

# An Enhanced Default Approach Bias Following Amygdala Lesions in Humans



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## Abstract

Approach and avoidance constitute a basic dimension of all animal behavior. Although a large number of studies have investigated approach and avoidance elicited by specific sensory stimuli, comparatively little is known about default approach biases when stimulus information is absent or reduced. The amygdala is well known to contribute to approach and avoidance behaviors in response to specific sensory stimuli; we tested whether the amygdala's role might extend to situations in which stimulus information is reduced. In a novel task, 3 patients with rare bilateral amygdala lesions (and control subjects) made approach-related judgments about photos of intact faces and of the same faces with all internal facial features occluded. Direct comparisons of the judgments of these stimuli isolated a default bias. The patients showed a greater tendency than the control subjects to rate occluded faces as more approachable than whole faces. These findings suggest that the amygdala's role in approach behavior extends beyond responses to specific stimuli.

## Keywords

amygdala, approach, avoidance, face processing, Urbach-Wiethe disease, lesion, ambiguity, open data

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From single-celled organisms to humans, all mobile species exhibit approach-avoidance behavior. In humans, approach-avoidance behavior is regulated by motivation and influenced by emotion (Elliot, Eder, & Harmon-Jones, 2013); at a more primitive level, it is related to instinctive defensive behaviors (Blanchard, Griebel, Pobbe, & Blanchard, 2011; McNaughton & Corr, 2004).

Although basic, approach-avoidance behavior shows large individual differences. Whereas some people would walk into and explore an unfamiliar dark room, others would pause and gather more information, and some might even flee. What accounts for this behavioral variability? Prior experience might sway one's response, but the situation in this example offers little information, and may not have been encountered previously. Nevertheless, a behavioral tendency will be observed. The amygdala is a brain structure known for its role in memory, learning, and emotion, and it has been implicated in psychiatric disorders, including anxiety. In the study reported here, we investigated what role the amygdala might play in regulating stimulus-independent behavior through a *default bias* to evaluate stimuli positively. We asked

whether patients with amygdala lesions exhibit an exaggerated tendency to approach low-information stimuli.

Research has demonstrated an abnormal tendency to approach other individuals, as well as stimuli that are normally threatening, in amygdala-lesioned monkeys (Klüver & Bucy, 1939), rodents (Choi & Kim, 2010), and humans (Feinstein, Adolphs, Damasio, & Tranel, 2011; Kennedy, Gläscher, Tyszka, & Adolphs, 2009). These findings point to the amygdala as being important in regulating approach-avoidance behavior. However, the basis of this approach tendency is unclear.

On the one hand, the bias may be specifically tuned for certain stimuli: Much of what is known about the amygdala's contribution to cognition and behavior has come from studies investigating responses to faces. Single-unit amygdala response selectivity has been found for faces in humans (Rutishauser et al., 2011) and monkeys (Gothard,

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Battaglia, Erickson, Spitzer, & Amaral, 2007), and these findings fit with the known connectivity of the amygdala with anterior temporal neocortex (Amaral, Price, Pitkänen, & Carmichael, 1992), a region containing face-selective cells (Perrett, Rolls, & Caan, 1982; Tsao, Freiwald, Tootell, & Livingstone, 2006). Lesions of the human amygdala can result in a remarkably specific impairment in recognizing fear (Adolphs, Tranel, Damasio, & Damasio, 1994; Adolphs et al., 1999; Broks et al., 1998) and trustworthiness (Adolphs, Tranel, & Damasio, 1998) in faces.

On the other hand, the amygdala might contribute to stimulus-independent baseline, or default, biases; such biases would be similar to the “tonic influence on behavior” theorized more than two decades ago (Amaral et al., 1992, p. 56). Studies have provided some preliminary evidence that patients with amygdala lesions have a propensity to approach other people or potentially dangerous situations regardless of context (Feinstein et al., 2011; Kennedy et al., 2009).

Conceivably, the amygdala could play a role in both a face-specific approach bias and a default approach bias. When S. M., a widely tested amygdala-lesion patient, rated the trustworthiness and approachability of whole faces, her evaluations hinted at two distinct processes: First, the fact that her judgments increasingly deviated from normal judgments as faces became less trustworthy suggests an inability to process facial cues to untrustworthiness. Second, there was evidence of a more uniform positive bias across all faces irrespective of their perceived trustworthiness (i.e., a global, potentially face-independent, bias toward trust; Adolphs et al., 1998; see Fig. S3 in Additional Results in the Supplemental Material available online). In the present study, we attempted to explicitly disentangle these two components, while also making two improvements to the method in this previous work (Adolphs et al., 1998): using more than a single case study and controlling for regression to the mean.

One mechanism by which a default bias could be achieved is through sensitivity to ambiguity. When a dangerous stimulus is detected, the amygdala, in conjunction with the cortex, must contextually assess the potential danger before launching a defensive response (Davis & Whalen, 2001). When signals are ambiguous, the amygdala may increase vigilance and the amount of predictive information available by lowering sensory thresholds (Whalen, 2007). Sensitivity to ambiguity has been found across species. In humans, the amygdala is more sensitive to ambiguity than to risk (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005). In mice and humans, temporal unpredictability in stimulus presentation elicits anxious behavior and amygdala activity (Herry et al., 2007). When stimulus duration is sufficiently long to permit appraisal (van der Zwaag, Da Costa, Zürcher, Adams, & Hadjikhani, 2012), ambiguous fearful faces with direct gaze elicit

greater amygdala activation, as measured by functional MRI (fMRI) in humans, than do unambiguous fearful faces with averted gaze (Adams, Gordon, Baird, Ambady, & Kleck, 2003). Individual variation in state anxiety correlates with the amygdala’s fMRI response to potentially ambiguous neutral faces (Somerville, Kim, Johnstone, Alexander, & Whalen, 2004). To our knowledge, we are the first to explore whether people with amygdala lesions have an abnormal tendency to approach ambiguous stimuli.

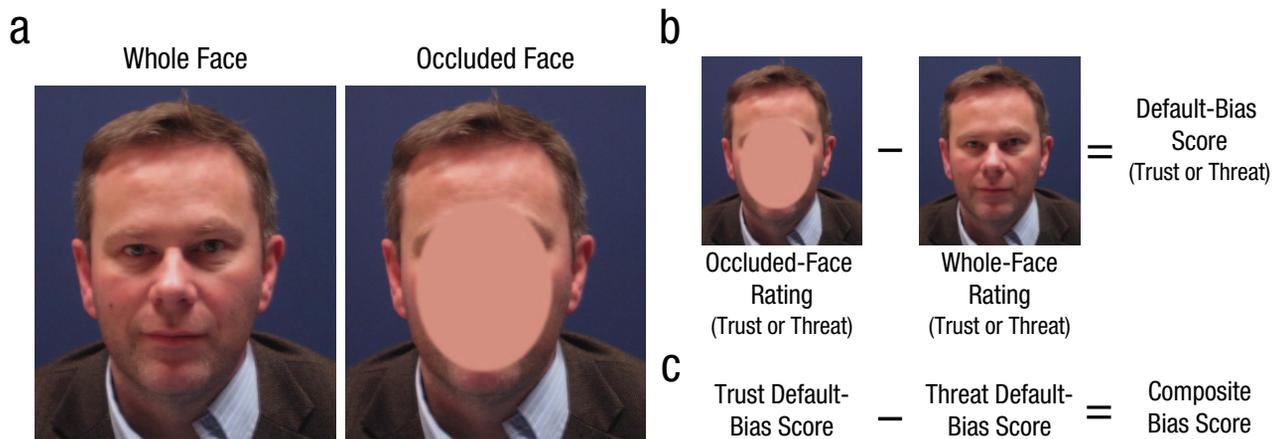
We tested the hypothesis that amygdala damage produces a stimulus-independent default bias by directly contrasting approach-related judgments for two sets of otherwise identical face stimuli: one set with the faces intact (whole-face condition) and the other modified such that the inner part of the faces was erased (occluded-face condition; see Fig. 1a). Subjects made trust and threat judgments, which are known to be processed relatively automatically during exposure to faces (Willis & Todorov, 2006). In the real world, distance (Sinha, Balas, Ostrovsky, & Russell, 2006), accessories (e.g., scarves, sunglasses), and other objects naturally occlude facial features. The same external facial cues (hairline, shape) were available for the faces in our two conditions, but information from facial features was available only in the whole-face condition. We operationalized an approach-related default bias as a tendency, within subjects, to judge low-information, occluded faces as more trustworthy and less threatening than the corresponding whole faces. Default-bias scores for both trust and threat judgments were calculated by subtracting whole-face ratings from occluded-face ratings (Fig. 1b). These default-bias scores for trust and threat were then combined to form composite bias scores (Fig. 1c), with more positive scores indicating a greater tendency to approach. The consistent default bias to approach that we hypothesized for the lesion patients would produce greater positive composite bias scores in the patients than the control subjects.

