Supplementary Materials for

Intact rapid detection of fearful faces in the absence of the amygdala

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Nature Neuroscience: doi:10.1038/nn.2380

Supplementary Methods

Subjects

Subjects were tested individually. For experiment 1, we tested SM in two separate sessions on separate days, and 12 healthy women of comparable age (control mean age = 41 years, range 36-45; SM = 42 years), IQ (control mean IQ = 102, range 84-123; SM = 88), and education (12 years for all). For control experiments 1A and 1B, we tested SM on a separate visit in several sessions, and compared her results to those from 7 female controls (mean age = 49 years, range 40-61; 12-14 years of education; mean IQ = 109, range 101-116). One subject was not tested in 1A (Ekman face) and 1B (NimStim close mouth), another subject was not tested in 1B (NimStim open mouth). For experiment 2 we tested SM and 23 healthy Caltech undergraduates (in this case not matched to SM on age or IQ); seven of the controls and SM also participated in the categorization task on the basis of which the search stimuli were constructed. We later repeated experiment 2 using a different set of face stimuli on SM (on a separate visit) and three age-matched controls. For experiment 3, we tested SM and 7 age-matched controls (the same cohort as experiment 1A and 1B). All subjects had normal visual acuity, corrected to 20/20, no history of psychiatric illness, and were naive to the experiment.

Stimuli and Task for Experiment 1

In a rapid discrimination task, visual images were shown as pairs for 40ms, unmasked, and subjects were asked to push a button as rapidly as possible to detect the emotional target's side of presentation (**Supplementary Fig. 1**). In three separate sessions, subjects were shown fearful faces paired with neutral faces (6 unique individuals), angry faces paired with neutral faces (6 unique individuals), or threatening scenes paired with neutral scenes (all different in each trial). Subjects were given the target to detect (fear, anger, or threat) before each session. For the faces, all face pairs showed the same individual. The faces were chosen from the Ekman and Friesen set[1]; the scenes from the International Affective Picture System[2]. 48 trials were presented for each of the 2 face sessions, and 100 trials for the threat scene session. The experiment began for each subject with two practice sessions that involved detection of cars and of disgust faces. All controls performed the experiment twice (for a total of 96 trials for the fear and anger faces, and 200 trials for the threat scenes); SM performed the experiment twice on each of two separate days, for a total of 192 fear face trials, 192 anger face trials, and 400 threat scene trials. We presented stimuli on a CRT display (refresh rate = 100Hz) using a PC running MATLAB with Psychtoolbox[3, 4]. Subjects sat 80 cm from the display. The visual angle of the display was 28 deg x 21 deg, and the face stimuli extended 8.2 deg x 11.0 deg and the scene stimuli extended 13.5 deg x 10.2 deg.

Stimuli and Task for Experiment 1A-1B

We performed two control tasks to examine the possible confounds of 1) afterimages, 2) neutral faces rendering the task an emotion-neutral discrimination not specific to fear, and 3) overtraining with the Ekman face set. Unless noted, the methods of experiment 1A and 1B were identical to those of experiment 1. In these experiments, we emphasized to subjects that they should respond as accurately as possible and allowed slow responses.

To remove any afterimages, we used backward masking with the images constructed by scrambling the phase of the face stimuli. An identical mask image was used in a given trial for both the target and the distractor. Stimulus onset asynchrony between the target and the mask was 140 ms for 1A and 40 ms (fear vs. happy), 80 ms (fear vs. neutral) and 140 ms (fear vs. sad) for 1B. The target was presented until the mask came on and the mask was presented for 150 ms. We used these timing values based on preliminary experiments to equate task performance across different emotions. To exclude the possibility that specific low-level image features of neutral

Nature Neuroscience: doi:10.1038/nn.2380

faces are utilized for discrimination of fearful faces, we intermixed trials that paired a fearful face with a neutral, a happy or a sad face using the Ekman set (1A; in total, 66 trials with 22 trials for each emotion pair [11 individual faces x 3 emotion categories for the distractor x 2 target position (left or right)]). We also controlled for 'familiarity' of the face stimulus set; we excluded the possibility that SM had learned to use some peculiar features of the Ekman faces to discriminate fearful faces over the many experiments with these stimuli in which she had participated over the years. For this purpose, we used the NimStim face set[5], which SM had never seen before. We used 40 individual pairs with an open mouth and 34 pairs with a closed mouth. In total, each subject performed 148 trials for each emotion pair (74 faces x 2 target positions).

