgments (i.e. approach or avoid) about ambiguous (i.e. neutral) or relatively unambiguous (i.e. angry or happy) facial expressions. We expected that the relatively difficult task of making such judgments about neutral faces would help to elucidate the neural substrate of such judgments via a comparison with angry faces. In a different session, participants were required to make sex discrimination judgments of the same stimuli. Many studies have supported the hypothesis that the amygdala and frontal cortex mutually influence and regulate the process of making approachability judgments [12, 15, 33, 34]. We hypothesized that perceptual evaluation of neutral face stimuli might require more attention and cognitive effort to render a decision, triggering greater responses within the amygdala and frontal cortex. Given the large body of evidence supporting the role of the amygdala in the processing of emotional stimuli, we predicted that the amygdala activity would be proportional to the participant's potential-threat sensitivity.

Method and Materials

Participants

Thirty right-handed healthy volunteers with normal vision (15 women and 15 men; 20–28 years of age, mean age ± SD, 23.4 ± 2.4 years) screened for psychiatric, neurological or major medical illness were included in this study. None of the participants had a history of exposure to psychotropic medications, and all were free of psychoactive medications at the time of scanning. All participants provided their written, informed consent to participate, according to the guidelines of the institutional review board and the ethics committee of Hiroshima University Hospital, Japan. The sex/approachability judgment task was explained to the partici-

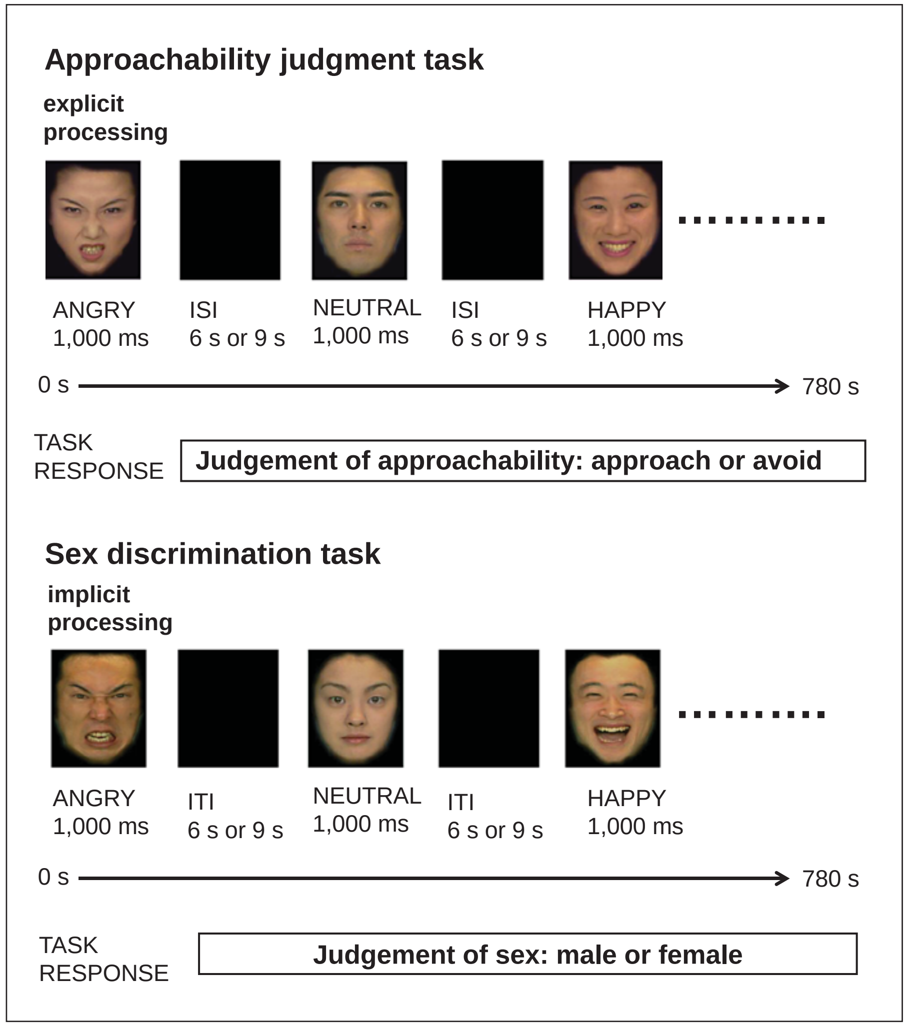

Fig. 1. Schematic of facial stimuli and task paradigm during fMRI.

Color version available online

pants, all of who were naïve to the facial stimuli used. Participants received course credit for their participation.

Stimuli and Task

The event-related fMRI paradigm consisted of two runs (fig. 1); each run presented people with angry, happy and neutral facial expressions derived from the standardized ATR facial expression image database [35]. A stimulus here is defined as the presentation of a face for 100 ms. The faces did not feature hair or jewelry cues, and were oriented to maximize interstimulus alignment of eyes and mouth. For each of the 30 subjects, exactly the same set of faces in exactly the same order was presented. Thirty-six stimuli were used in total: 12 angry, 12 happy and 12 neutral faces. The faces with the same identities and expressions were presented three times in one run. Stimulus order was random across the session.