## Method

### Subjects

All subjects gave informed consent or assent (when the experiment was completed online) in accordance with a protocol approved by the institutional review board of the California Institute of Technology.

**Amygdala patients.** Selective bilateral damage to the human amygdala is extremely rare, but can arise from the genetic disease Urbach-Wiethe disease (Hofer, 1973). We tested 3 women with bilateral amygdala calcification lesions (Fig. S1 in Additional Results in the Supplemental Material) caused by this disease. At testing, 2 of the patients,



**Fig. 1.** Illustration of the stimuli and calculation of bias scores. As illustrated in (a), each face was shown both intact (whole-face condition) and with the internal portion of the face erased (occluded-face condition); the occluded faces contained less information than the whole faces. Subjects rated how trustworthy and threatening each face was. For each face, for each subject, a default-bias score (b) was calculated by subtracting the rating of the whole face from the rating of the occluded face. Thus, positive default-bias scores for trust indicated a tendency to find occluded faces more trustworthy than whole faces; negative default-bias scores for threat indicated a tendency to find occluded faces less threatening than whole faces. A composite bias score was calculated by subtracting the default-bias score for threat from the default-bias score for trust, so that the two measures had the same directionality (c). Thus, larger positive composite bias scores indicated a greater tendency to approach faces in the occluded- compared with the whole-face condition (i.e., judgment that occluded faces were more trustworthy and less threatening than whole faces).

A. M. and B. G., identical twin sisters from rural southern Germany, were 36 years of age, were married with children, and had been in full-time employment since receiving their 13 years of education in Germany. The third patient, A. P., was American. She was 27 years of age and had worked since she obtained her bachelor's degree. All 3 patients had an IQ in the average range, as measured by the Hamburg-Wechsler-Intelligenztest für Erwachsene Revision (A. M.: 101; B. G.: 96; Becker et al., 2012) or the Wechsler Abbreviated Scale of Intelligence (A. P.: 98). Their lesions were all similarly symmetric and confined to the amygdala (A. M.: 1.12 cc bilaterally; B. G.: 1.15 cc; A. P.: 0.71 cc). The damage included complete ablation of the basolateral amygdala with minor damage of other amygdaloid regions, including anterior and ventral cortical regions at the rostral level and lateral and medial parts of the central nucleus and amygdalo-hippocampal area at the caudal level (Fig. S1). All 3 patients were tested individually in the laboratory.

**Healthy comparison subjects.** Eighty-one age-, gender-, and education-matched control subjects with no current mental-health diagnoses were tested. This group included 61 Americans (mean age = 30.5 years,  $SD = 8.0$  years) and 20 Germans (mean age = 35.1 years,  $SD = 6.1$  years). The Americans were recruited through Amazon's Mechanical Turk, and the Germans were recruited through e-mails forwarded to acquaintances of the authors' German colleagues. All control subjects completed the experiment using Qualtrics, an online survey-hosting platform, under conditions that were otherwise

identical to those of the laboratory sessions at which the lesion patients were tested.

**Sample size.** For our control group, we decided to test a sample ( $N = 81$ ) larger than the samples that have been investigated in previous approach-withdrawal research (e.g.,  $N = 46$  in Adolphs et al., 1998). Previous approach-withdrawal research on patients with amygdala lesions has typically been in the form of single case studies; here, we report results for 3 patients. We present their results both as individuals and as a small group, and report bootstrap analyses comparing them statistically with the control group.

### Stimuli

Our original stimulus set consisted of 34 high-resolution color images (16 females and 18 males, 20 to 50 years of age, who were instructed to adopt natural poses) showing essentially neutral facial expressions. The photographs were all taken with the same camera, at the same angle with controlled lighting and in front of the same plain background. After image capture, the images were luminance matched on each RGB channel, using the SHINE toolbox (Willenbockel et al., 2012). These 34 luminance-matched images were used in the whole-face condition. To create the stimuli for the occluded-face condition, we placed an oval mask over each face, adjusting the mask so that no inner facial features were visible (Fig. 1). All 68 images were resized so that the interocular distance for all images was constant. All faces were unfamiliar to the subjects.

## Experimental design

Subjects indicated the degree to which they found the person depicted in each image threatening or trustworthy. Response options on the 6-point scale were “strong no,” “no,” “weak no,” “weak yes,” “yes,” and “strong yes.” The directionality of the rating scale was counterbalanced across subjects. The task was self-paced. The occluded stimuli were always presented first; in separate blocks, subjects rated these stimuli for trust and threat, with the order of the two blocks counterbalanced across subjects. Next, subjects rated the whole faces for trust and threat, again in separate blocks with block order counterbalanced across subjects. Within each of the four blocks—two stimulus conditions (occluded, whole)  $\times$  2 judgments (trust, threat)—all 34 facial images were presented in randomized order. We note that it would have been preferable for the presentation order of the whole- and occluded-face blocks to be counterbalanced or randomized, but counterbalancing was not possible with a patient sample of 3, and without a much larger stimulus set, it would have been difficult to control for unintended memory effects if the order were randomized. Although our design included a fixed presentation order for whole- and occluded-face blocks, the same order was used for both subject groups, and presentation order therefore did not affect conclusions regarding our main question of interest—whether within-subjects differences in ratings between the stimulus conditions differed between the subject groups.

## German translations

For the German subjects, the entire experiment was translated into German: “threatening” was translated as “bedrohlich” (English translations: “menacing,” “ominous”); “trustworthy” was translated as “zuverlässig” (English translations: “reliable,” “trustworthy”). The translations were independently verified by five bilingual German-English speakers (100% agreement).

## Analysis

**Rescaling German subjects’ scores.** To control for cultural and language differences between the two nationalities, we minimally rescaled all German subjects’ ratings with a fixed offset. The average trust rating across all faces (whole and occluded) and all control American subjects was subtracted from the average trust rating across all faces and all German control subjects; the value of this difference between the two groups was subtracted from every German trust rating, including the ratings of the 2 German lesion patients. German subjects’ threat ratings were rescaled following the same procedure. The rescaling factors were small: 0.429 for trust ratings and

–0.188 for threat ratings. Given that there were no mean differences between American and German control subjects after rescaling (see Fig. S2 in Additional Results), we pooled the data from these control groups in all subsequent analyses.