Each interstimulus interval (ISI) was randomly set to between 6 and 9 s. With each stimulus being presented for 100 ms, the total run time was 13 min, on average. A black screen was presented during the ISI. All stimuli were presented using a back-projection system.

During one of the two runs, participants were instructed to decide whether they would 'approach' or 'avoid' the actor in the picture (approachability judgment task). In the other run, subjects were asked to identify the sex of each actor (sex discrimination task). Presentation order of the two runs was counterbalanced across participants. A fiber optic response box was used to record participant judgments [and reaction times (RTs)] for each stimulus: left button for approach/male response and right button for avoid/female response. After scanning, participants undertook a self-paced task in which they rated all the faces on a scale of approachability from 1 (high approachability) to 9 (high unapproachability).

Questionnaires

Volunteers had completed the Spielberger STAI-T [30] before the fMRI session. In our study, the TAs ranged from 29 to 63 (mean ± SD: 46.60 ± 10.06).

Image Acquisition

fMRI scans were performed with a MAGNEX ECLIPSE 1.5 T Power Drive 250 (Shimadzu, Japan). A time-course series of 360

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volumes was acquired with T_2-weighted, gradient echo, echo planar imaging sequences. Each volume consisted of 28 slices, and the thickness of each slice was 4.0 mm with no gap, encompassing the entire brain. The interval between two successive acquisitions of the same image (repetition time, TR) was 3,000 ms, the echo time (TE) was 55 ms and the flip angle was 90°. The field of view was 256 mm and the matrix size was 64 × 64, giving voxel dimensions of 4.0 × 4.0 × 4.0 mm. After functional MRI scanning, structural scans were acquired using a T_1-weighted gradient echo pulse sequence (TR = 12 ms, TE = 4.5 ms, flip angle = 20°, field of view = 256 mm and voxel dimensions 1.0 × 1.0 × 1.0 mm), which facilitated localization and coregistration of the functional data.

Behavioral Analysis

Accuracy of sex discrimination judgments, rates of avoidance choice RTs and mean approachability scores were analyzed using one- and two-way repeated-measures analyses of variance (ANOVAs) along with the Tukey test for post hoc comparisons, using SPSS software. A probability level of $p < 0.05$ was considered statistically significant. All data presented in the text are expressed as (means ± SD). In addition, difference scores for sex discrimination, avoidance scores, RTs and mean approachability were calculated by subtracting averaged performance scores for happy trials for each participant from their corresponding angry and neutral averages. Because neutral faces tend to be recognized as threatening or ambiguous, activating neural responses within the amygdala [36–38], and happy faces are typically judged to be more approachable compared to all other emotions [13, 37, 39], we used happy faces as the baseline condition.

Item-Based Analysis

In order to elucidate the effects of facial expression on consistent response, we conducted an item-based analysis of the relationship between the facial expression and the response rate for consistent discrimination of sex and judgments of approachability over all 3 trials. For each facial stimulus, we calculated the mean rate of consistent approachability and gender decision among the thirty participants. These rates were analyzed using one-way repeated-measures ANOVA. A probability level of $p < 0.05$ was considered statistically significant. All data presented in the text are expressed as mean ± SD.

fMRI Analysis

Datasets from all 30 participants met our criteria for high quality and scan stability with minimum motion correction (<2 mm or 2 degrees displacement in any of the six motion parameters) and were subsequently included in the fMRI analyses. Residual movement was modeled as a regressor of no interest. Functional brain analysis depicting the cognitive subtraction between the presentations of angry or neutral expressions and happy expressions was performed using Statistical Parametric Mapping 5 (SPM5) software, according to standard procedures [40, 41]. After excluding the first three 'dummy' volumes, the remaining 357 volumes were used for the statistical analysis. Images were corrected for motion and realigned with the first scan of the session, which served as the reference. The T_1 anatomical images were coregistered to the first functional image for each participant and aligned to a standard stereotaxic space, using the Montreal Neurological Institute (MNI) T_1 template in SPM5. A calculated nonlinear transformation was applied to all functional images for spatial normalization. Finally, the functional MRIs were smoothed with an 8-mm full-width, half-maximum Gaussian filter. The fMRI response was temporally filtered using a high-pass filter of 128 Hz to minimize scanner drift. The result from the filtering was modeled using a canonical hemodynamic response function with its temporal and dispersion derivatives. Using both derivatives in addition to the canonical HRF allowed us to characterize HRFs with late-onset or longer duration.

Data were analyzed using a general linear model for each voxel in a two-stage random effects procedure. First, regions of activation common to all unapproachable conditions were determined using a whole-brain conjunction analysis [42] of the angry minus happy (AH) faces and neutral minus happy (NH) faces during sex discrimination as well as the AH and NH faces during approachability judgments. We used happy faces as the baseline as was done for the behavioral analysis. Second, a whole-brain ANOVA with task and emotion as within-subject factors was performed to identify differential activity between brain regions. We focused on the bilateral amygdala as a test of our hypothesis. We report predicted regions within amygdala surviving a threshold of $p < 0.005$ uncorrected with an extent threshold of 5 contiguous voxels. Consistent with the previous studies [43–46], because the activation of the amygdala has been relatively difficult to detect [47, 48], we use the less conservative threshold. In addition, we descriptively report activations outside of the amygdala regions of interest (ROIs) that survived a threshold of $p < 0.001$ uncorrected with an extent threshold of 30 contiguous voxels [49]. Moreover, small volume corrections were applied to the amygdala using an Anatomical Automatic Labeling Atlas-based mask [50]. The amygdala mask was created by the WFU PickAtlas [51]. Entire volume corrections were also applied to the significantly activated regions outside of the amygdala ROIs. We described significant results of them complementarily. Activations are reported in standard MNI space. An identification of resulting brain structures was ascertained by using Talairach Daemon client (http://www.talairach.org). The participant-specific parameter estimates at these locations were extracted for each face contrast from the significant clusters of peak activation, using the eigenvariate function in SPM5 and further examined by two-way repeated-measures ANOVA analyses, using the SPSS software package.

Correlation Analyses

To examine a possible correlation between the amygdala activity during the rating of approachability and the participant's potential-threat sensitivity, a Pearson's correlation analysis was conducted between the TA and the signal change within the amygdala. To provide data that might generate further hypotheses, we also conducted correlation analyses using the TA, sex discrimination difference, avoidance score differences, RT differences, mean approachability differences and the signal change within the amygdala and that within other activated areas. These fMRI signals were extracted from the significant clusters of the SPM ANOVA analysis. The significance level for the correlations was set at $p < 0.05$.

Results

Behavioral Data

A one-way repeated-measures ANOVA was performed on the accuracy scores for sex discrimination of

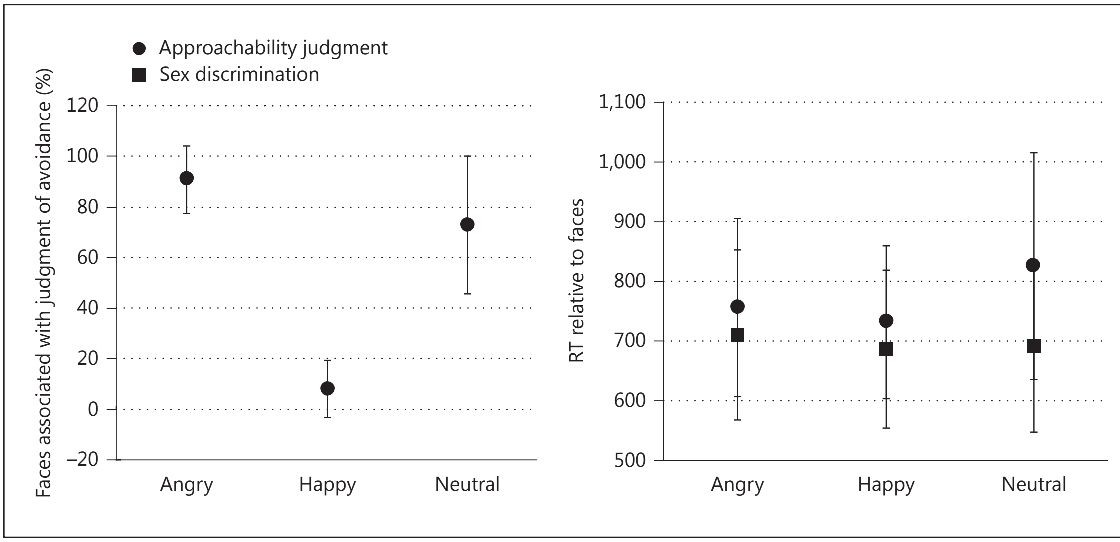

Fig. 2. Plots showing the number of faces associated with avoidance judgments (as percentage of total) during the approachability judgment task (**a**) and RT during the approachability judgment and sex discrimination tasks (**b**). See text for statistics.

faces. There was no significant main effect of face type, $F(2, 58) = 0.8$, $p = 0.423$. Accuracy scores (±SD) for each face type were 89.8 ± 11.7% for angry faces, 90.2 ± 9.8% for happy faces and 91.3 ± 10.3% for neutral faces.

There was an effect of emotional expression on the number of faces that participants judged they would avoid, $F (2, 58) = 152.0$, $p < 0.001$. Post hoc analysis showed that participants judged that they would avoid a significantly lower number of happy faces when compared to neutral and angry faces (both $p < 0.001$). The number of angry faces that participants judged they would avoid was greater than the number of neutral faces associated with a similar judgment ($p = 0.001$; fig. 2). The number of faces associated with avoidance judgments (as a percentage of the total) during the approachability judgment task was 88.6 ± 19.0% for angry faces, 11.5 ± 20.6% for happy faces and 72.8 ± 27.2% for neutral faces.

A 2 (task) × 3 (face type) repeated-measures ANOVA was performed on the RTs for face judgments. There were main effects of task and face type, and the task by face type interaction was also significant (all $p < 0.001$). Post hoc analysis indicated greater RTs during approachability judgments than during sex discrimination, for all face types (all $p < 0.01$). Furthermore, while RTs were greater for angry compared to neutral and happy faces during sex discrimination (all $p < 0.04$), RTs were greater for neutral as compared to happy and angry faces during approachability judgments (all $p < 0.001$; fig. 2).