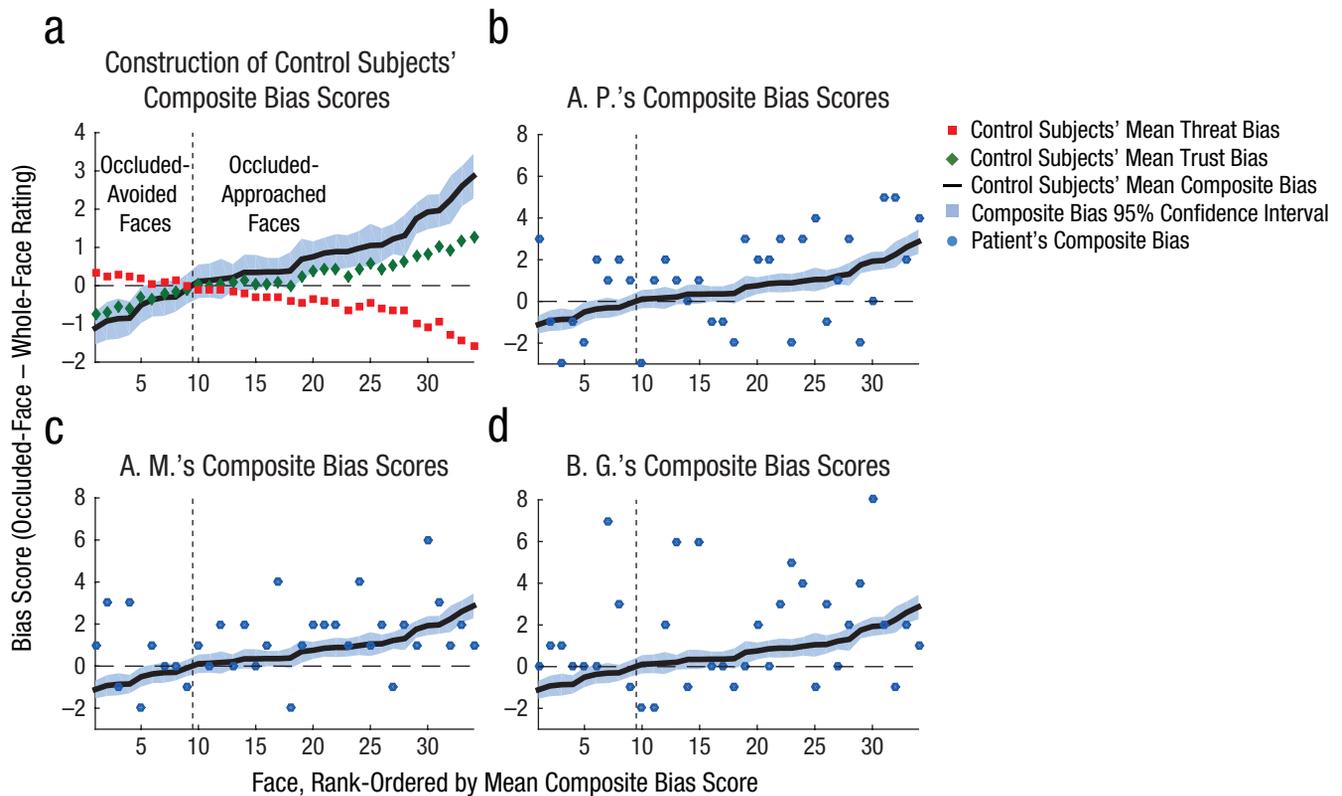
Note that the rescaling does not affect the derived bias scores discussed later, which constitute our main effects of interest. Those bias scores were calculated as within-subjects rating differences and consequently were not affected by group-level manipulations applied uniformly to individuals’ scores.

**Defining default bias.** For each type of judgment, we calculated a default-bias score (Fig. 1b) for each face by subtracting the whole-face rating from the occluded-face rating for that face. Positive scores for trust judgments and negative scores for threat judgments represented a default approach bias.

**Calculating composite bias scores.** For each face, we calculated a composite bias score for each subject by subtracting that subject’s threat bias score from his or her trust bias score (Fig. 1c). A mean negative composite bias score across subjects indicated that a face was avoided in the occluded-face condition relative to the whole-face condition (*occluded-avoided face*), receiving higher threat and lower trust ratings in the occluded than in the whole condition. A mean positive composite bias score across subjects indicated that a face was approached in the occluded-face condition relative to the whole-face condition (*occluded-approached face*), receiving lower threat and higher trust ratings in the occluded than in the whole condition. To determine the consistency of the directionality of approach bias between trust and threat judgments, we overlaid plots of control subjects’ mean trust and threat bias scores as a function of rank order of the faces’ mean composite bias scores (Fig. 2a). These plots demonstrated that trust and threat default biases moved together in a consistent fashion.

**Comparing patients with control subjects.** Each individual patient’s composite bias scores were qualitatively compared with those of control subjects by overlaying the patient’s composite bias scores for the faces on a plot of the 95% confidence interval (CI) of the control subjects’ mean composite bias scores for the faces.

In addition, we took a quantitative approach to comparing the lesion patients and control subjects, estimating how the 3 lesion patients would compare with 3 people randomly drawn from the general population. Separately for (a) all faces, (b) occluded-avoided faces, and (c) occluded-approached faces, we built a bootstrapped population estimate from 100,000 bootstrap samples of 3 randomly sampled control subjects’ average bias score. To remove any statistical dependency between the face



**Fig. 2.** Construction of composite bias scores and comparison of control subjects' and patients' composite bias scores. The graph in (a) shows the 81 control subjects' mean trust and threat bias scores. Given that the directionality of the trust and threat judgments was consistent, the two bias scores were combined to form composite bias scores. The graphs in (b) through (d) show the individual patients' composite bias scores; for purposes of comparison, the control subjects' mean composite bias scores, from (a), are shown as well. In all the graphs, the face stimuli (x-axis) have been rank-ordered according to the control subjects' mean composite bias score. The vertical dashed lines represent the boundary between faces with a negative composite bias score (which tended to be avoided more in the occluded-face relative to the whole-face condition) and faces with a positive composite bias score (which tended to be approached more in the occluded-face relative to the whole-face condition).

classification and comparison of control subjects' and patients' scores, on each bootstrap iteration we reclassified faces as occluded-avoided or occluded-approached according to the mean bias score of the 78 control subjects who were not randomly sampled on that bootstrap iteration.

**Testing for a difference in general approach tendency between occluded and whole faces.** To disentangle the contributions of occluded-face and whole-face ratings to the default approach bias we found, we separately calculated an approach-related *positivity* score (cf. Norris, Gollan, Bertson, & Cacioppo, 2010), the trust rating minus the threat rating, for each whole and occluded face. A positive positivity score indicated a general approach tendency (i.e., the face was more trustworthy than threatening), whereas a negative positivity score indicated avoidance (i.e., the face was more threatening than trustworthy). We used bootstrap resampling to compare patients' and control subjects' positivity scores for whole and occluded faces.

## Results

Results are fully detailed in this section and are summarized in Table 1 to quickly orient readers to our findings.

### *Comparison of lesion patients' and control subjects' composite bias scores*

We tested for a default approach bias in our amygdala-lesion patients by exploring whether they tended to approach occluded face stimuli more than whole face stimuli, relative to our control subjects. As already noted, we first confirmed the validity of our composite bias score. Control subjects' trust and threat bias scores moved together in an expected manner (Fig. 2a), such that faces that tended to be rated as more trustworthy when occluded were also rated as less threatening when occluded, and vice versa.

Each patient's composite bias scores were compared with the control subjects' mean bias scores (Figs. 2b–2d): Overall, the patients' bias scores indicated a heightened

**Table 1.** Summary of the Information Provided in Figures 2 Through 5 and Table 2

Figure 2a: This figure illustrates how composite bias scores were derived by combining separate trust and threat default-bias scores, which moved in opposite directions: Faces that tended to be trusted in the occluded condition were not found threatening in that condition, and faces that tended to not be trusted in the occluded condition were found to be threatening in that condition.

Figures 2b–2d: These graphs show that for each face, patients' composite bias scores tended to be more positive than control subjects' composite bias scores. That is, the patients exhibited an enhanced default approach bias.