A one-way repeated-measures ANOVA was performed on the approachability scores. There was a significant main effect of face type, $F(2, 58) = 330.4$, $p < 0.001$. Mean approachability scores (± SD) for each face type were 7.922 ± 0.822 for angry faces, 2.272 ± 0.755 for happy faces and 5.330 ± 0.787 for neutral faces.

Item-Based Analysis

A one-way repeated-measures ANOVA was performed on the rates of consistent response for sex discrimination of faces. There was no significant main effect of face type, $F(2, 22) = 0.1$, $p = 0.916$. Consistent response rates (±SD) for each face type were 83.6 ± 10.6% for angry faces, 82.5 ± 15.4% for happy faces and 83.3 ± 13.9% for neutral faces.

There was a significant main effect of face type on the rates of consistent response for approachability judgment for faces, $F (2, 22) = 15.4$, $p < 0.001$. Consistent response rates (±SD) for each face type were 86.4 ± 5.0% for angry faces, 81.9 ± 5.6% for happy faces and 68.9 ± 11.0% for neutral faces. Neutral faces elicited less consistent responses within participants, suggesting the apparent effects of ambiguity on the decision.

Brain Activation

ANOVA Analyses

Linear contrasts were performed to produce SPMs of the main effect of task (sex or approachability judg-

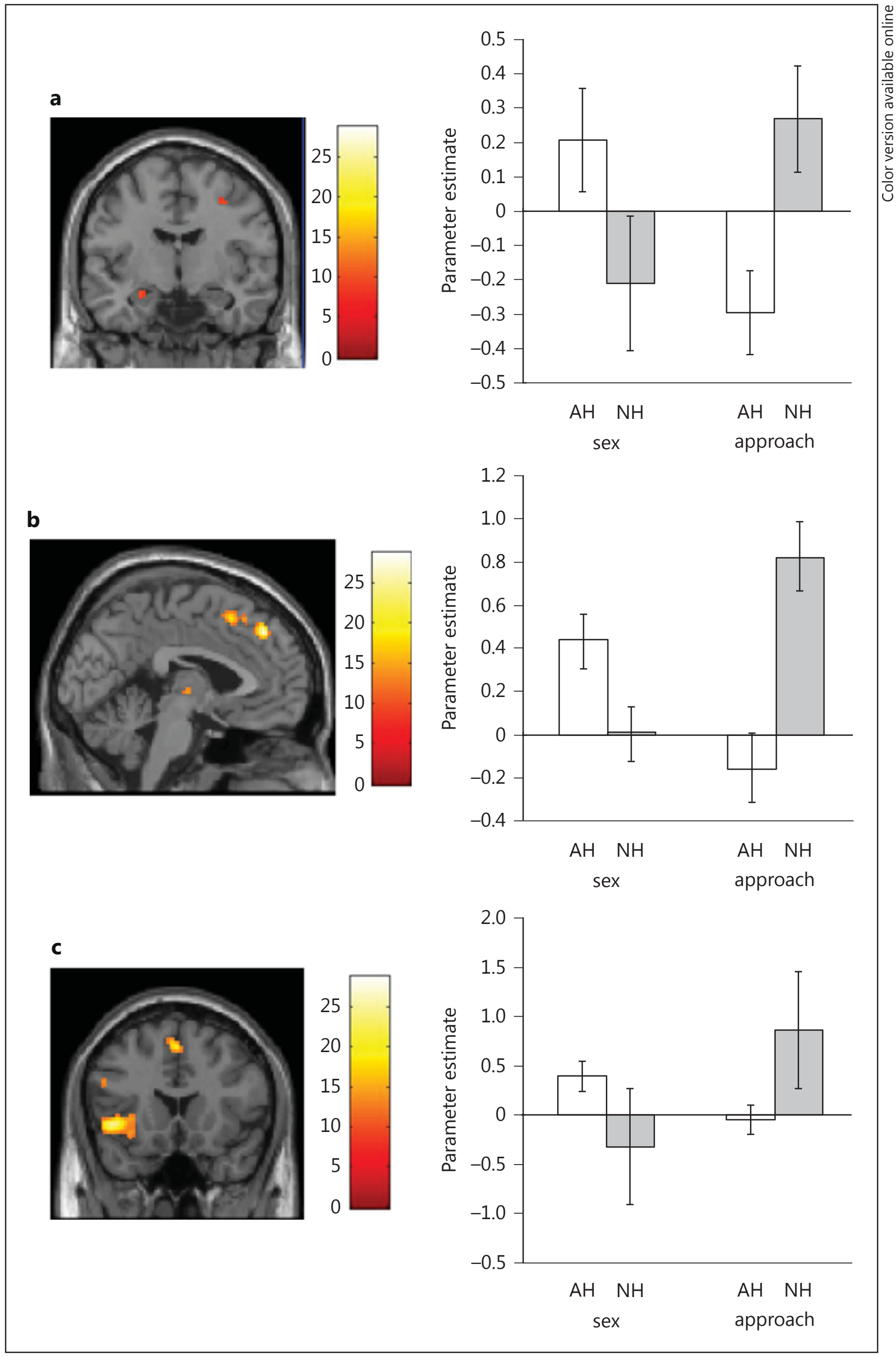

Fig. 3. a Regions showing the interaction effect of task and face on the activation magnitude within the left amygdala. **b** Regions showing the interaction effect on the activation magnitude within the left medial frontal gyrus. **c** Regions showing the interaction effect on the activation magnitude within the left inferior frontal gyrus. Mean participant-specific parameter estimates for activity in a significant cluster including the peak coordinate. AH = Angry versus happy condition; approach = approachability judgment; NH = neutral versus happy condition; sex = sex discrimination.

ment), the main effect of face type (AH or NH) and the interaction between these two factors. An ANOVA analysis revealed that the contrast pertaining to the interaction of task and face type demonstrated several areas of activation within the left amygdala (fig. 3a; table 1), the medial (fig. 3b; table 1) and inferior, middle frontal gyri (fig. 3c; table 1) and the thalamus (table 1). The interaction on amygdala activation survived FWE correction for the AAL-based amygdala mask (voxels = 1, $p < 0.05$). In addition, the interaction on medial frontal gyrus activation survived FWE correction for the entire brain (voxels = 4, $p < 0.05$). The significant main

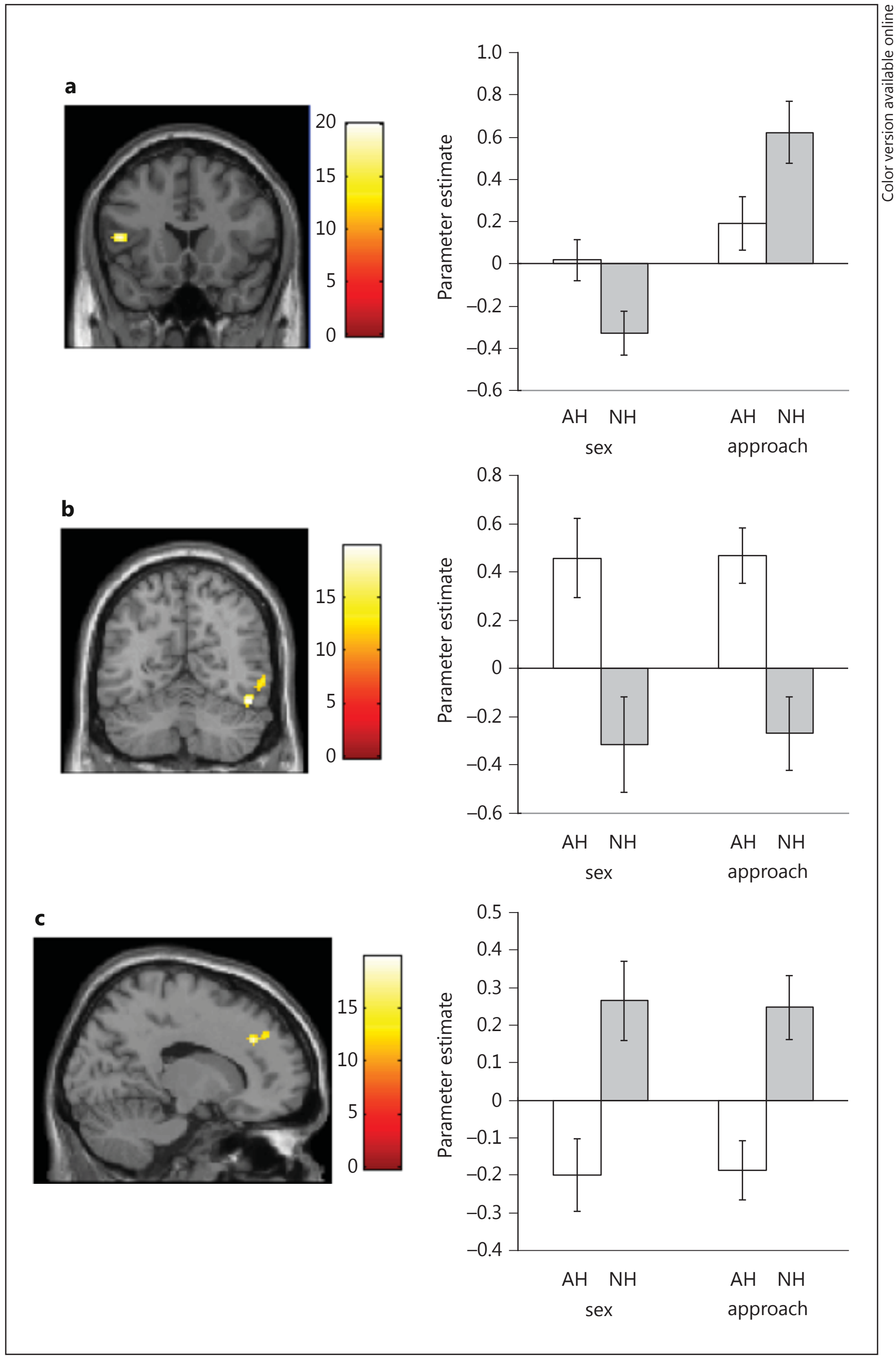

Fig. 4. a Regions showing the main effect of task on the activation magnitude within the left precentral and inferior frontal gyri. **b** Regions showing the main effect of face on the activation magnitude within the right fusiform gyrus. **c** Regions showing the main effect of face on the activation magnitude within the right inferior frontal gyrus. Mean participant-specific parameter estimates for activity in a significant cluster including the peak coordinate. AH = Angry versus happy condition; approach = approachability judgment; NH = neutral versus happy condition; sex = sex discrimination.