Figure 3: This figure presents the results of the bootstrap analysis comparing 3 randomly sampled control subjects' mean composite bias score with the patients' actual mean score. It shows that patients had a stronger default approach tendency for all faces, and especially for faces that control subjects tended to avoid in the occluded condition.

Figure 4: This figure provides a parametric visualization of the bias shown in Figure 3. To test whether patients' bias resulted from a specific difficulty in rating occluded faces, we generated synthetic bias scores derived from patients' actual whole-face ratings and random occluded-face ratings. These synthetic scores were lower, not higher, than control subjects' composite bias scores; therefore, the patients' enhanced default bias relied on their abnormally positive evaluation of occluded faces.

Figure 5: This figure presents the results of the bootstrap comparison of control subjects' and patients' approach-related positivity scores (trust rating minus threat rating) for whole and occluded faces separately. It shows that all subjects had a bias to approach occluded faces more than whole faces, but also confirms that this bias was greatly enhanced in the patients.

Table 2: This table provides the 3 patients' individual ratings and bias scores, the 95% confidence intervals of the control subjects' mean ratings and bias scores, and a summary of how the patients compared with the control group.

tendency to approach faces in the occluded condition (this bias was not driven by a heightened tendency to avoid faces in the whole-face condition, as patients' ratings of whole faces did not differ from control subjects' ratings; see Table 2). Each patient's mean bias score was higher than that of the control subjects ( $M = 0.59$ ,  $SD = 0.76$ ): Compared with the control subjects' mean score, A. P.'s mean score was 0.46  $SD$  higher, A. M.'s mean score was 0.85  $SD$  higher, and B. G.'s mean score was 1.28  $SD$  higher.

Further confirming that the patients had a general bias to rate occluded faces as more trustworthy and less threatening than whole faces, our bootstrap analysis showed that the patients' composite bias scores were indeed higher than the control subjects'; only 7.6% of the bootstrap samples of control subjects had mean bias scores that exceeded the mean bias score of the patients (Fig. 3a). In addition, the patients' and control subjects' averages were strongly distinct ( $d = 1.13$ ), with nonoverlapping 95% CIs, [0.90, 1.59] and [0.43, 0.76], respectively. The difference between the two groups was weaker when the analysis was restricted to those faces that control subjects had a bias to approach in the occluded condition (Fig. 3c); for this subset of the faces, 15.8% of the bootstrap samples of control subjects had mean bias scores that exceeded the patients' mean, and the group averages were only moderately distinct ( $d = 0.74$ ), with 95% CIs of [0.84, 1.20] for control subjects and [1.19, 1.74] for patients. As expected, however, the between-groups difference was more pronounced for those faces that control subjects had a tendency to avoid in the occluded condition (Fig. 3b); for these faces, a mere 1.9% of the bootstrap samples of control subjects had mean bias

scores that exceeded the patients' mean, and the two groups' averages were strongly distinct ( $d = 1.53$ ), with 95% CIs of [−0.81, −0.37] for control subjects and [0.04, 1.22] for patients.

To test the possibility that these effects were driven by regression to the mean (i.e., that the amygdala-lesion patients' ratings were simply noisier, or more random, than the control subjects'), we estimated random bootstrapped distributions from samples of 3 artificial control subjects with random composite bias scores (built from raw trust and threat scores evenly distributed on the 6-point scale). Building a control distribution from random scores (i.e., noise) strengthened the separation of the control subjects' distribution and patients' mean bias scores for all faces (Fig. 3a) and occluded-approached faces alone (Fig. 3c), as the random distributions moved below the actual distributions for control subjects, which increased the separation between the control subjects' and patients' means. Although this increased separation was not observed for the occluded-avoided faces (Fig. 3b), the patients' default bias for those faces was particularly strong. Thus, regression to the mean is an unlikely explanation. In conclusion, the abnormal ratings given by the 3 patients with amygdala lesions are unlikely to have arisen simply from noisier ratings.

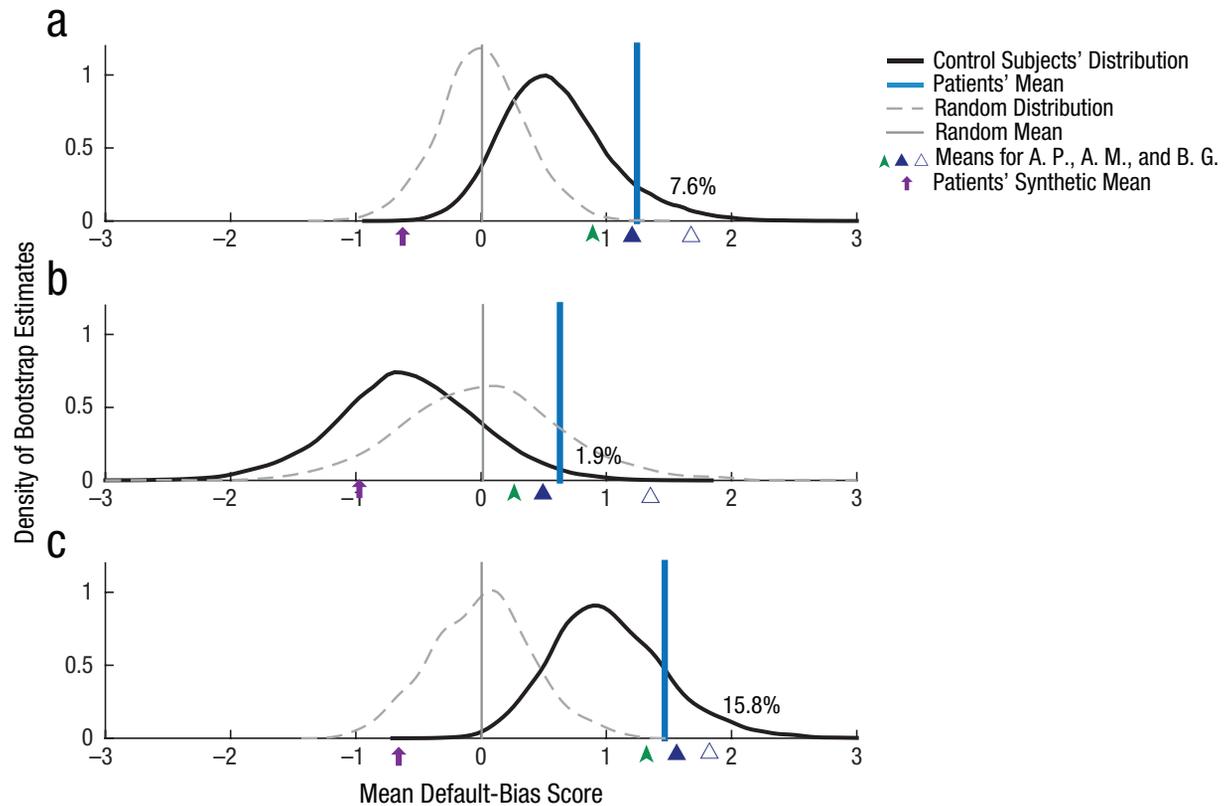
Finally, a more subtle possibility is that the 3 amygdala patients did not give globally noisier ratings, but gave random ratings specifically in the most difficult stimulus condition (i.e., for the occluded faces only). To test if this could have produced our data, we next derived synthetic mean default-bias scores by subtracting actual whole-face ratings of the patients from chance occluded-face ratings (i.e., 3.5, with a fixed bias offset for the German

**Table 2.** Comparison of Raw Scores and Derived Bias Scores of Bootstrapped Control Samples and the Individual Patients

Variable	Control samples with mean values exceeding the patients' (%) <sup>a</sup>	95% CI of control subjects' mean	Patients' means			Summary comparison of patients and control subjects
			A. P.	A. M.	B. G.	
Ratings of whole faces	19.9	[3.2, 3.4]	3.3	2.7	3.2	A. P.'s and B. G.'s means did not differ from control subjects', but A. M.'s mean was lower.
Ratings of occluded faces	4.7	[2.8, 3.1]	2.6	2.2	2.1	All 3 patients' means were lower than control subjects'.
Default-bias score	12.1	[-0.5, -0.3]	-0.7	-0.4	-1.1	A. P.'s and B. G.'s scores were lower than control subjects'; A. M.'s score did not differ from control subjects', but her whole-face ratings already indicated impairment.
Threat judgments						
Ratings of whole faces	23.7	[3.1, 3.3]	3.1	2.6	4.6	A. P.'s mean did not differ from control subjects'; A. M.'s mean was lower; B. G.'s mean was higher.
Ratings of occluded faces	3.9	[3.3, 3.5]	3.3	3.4	5.0	A. P.'s and A. M.'s means did not differ from control subjects'; B. G.'s mean was very high.
Default-bias score	8.9	[0.1, 0.3]	0.2	0.8	0.4	A. P.'s mean did not differ from control subjects'; A. M.'s and B. G.'s means were high.
Combined judgments						
Composite bias score across all faces	7.6	[0.4, 0.8]	0.9	1.2	1.6	All 3 patients had higher scores than the control group.
Composite bias score across occluded-avoided faces	1.9	[-0.8, -0.4]	0.2	0.4	1.2	All 3 patients had higher scores than the control group.
Composite bias score across occluded-approached faces	15.8	[0.8, 1.2]	1.2	1.5	1.7	A. P.'s score was within the 95% CI of the control group; A. M.'s and B. G.'s scores were higher.

Note: Default-bias scores were calculated by subtracting ratings of whole faces from ratings of occluded faces. Composite bias scores were calculated by subtracting default-bias scores for threat ratings from default-bias scores for trust ratings. Occluded-avoided faces are those for which control subjects' average composite bias score was negative; occluded-approached faces are those with a positive average composite bias score. CI = confidence interval.

<sup>a</sup>For threat, this column shows the percentage of bootstrapped control samples whose average ratings and bias scores were lower than those of the patients; for trust and composite bias, this column shows the percentage of bootstrapped control samples whose average ratings and bias scores were higher than those of the patients.

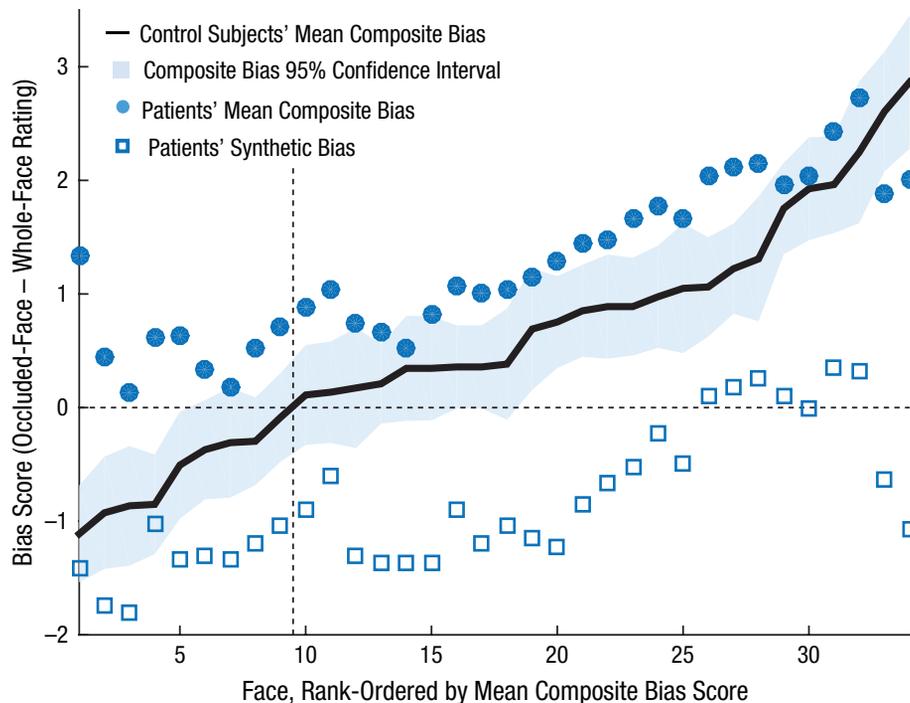


**Fig. 3.** Comparison of patients' mean composite bias scores with bootstrapped distributions of control subjects' scores. The density plots show bootstrapped estimates of the distribution of 3 randomly sampled control subjects' mean composite bias scores for (a) all faces ( $n = 34$ ), (b) occluded-avoided faces ( $n = 9$ ), and (c) occluded-approached faces ( $n = 25$ ), with the 3 patients' actual mean bias score overlaid. (Occluded-avoided and occluded-approached faces were identified by the mean composite bias score of the 78 control subjects not included on a given bootstrap iteration.) The individual patients' mean scores are indicated along the  $x$ -axes. The percentage of bootstrap samples in which the control subjects' mean score was higher than the patients' mean is indicated on each plot. As a test against regression to the mean, random bootstrapped control distributions, built from samples of 3 artificial control subjects with random composite bias scores (built from raw trust and threat scores evenly distributed on the 6-point scale), are overlaid on each plot, with the mean of each distribution indicated by a vertical line through that distribution. As a test of the contribution of occluded-face ratings to the patients' enhanced default bias, operationalized as higher composite bias scores, a *synthetic* mean composite bias score for the patients was derived from synthetic default-bias scores created by subtracting the patients' actual whole-face ratings from chance occluded-face ratings. The patients' mean synthetic composite bias score is indicated along the  $x$ -axis of each plot.

patients). The composite scores derived from these synthetic default-bias scores tended to be lower than control subjects' composite bias scores (Fig. 3), once again going in a direction opposite to that seen for the actual ratings given by the amygdala-lesion patients, which were higher than control subjects' ratings.

Binary classification of faces as occluded-avoided (Fig. 3b) or occluded-approached (Fig. 3c) indicated that the patients' default approach bias, operationalized as composite bias scores, was strongest for faces avoided by control subjects in the occluded condition. We visualized how the patients differed from control subjects in response to each face by overlaying the patients' mean composite bias score for each face on a plot of control subjects' rank-ordered mean composite bias scores

(Fig. 4). The patients' scores were smoothed with a 10-face moving average to improve visualization of the general parametric trend. Although the patients tended to have higher bias scores than control subjects across all faces, the patients' bias scores became less distinct from control subjects' as control subjects' composite bias scores increased. We also plotted synthetic bias scores derived by subtracting the patients' actual raw scores for whole-face stimuli from chance occluded-face ratings (Fig. 4). Unlike the patients' bias scores, these synthetic bias scores were not higher than control subjects'—in fact, they were lower. These results once again indicate that the deviation of the patients' bias scores from control subjects' bias scores was indeed driven by abnormal, but consistent, occluded-face ratings.