effect of task was present in the left prefrontal and inferior frontal gyri (fig. 4a; table 1). The significant main effect of face type was present both in the right fusiform and inferior temporal gyri (fig. 4b; table 1) and in the right medial frontal and superior frontal gyri (fig. 4c; table 1). While angry faces elicited greater fusiform gyrus activity, neutral faces elicited greater medial frontal gyrus activity.

The SPSS ANOVA analysis about neural activation within the left amygdala, the medial and inferior, middle frontal gyri and thalamus confirmed significant task by face type interactions (all $p \leq 0.002$). The ANOVA about

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Table 1. ANOVA analysis of canonical HRF during judgements of sex and approachability

Brain region	Side	Vox-els	x[a]	y[a]	z[a]	Z score	Effect
Task by face type interaction							
AMG*	L	5	–26	–8	–18	2.88	sex: AH > NH
MeFG	L	149	–2	40	42	4.92	approach: NH > AH
IFG	L	482	–44	18	–4	4.55	
IFG	L		–36	22	–6	4.29	
MiFG	L		–44	36	–4	3.52	
MeFG	L	100	0	18	50	4.00	
MeFG	L		–4	26	52	3.59	
Thalamus	R	33	4	–14	0	3.96	
IFG	R	44	48	24	16	3.70	
IFG	L	33	–50	20	24	3.50	
IFG	L	31	–48	32	16	3.47	
Main effect of task							
PG	L	89	–48	18	10	4.14	approach > sex
IFG	L		–48	22	–4	3.28	
Main effect of face type							
FG	R	129	46	–60	–18	4.11	AH > NH
ITG	R		56	–56	–8	3.55	
ITG	R		52	–64	–6	3.45	
MeFG	R	47	16	34	34	4.00	NH > AH
SFG	R		16	42	36	3.41	

All values $p < 0.001$. * $p < 0.005$ uncorrected.

AMG = amygdala; approach = approachability judgment; FG = fusiform gyrus; IFG = inferior frontal gyrus; ITG = inferior temporal gyrus; L = left; MeFG = medial frontal gyrus; MiFG = middle frontal gyrus; PG = precentral gyrus; R = right; sex = sex discrimination; SFG = superior frontal gyrus.

[a] MNI coordinates referring the center of gravity of the cluster.

neural activation within the left precentral and inferior frontal gyri confirmed a significant main effect of task (all $p < 0.001$). In addition, the ANOVA about neural activation within the right fusiform and right medial frontal gyri confirmed a significant main effect of face (all $p < 0.001$).

Relationships between Psychological/Behavioral Data and Activation within the Amygdala and Other Areas

Under approachability judgment, during the presentations of neutral versus happy faces, TA was positively correlated with activation in the left amygdala ($r = 0.376$, $p = 0.041$; fig. 5a). When the one outlier was removed, more robust significance was found in the correlation between TA and amygdala activity ($r = 0.437$, $p = 0.018$). During the presentations of angry versus happy faces, RT difference was positively correlated with activation in the left medial [(–2, 40, 42), $r = 0.508$, $p = 0.004$] (fig. 5b) and inferior frontal gyri [(–44, 18, –4), $r = 0.384$, $p = 0.036$].

Under sex discrimination, during the presentations of angry versus happy faces, mean approachability difference was negatively correlated with activation in the left medial frontal gyrus [(–2, 40, 42), $r = –0.481$, $p = 0.007$; fig. 5c]. Moreover, the accuracy score difference was negatively correlated with activation in the right fusiform gyrus ($r = –0.381$, $p = 0.038$; fig. 5d). For the presentations of neutral versus happy faces, there were no significant correlations among these variables.

Discussion

We investigated the neural substrates underlying implicit and explicit evaluation of approachability of faces, using faces with several different expressions. We also intended to establish whether there was a significant relationship between brain region activation, task performance and participant threat sensitivity. Ours appears to be the first study to reveal specific involvement of the amygdala in explicit approachability judgments of ambiguous stimuli and the relationship between such judgments and TA.

Participants took longer to respond during sex discrimination of angry faces, as well as during approachability judgments of neutral faces. In addition, neutral faces elicited more inconsistent responses from participants only during approachability judgment. These behavioral data suggest increased processing of angry faces due to the distracting effects of such affect on sex discrimination, and increased processing of neutral faces associated with greater ambiguity during approachability judgments. Consistent with the behavioral results, the neurobiological analysis showed that the left amygdala, the medial, inferior and middle frontal gyri and the thalamus were activated by angry faces during sex discrimination, with the same structures being activated by neutral faces during approachability judgments. Because activity in these structures has been consistently related to emotional face processing [52, 53], neural activation within this circuit may contribute to the decoding and integration of facial information, with such information being subsequently used in various judgments such as approachability.

Interestingly, we found the interaction between task and face valence within these structures including the amygdala was a stronger response to angry in the im-

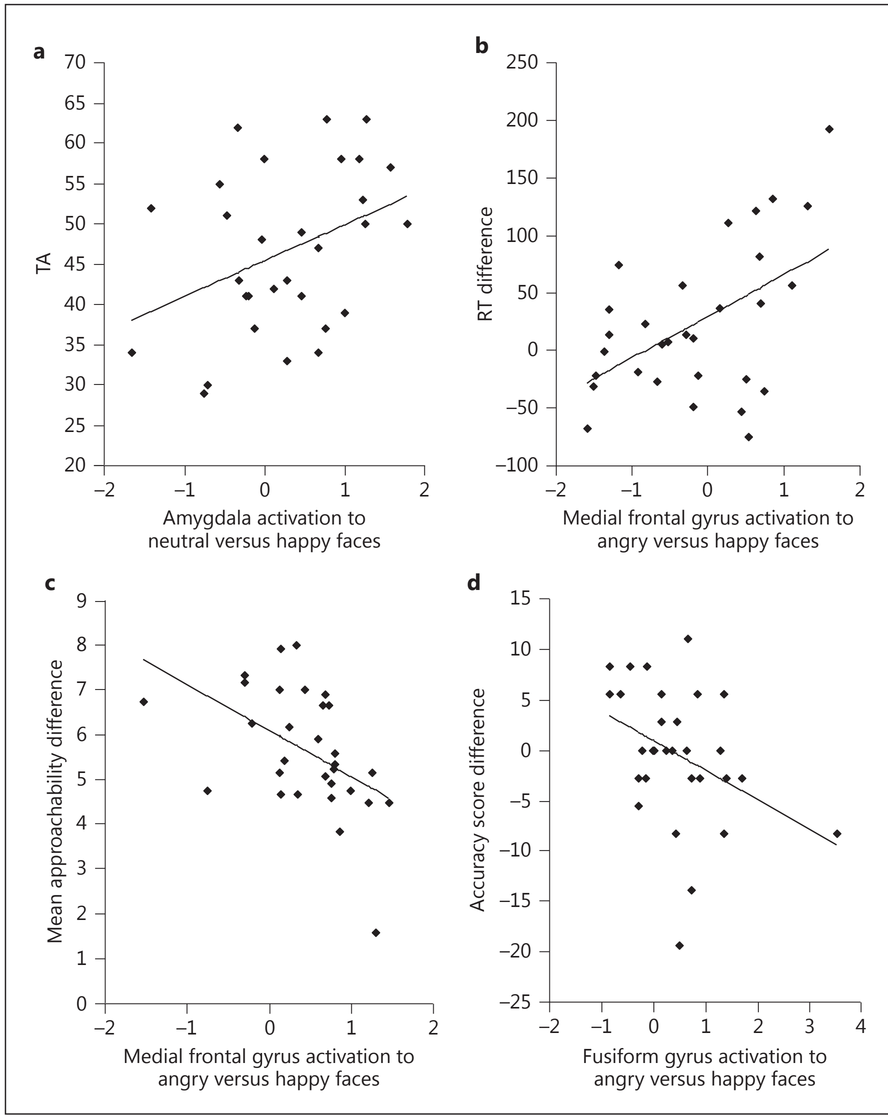

Fig. 5. a Plot showing the degree of correlation of TA with the activation magnitude within the left amygdala in response to neutral compared with happy faces during approachability judgment. **b** Plot showing the degree of correlation of RT difference with the activation magnitude within the left medial frontal gyrus in response to angry compared with happy faces during approachability judgment. **c** Plot showing the degree of correlation of mean approachability difference with the activation magnitude within the left medial frontal gyrus in response to angry compared with happy faces during gender discrimination. **d** Plot showing the degree of correlation of accuracy score difference with the activation magnitude within the right fusiform gyrus in response to angry compared with happy faces during gender discrimination.

plicit condition, but stronger to neutral in the explicit condition. The difficulty of neutral stimuli in attributing emotional significance to a facial expression may in turn lead to heightened vigilance, as well as to increased amygdala activity [15, 54, 55]. Our results were consistent with previous studies, indicating that the greater ambiguity of facial threat stimuli elicited greater amygdala activity [15, 56, 57]. Overall, we concluded that the neural response to neutral faces during approachability judgments was greater than the responses to the other face types. When judging approachability of faces, the left amygdala might take the critical role of preparing for, orienting around and evaluating the target faces. We also found an increased activation of the left precentral and inferior frontal gyri during approachability judgment compared with that during sex discrimination. Consistent with the previous study [58], this finding suggests a critical role for these structures in approachability rating that is independent of face type. These neural areas are associated with sensation integration and behavior planning [59, 60], and may play an important role in precipitating approachability decisions. Moreover, we found the main effect of face type in neural activation within the right fusiform gyrus and medial frontal gyrus. Independent of task condition, while the former responded to angry faces, the latter responded to neutral faces, suggesting the existence of expression-specific activation within both areas.