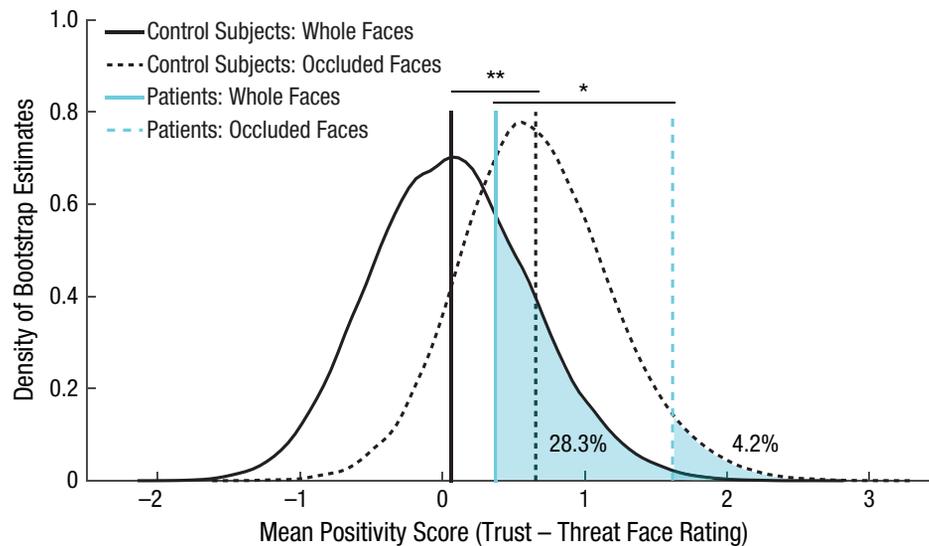
**Fig. 4.** Parametric trend in bias scores. The mean composite bias scores of the 3 patients are overlaid on a plot of the 81 control subjects' mean composite bias scores. The patients' scores were smoothed with a 10-face moving average, with a step size of 1 face. The face stimuli ( $x$ -axis) have been rank-ordered according to the control subjects' mean composite bias scores. Faces classified as occluded-avoided lie to the left of the vertical dashed line; occluded-approached faces lie to the right. Also shown are mean synthetic bias scores, derived by subtracting the patients' actual raw scores for whole-face stimuli from chance occluded-face ratings and smoothing with a 10-face moving average.

### ***Approach-related positivity scores for whole- and occluded-face stimuli***

Examination of positivity scores (positive for faces that were approached, i.e., that had stronger trust than threat ratings) for both classes of stimuli (whole and occluded faces) confirmed that the observed default bias was driven by greater positive evaluations of occluded faces. Approach-related positivity scores were higher in the occluded-face condition than in the whole-face condition in both control subjects and patients (Fig. 5). Although control subjects' positivity scores (trust minus threat rating for each face) exhibited a shift from relatively neutral evaluations of whole faces ( $M = 0.063$ ) to positive evaluations of occluded faces ( $M = 0.656$ ),  $p = 5.90 \times 10^{-10}$ , the increase in positivity scores for occluded compared with whole faces was markedly greater in the patients (whole faces:  $M = 0.373$ ; occluded faces:  $M = 1.618$ ),  $p = .0199$ . These results are inconsistent with alternative explanations of the default bias, such as that it arises from negative whole-face evaluations in combination with neutral occluded-face evaluations.

### ***Results separated by judgment and stimulus type***

Our analyses thus far were performed on a default bias defined as a tendency to give both higher trust ratings and lower threat ratings to occluded faces than to whole faces. Although the composite bias scores provided the most comprehensive way to present our results, separate trust and threat biases obviously contributed to the overall bias. We therefore also performed bootstrap comparisons of control subjects' and patients' mean trust and threat biases for whole and occluded faces separately (Table 2). These comparisons confirmed that the patients' observed approach bias was driven by abnormal ratings of occluded faces. As a group, the patients' whole-face ratings were not different from those of the control subjects, which was somewhat unexpected given the previous finding that patient S. M. (who also has bilateral amygdala lesions from Urbach-Wiethe disease, albeit lesions that are more substantial than those of any of our 3 patients) gave abnormally high trustworthiness judgments to whole faces (though a different set of faces than the ones used in the present study; Adolphs et al., 1998).



**Fig. 5.** Bootstrap comparison of patients' and control subjects' approach-related positivity scores. The density plot shows estimates of the bootstrap distribution of 3 randomly sampled control subjects' mean positivity scores (trust minus threat ratings for each face), separately for whole faces and occluded faces. Also shown are the means for these control bootstrap distributions and the patients' actual mean positivity scores for whole and occluded faces. Asterisks indicate significant differences between means ( $*p < .05$ ,  $**p < .001$ ). The percentage of bootstrap samples in which the control subjects' mean positivity score was greater than the patients' mean positivity score is indicated for each face condition and highlighted by the blue shading.

To verify that this discrepancy between S. M. and our amygdala-lesion patients was not driven by differences in the stimulus sets, we tested 2 of our patients (A. M. and B. G.) on the original stimuli from the experiment with S. M. Although the judgments of A. M. and B. G. tended to deviate from those of control subjects, especially for the faces control subjects avoided most (Fig. S3 in Additional Analyses), these patients exhibited only a weak trend to rate whole faces more favorably (i.e., as less threatening and more trustworthy) than control subjects, as S. M. had. Unfortunately, S. M. was not available for testing on our new task, and A. P. was not available for testing on the original task used by Adolphs et al. Results from the data available indicate that the default bias observed in this study results primarily from the patients' enhanced positive evaluation of the occluded-face stimuli.

## Discussion

By comparing ratings of whole and occluded faces, we found that 3 patients with rare selective bilateral amygdala lesions exhibited a significantly enhanced default approach bias relative to control subjects. Specifically, the increase in trust ratings and decrease in threat ratings in the low-information, occluded-face condition, compared with the whole-face condition, was greater for the patients than for the control subjects.

Consider again our example situation of walking into a dark room. The normal response to an ambiguous

situation is risk assessment (Blanchard et al., 2011); given insufficient information to determine whether a threat is present, one should pause and gather more information before proceeding. Our patients' ratings indicated that they would simply enter the room, whereas at the other end of the spectrum, anxious individuals might flee the dark room before gathering further evidence. Future experiments exploring individual differences (e.g., trait and state anxiety, perceived dominance, history of exposure to physical and social threat or betrayal) will be important to both validate our task and determine what factors beyond amygdala damage relate to heightened approach tendencies. It is worth noting that a few of our control subjects had an approach bias similar to that of the patients; future studies are needed to determine the cause of these individual differences.

In humans, given a lack of stimulus information, an exploratory tendency may normally promote a default approach bias, the *positivity offset* predicted for evaluation of low-information stimuli in the evaluative space model (Norris et al., 2010). This positivity offset is similar to the increase in approach-related positivity scores (trust minus threat ratings) in the occluded-face condition compared with the whole-face condition in the present study (Fig. 5). We observed this shift in positivity scores in both control subjects and patients, but it was enhanced in the patients.

Although patients' approach ratings were higher than control subjects', the patients were not completely

indiscriminate: Their judgments differed more in degree than in direction (Table 2). Future work should test whether their enhanced approach bias extends to (a) other classes of degraded stimuli and (b) the real world. If our 3 patients, like S. M. (Feinstein et al., 2011; Kennedy et al., 2009), were shown to exhibit abnormal proxemic (i.e., personal space) behavior and a tendency to approach real threatening stimuli (e.g., snakes), this would further corroborate a default approach bias. Preliminary testing has confirmed that B. G. has abnormally small personal space and fear responses (D. P. Kennedy & J. Feinstein, personal communication, August 21, 2014). Testing subjects' actual behavior is crucial, as compensatory processing may allow them to give explicit ratings that are more "correct" than their real-world behavior would be: For example, although S. M. abnormally approached actual snakes without showing any fear, beforehand she verbally insisted that she "hates" snakes and "tries to avoid them" (Feinstein et al., 2011, p. 34).

Differences among the amygdala-lesion patients need to be explained. Amygdala damage can prompt two distinct approach processes—a default bias and a face-specific bias—which can operate simultaneously. Removing facial-feature information from our stimuli allowed us to observe a default bias while working within the general category of facial stimuli. Across all subjects, responses to facial features were variable, and the patients' whole-face ratings were similar to those of control subjects. In contrast, S. M.'s ratings of whole faces were different from control subjects' (Adolphs et al., 1998). This deviation between S. M. and the patients in the current study is in line with the heterogeneity of impairments reported in cases of bilateral amygdala damage (Adolphs et al., 1999; Hamann et al., 1996; Siebert, Markowitsch, & Bartel, 2003; van Honk, Terburg, Thornton, Stein, & Morgan, in press), and may reflect compensatory processing (Becker et al., 2012; Scheele et al., 2012). S. M.'s impairment in evaluating whole faces hints at progressive amygdala damage (impairment), which is expected in Urbach-Wiethe disease (Appenzeller et al., 2006) and which may encompass more, and different, amygdala nuclei than in other cases of Urbach-Wiethe disease (van Honk et al., in press).