In addition, TA was positively correlated with left amygdala response to neutral faces during approachability judgment, suggesting that participants who had reported higher TA tended to have higher amygdala reactivity. Our result supports the notion that the left amygdala is more responsive to explicit evaluative processing [61–64]. That is to say, it is possible that the heightened left amygdala activity observed during approachability judgment may be due to a greater sensitivity or evaluative ability associated with explicit processing of socially ambiguous stimuli in high TA subjects. By presenting facial stimuli for 200 ms in a block design, Somerville et al. [37] observed a positive relationship between state anxiety and neural response within the bilateral amygdala to neutral faces during passive viewing. Our stimulus paradigm and task instructions might elicit more evaluative and analytical processing, leading to the observed left lateralized activation, compared with previous work. We found a significant relationship between TA and ventral amygdala activity, not for angry but for neutral faces, despite the threatening meaning of the former stimuli; this suggests the possibility that the psychological construct of TA includes not only sensitivity but also a predictive process for potential threat. This result is also consistent with earlier work that reported that the ventral amygdala is heavily involved in coding signals of ambiguity and responds more to an ambiguous or probable threat [22, 54]. Many studies found that individual levels of anxiety only influence amygdala activities to ambiguous or subthreshold threat information, but not to apparent or suprathreshold threat information [18–22]. These results parallel our findings that TA influences ventral amygdala activity in response to ambiguous, neutral stimuli. In the Introduction, according to the traditional theory of anxiety, we defined threat sensitivity as the tendency to recognize either an ambiguous or a potential threat; in humans, this tendency is considered to be related to anxiety [7, 8]. Our findings about amygdala reactivity support, at least in part, the possible link between the classic theory of anxiety and the neural functioning within the amygdala during the rating of approachability.

Beyond the relationships between amygdala activity and other variables, we found several significant correlations. During the sex discrimination task, there was a significant negative correlation between mean approachability differences between angry and happy faces and activation of the left medial frontal gyrus. Recently, it was proposed that the medial frontal cortex contains cortical relay nodes that afford the attribution of self-relevant, implicit meaning that subserves egocentric 'value' judgments, which are critical for self-control [65]. Avoidant behavioral tendencies might serve to weaken the self-relevant meaning attribution function. Moreover, the accuracy of gender discrimination in angry faces was negatively correlated with the right fusiform gyrus activation. Considering about the expression-specific activation revealed by ANOVA analysis, it is understandable that participants with higher activation of the fusiform gyrus might be more distracted by the angry expressions, resulting in lower scores in sex discrimination. During approachability judgment, there was a significant positive correlation between RT differences and activation of the left medial and inferior frontal gyri in response to angry faces. These enhanced activations might afford self-control and risk-aversion, resulting in delayed responses in assessing approachability.

Our study displays several limitations. First, it is noteworthy that TA scores were relatively high among our subjects, compared with the normative American adults in the test manual [66]. This finding has consistently emerged in Japanese samples, possibly due to the Japanese tendency toward suppressing expression of positive feelings [67, 68]. It is thus possible that TA could show a different relationship with amygdala response in European or North American participants. Such studies would provide important data for predictions concerning application of the present paradigm to the study of cultural differences in anxiety. Second, because we used no imaging method for magnetic field inhomogeneity within the medial temporal lobe, such as selection of voxel size and slice orientation [69], we cannot rule out the possibility that our results were influenced by susceptibility effects within the amygdala. Third, we investigated brain response by the slow presentation of stimuli with an ISI of 6–9 s. According to the previous technical report [70], we would maybe find stronger effects by using a more rapid presentation of stimuli; further studies using such a method could provide support for our results. Fourth, we used happy faces as a baseline. We did so because neutral faces tended to be recognized as 'threatening' or 'ambiguous'. Taking previous studies and our results together, we conclude that the amygdala response to neutral faces reflects the individual level of reactivity to an ambiguous threat. However, based on the current data only, the neurophysiological meaning of the different neural activation when a happy face is presented to the subject versus a neutral face remains unclear. We need to verify our results by using other stimuli (i.e. scrambled faces or fixation cross) as a baseline. Fifth, without correction for multiple comparisons, some of our data could reflect spurious activation and correlation among variables. Thus, caution should be used while interpreting our findings until the results have been replicated.

In conclusion, our findings extend a proposed model of social cognition by highlighting the functional engagement of the amygdala in the explicit judgment of approachability, which is thought to reflect an individual's ambiguous threat sensitivity. Neural responses during approachability judgments varied with task instructions and facial stimuli, reflecting complex human responses to the social environment. Because fMRI does not differentiate between function-specific processing and neuromodulation, between bottom-up and top-down signals, and occasionally between excitation and inhibition [71], to support our conclusions we should conduct a multimodal study that includes electrophysiological measurements of brain activity.

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