Although patients' differences in a face-specific deficit need to be further explored and explained on the basis of precise anatomical differences, the present study focused on isolating a stimulus-independent effect that will clearly interact with responses to facial features in influencing approach-avoidance behavior. However, across the entire stimulus set, a general default approach bias could be observed independently of specific responses to facial features.

Mechanistically, the patients' approach bias may relate to a specific deficit related to disrupted vigilance

(Davis & Whalen, 2001; Whalen, 2007), a possibility compatible with the idea that the amygdala launches a defensive behavioral response to coincident sensory and contextual danger signals (Freese & Amaral, 2009). However, the patients' approach bias can be explained by a more general mechanism of amygdala function. The possibility that the amygdala plays a general role in processing salience and self-relevance (Cunningham & Brosch, 2012; Harrison & Adolphs, 2015; Sander, Grafman, & Zalla, 2003) is compatible with a wide array of findings regarding the amygdala. The amygdala contributes to both negative and positive reinforcement (Murray, Izquierdo, & Malkova, 2009) and processes positively and negatively valenced stimuli (Anderson et al., 2003; Hamann, Ely, Hoffman, & Kilts, 2002). In rats (Hatfield, Han, Conley, Gallagher, & Holland, 1996) and nonhuman primates (Izquierdo & Murray, 2007; Málková, Gaffan, & Murray, 1997), basolateral amygdala lesions interfere with reinforcer devaluation, such that an animal will indiscriminately approach devalued food items, an effect similar to our patients' default approach bias. Hypothetically, the basolateral nucleus, which is damaged in our patients, updates the value of a stimulus (Murray et al., 2009). All of these findings indicate that the amygdala contributes more than merely a role in detecting threats, and instead processes any stimuli of high relevance.

A salience, or relevance, explanation not only is compatible with our observed default bias but also accounts for prior findings in amygdala-lesion patients. For example, amygdala lesions inhibit proper orienting to stimuli (Spezio, Huang, Castelli, & Adolphs, 2007), which in turn results in a diminished ability to experience (Feinstein et al., 2011) or recognize (Adolphs et al., 2005) fear. Proper orienting can lead to recovery of this ability: S. M. correctly identified fear in facial stimuli after being given explicit top-down instruction to look at the eyes (Adolphs et al., 2005).

Our finding of an enhanced default approach bias in amygdala-lesion patients suggests a further role for the amygdala in setting a default for what is potentially relevant or salient. This default normally prevents individuals from approaching situations that may be threatening while simultaneously permitting exploration of those situations. In our patients, this balance is shifted. Similarly, in psychiatric disorders featuring dysregulation of the amygdala (e.g., anxiety disorders—Davis, 1992; Etkin & Wager, 2007; autism—Baron-Cohen et al., 2000; Castelli, Frith, Happé, & Frith, 2002; Dalton et al., 2005), stimuli are not evaluated correctly as a result of shifted baseline biases as well as under- and overweighting of the threat, social importance, and relevance of stimuli.

In summary, contrasting judgments of occluded and whole faces, we uncovered a default approach bias following bilateral amygdala damage. Future research is needed to test for a default approach or avoidance bias

in psychiatric disorders in which the amygdala is implicated, to develop implicit tests of approach bias in order to circumvent potential compensatory mechanisms, and to devise tests that can provide a clearer mechanistic account of our findings.

### Author Contributions

L. A. Harrison and R. Adolphs developed the study concept and design. Testing and data collection were performed by L. A. Harrison and R. Hurlmann. L. A. Harrison performed the data analysis and interpretation under the supervision of R. Adolphs. L. A. Harrison drafted the manuscript, and R. Adolphs provided critical revisions. All authors approved the final version of the manuscript for submission.

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The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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### Supplemental Material

Additional supporting information can be found at <http://pss.sagepub.com/content/by/supplemental-data>

### Open Practices



All data have been made publicly available via Open Science Framework and can be accessed at <https://osf.io/8cktf/>. Task instructions can also be accessed at <https://osf.io/8cktf/>. Because of confidentiality concerns, the photographs used as stimuli are not available at Open Science Framework, but they can be obtained for research use by contacting Laura A. Harrison, [lauraharrison@caltech.edu](mailto:lauraharrison@caltech.edu). The complete Open Practices Disclosure for this article can be found at <http://pss.sagepub.com/content/by/supplemental-data>. This article has received the badge for Open Data. More information about the Open Practices badges can be found at <https://osf.io/tvyxz/wiki/1.%20View%20the%20Badges/> and <http://pss.sagepub.com/content/25/1/3.full>.

### References

- Adams, R. B., Gordon, H. L., Baird, A. A., Ambady, N., & Kleck, R. E. (2003). Effects of gaze on amygdala sensitivity to anger and fear faces. *Science*, *300*, 1536.
- Adolphs, R., Gosselin, F., Buchanan, T. W., Tranel, D., Schyns, P., & Damasio, A. R. (2005). A mechanism for impaired fear recognition after amygdala damage. *Nature*, *433*, 68–72.
- Adolphs, R., Tranel, D., & Damasio, A. R. (1998). The human amygdala in social judgment. *Nature*, *393*, 470–474.
- Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, *372*, 669–672.
- Adolphs, R., Tranel, D., Hamann, S., Young, A., Calder, A., Anderson, A., . . . Damasio, A. R. (1999). Recognition of facial emotion in nine subjects with bilateral amygdala damage. *Neuropsychologia*, *37*, 1111–1117.
- Amaral, D. G., Price, J. L., Pitkänen, A., & Carmichael, S. T. (1992). Anatomical organization of the primate amygdaloid complex. In J. P. Aggleton (Ed.), *The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction* (pp. 1–66). New York, NY: Wiley-Liss.
- Anderson, A. K., Christoff, K., Stappen, I., Panitz, D., Ghahremani, D. G., Glover, G., . . . Sobel, N. (2003). Dissociated neural representations of intensity and valence in human olfaction. *Nature Neuroscience*, *6*, 196–202.
- Appenzeller, S., Chaloult, E., Velho, P., de Souza, E. M., Araujo, V. Z., Cendes, F., & Li, L. M. (2006). Amygdalae calcifications associated with disease duration in lipid proteinosis. *Journal of Neuroimaging*, *16*, 154–156.
- Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C., & Williams, S. C. R. (2000). The amygdala theory of autism. *Neuroscience & Biobehavioral Reviews*, *24*, 355–364.
- Becker, B., Mihov, Y., Scheele, D., Kendrick, K. M., Feinstein, J. S., Matusch, A., . . . Hurlmann, R. (2012). Fear processing and social networking in the absence of a functional amygdala. *Biological Psychiatry*, *72*, 70–77.
- Blanchard, D. C., Griebel, G., Pobbe, R., & Blanchard, R. J. (2011). Risk assessment as an evolved threat detection and analysis process. *Neuroscience & Biobehavioral Reviews*, *35*, 991–998.
- Broks, P., Young, A. W., Maratos, E. J., Coffey, P. J., Calder, A. J., Isaac, C., . . . Hadley, D. (1998). Face processing impairments after encephalitis: Amygdala damage and recognition of fear. *Neuropsychologia*, *36*, 59–70.
- Castelli, F., Frith, C., Happé, F., & Frith, U. (2002). Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain*, *125*, 1839–1849.
- Choi, J., & Kim, J. J. (2010). Amygdala regulates risk of predation in rats foraging in a dynamic fear environment. *Proceedings of the National Academy of Sciences, USA*, *107*, 21773–21777.
- Cunningham, W. A., & Brosch, T. (2012). Motivational salience: Amygdala tuning from traits, needs, values, and goals. *Current Directions in Psychological Science*, *21*, 54–59.
- Dalton, K. M., Nacewicz, B. M., Johnstone, T., Schaefer, H. S., Gernsbacher, M. A., Goldsmith, H. H., . . . Davidson, R. J. (2005). Gaze fixation and the neural circuitry of face processing in autism. *Nature Neuroscience*, *8*, 519–526.
- Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual Review of Neuroscience*, *15*, 353–375.

- Davis, M., & Whalen, P. J. (2001). The amygdala: Vigilance and emotion. *Molecular Psychiatry*, *6*, 13–34.
- Elliot, A. J., Eder, A. B., & Harmon-Jones, E. (2013). Approach-avoidance motivation and emotion: Convergence and divergence. *Emotion Review*, *5*, 308–311.
- Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry*, *164*, 1476–1488.
- Feinstein, J. S., Adolphs, R., Damasio, A., & Tranel, D. (2011). The human amygdala and the induction and experience of fear. *Current Biology*, *21*, 34–38.
- Freese, J. L., & Amaral, D. G. (2009). Neuroanatomy of the primate amygdala. In P. J. Whalen & E. A. Phelps (Eds.), *The human amygdala* (pp. 3–42). New York, NY: Guilford Press.
- Gothard, K. M., Battaglia, F. P., Erickson, C. A., Spitler, K. M., & Amaral, D. G. (2007). Neural responses to facial expression and face identity in the monkey amygdala. *Journal of Neurophysiology*, *97*, 1671–1683.
- Hamann, S. B., Ely, T. D., Hoffman, J. M., & Kilts, C. D. (2002). Ecstasy and agony: Activation of the human amygdala in positive and negative emotion. *Psychological Science*, *13*, 135–141.
- Hamann, S. B., Stefanacci, L., Squire, L. R., Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1996). Recognizing facial emotion. *Nature*, *379*, 497.
- Harrison, L., & Adolphs, R. (2015). The amygdala and social perception. In A. W. Toga (Ed.), *Brain mapping* (pp. 91–96). Waltham, MA: Academic Press.
- Hatfield, T., Han, J.-S., Conley, M., Gallagher, M., & Holland, P. (1996). Neurotoxic lesions of basolateral, but not central, amygdala interfere with Pavlovian second-order conditioning and reinforcer devaluation effects. *The Journal of Neuroscience*, *16*, 5256–5265.
- Herry, C., Bach, D. R., Esposito, F., Di Salle, F., Perrig, W. J., Scheffler, K., & Seifritz, E. (2007). Processing of temporal unpredictability in human and animal amygdala. *The Journal of Neuroscience*, *27*, 5958–5966.
- Hofer, P. A. (1973). Urbach-Wiethe disease (lipoglycoproteinosis; lipid proteinosis; hyalinosi cutis et mucosae): A review. *Acta Dermato-Venereologica. Supplementum*, *53*, 1–52.
- Hsu, M., Bhatt, M., Adolphs, R., Tranel, D., & Camerer, C. F. (2005). Neural systems responding to degrees of uncertainty in human decision-making. *Science*, *310*, 1680–1683.
- Izquierdo, A., & Murray, E. A. (2007). Selective bilateral amygdala lesions in rhesus monkeys fail to disrupt object reversal learning. *The Journal of Neuroscience*, *27*, 1054–1062.
- Kennedy, D. P., Gläscher, J., Tyszka, J. M., & Adolphs, R. (2009). Personal space regulation by the human amygdala. *Nature Neuroscience*, *12*, 1226–1227.
- Klüver, H., & Bucy, P. C. (1939). Preliminary analysis of functions of the temporal lobes in monkeys. *Archives of Neurology & Psychiatry*, *42*, 979–1000.
- Málková, L., Gaffan, D., & Murray, E. A. (1997). Excitotoxic lesions of the amygdala fail to produce impairment in visual learning for auditory secondary reinforcement but interfere with reinforcer devaluation effects in rhesus monkeys. *The Journal of Neuroscience*, *17*, 6011–6020.
- McNaughton, N., & Corr, P. J. (2004). A two-dimensional neuropsychology of defense: Fear/anxiety and defensive distance. *Neuroscience & Biobehavioral Reviews*, *28*, 285–305.
- Murray, E. A., Izquierdo, A., & Malkova, L. (2009). Amygdala function in positive reinforcement: Contributions from studies of nonhuman primates. In P. J. Whalen & E. A. Phelps (Eds.), *The human amygdala* (pp. 82–104). New York, NY: Guilford Press.
- Norris, C. J., Gollan, J., Berntson, G. G., & Cacioppo, J. T. (2010). The current status of research on the structure of evaluative space. *Biological Psychology*, *84*, 422–436.
- Perrett, D. I., Rolls, E. T., & Caan, W. (1982). Visual neurons responsive to faces in the monkey temporal cortex. *Experimental Brain Research*, *47*, 329–342.
- Rutishauser, U., Tudusciuc, O., Neumann, D., Mamelak, A., Heller, A. C., Ross, I. B., . . . Adolphs, R. (2011). Single-unit responses selective for whole faces in the human amygdala. *Current Biology*, *21*, 1654–1660.
- Sander, D., Grafman, J., & Zalla, T. (2003). The human amygdala: An evolved system for relevance detection. *Reviews in the Neurosciences*, *14*, 303–316.
- Scheele, D., Mihov, Y., Kendrick, K. M., Feinstein, J. S., Reich, H., Maier, W., & Hurlmann, R. (2012). Amygdala lesion profoundly alters altruistic punishment. *Biological Psychiatry*, *72*, e5–e7.
- Siebert, M., Markowitsch, H. J., & Bartel, P. (2003). Amygdala, affect and cognition: Evidence from 10 patients with Urbach-Wiethe disease. *Brain*, *126*, 2627–2637.
- Sinha, P., Balas, B., Ostrovsky, Y., & Russell, R. (2006). Face recognition by humans: Nineteen results all computer vision researchers should know about. *Proceedings of the IEEE*, *94*, 1948–1962.
- Somerville, L. H., Kim, H., Johnstone, T., Alexander, A. L., & Whalen, P. J. (2004). Human amygdala responses during presentation of happy and neutral faces: Correlations with state anxiety. *Biological Psychiatry*, *55*, 897–903.
- Spezio, L., Huang, P. S., Castelli, F., & Adolphs, R. (2007). Amygdala damage impairs eye contact during conversations with real people. *The Journal of Neuroscience*, *27*, 3994–3997.
- Tsao, D. Y., Freiwald, W. A., Tootell, R. B. H., & Livingstone, M. S. (2006). A cortical region consisting entirely of face-selective cells. *Science*, *311*, 670–674.
- van der Zwaag, W., Da Costa, S. E., Zürcher, N. R., Adams, R. B., Jr., & Hadjikhani, N. (2012). A 7 tesla fMRI study of amygdala responses to fearful faces. *Brain Topography*, *25*, 125–128.
- van Honk, J., Terburg, D., Thornton, H., Stein, D. J., & Morgan, B. (in press). Consequences of selective bilateral lesions to the basolateral amygdala in humans. In D. G. Amaral & R. Adolphs (Eds.), *Living without an amygdala*. New York, NY: Guilford Press.
- Whalen, P. J. (2007). The uncertainty of it all. *Trends in Cognitive Sciences*, *11*, 499–500.
- Willenbockel, V., Sadr, J., Fiset, D., Horne, G., Gosselin, F., & Tanaka, J. W. (2012). Controlling low-level image properties: The SHINE toolbox. *Behavior Research Methods*, *42*, 671–684.
- Willis, J., & Todorov, A. (2006). First impressions: Making up your mind after a 100-ms exposure to a face. *Psychological Science*, *17*, 592–598.