To ensure proper fixation, we presented all stimuli in a gaze-contingent manner using an Eyelink 2 eyetracker and the Eyelink toolbox[6]. We calibrated the eye tracker before the first session and re-calibrated as needed. We confirmed accuracy of the eye tracker using the built-in validation procedure. In each trial, we briefly flashed the stimuli only once subjects had properly fixated. The size of the fixation cross was 0.27 deg x 0.27 deg and the accepted fixation window was a square area of 1.4 x 1.4 deg containing the fixation cross at the center. Fifty milliseconds fixation within the fixation window was required to trigger a trial. When the drift was detected, the built-in drift correction was applied, in addition to a mandatory drift correction for every 23 trials.

Results for Experiment 1A and 1B

Overall, SM's performance (mean d'= 1.03 across 7 conditions, mean z-score = -0.85) was slightly, but not significantly, worse than controls (n=7, mean d' = 1.90, mean std for d' = 0.99). In **Supplementary Table 1** below, we show the breakdown of performance.

Stimuli and Task for Experiment 2

We morphed the faces of six individuals from the Ekman and Friesen set in 25 steps from neutral to fearful (always within the same individual), thus creating 6 separate morph sequences. Morphing was carried out using SMartMorph (version 1.55, MeeSoft, http://meesoft.logicnet.dk) and based on manually defined corresponding features between the beginning and end images. We first carried out a categorization task in 7 of the controls and SM. In this task, subjects viewed all of the morphs, in randomized order, for 100ms (unmasked) at fixation and then pressed one of two keys to indicate the category (neutral or fear) (Results are shown in **Supplementary Fig. 3**). The average probability of reporting each option was fitted with a sigmoid curve for each subject. The pooled normal categorization data was used to determine the category boundary on which the search task stimuli were based (i.e., SM and controls saw the identical stimulus set in the search experiment).

For the search task, subjects were shown, in randomized order, 12 different versions resulting from the manipulation of 3x2x2 factors. The first factor was the set size array, which was either 4, 8, or 12 faces. The second factor was the categorical condition, which either showed both target and distractors as perceived to be within the same category, or as perceived to be in two different categories. The third factor was the physical degree of morphing between target and distractors, which was either 0.33 or 0.40 distance in morph space, where 1.0 is the whole range from neutral to fear. Trials were intermixed with other conditions in which target and distractors differed in anger, happiness, or gaze direction (these additional conditions were not analyzed in the present study). On each trial, subjects saw 4, 8, or 16 images displayed simultaneously at random locations within a 5x5 grid (subtending 18 x 18 degrees of visual angle total, with each face subtending approximately 2 x 3 degrees). All images except one (the target) were identical, and all were morphs of the same individual. Subjects were instructed to press a button as soon as they detected an oddball image, which resulted in the faces all being replaced by blank gray rectangles. The subject was then asked to click on the location of the rectangle that had been the

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target. Only correct trials were analyzed, which was the vast majority of trials for all subjects including SM.

To analyze data from the search task, we began with each subject's mean reaction time (averaged over the 6 individuals whose faces were morphed) for the 12 conditions resulting from the 3x2x2 factors described above. To estimate the effect of interest, the category factor, we calculated an index that describes how much reaction time improves if the target and distractors fall into different categories than when they are within the same category, as Normalized RT improvement = ((RTsame_category)-(RTdifferent_category))/RTsame_category. We found that this index did not differ significantly as a function of array set size, and only marginally as a function of morph degree (an 18% improvement for the different-category condition in the case of the 0.33 morph distance; a 12% improvement in the case of the 0.4 morph distance; both significantly greater than zero). For the data we report, we averaged our category index over all array sizes and morph degrees. The results were the same when we analyzed the data according to SM's or controls' category boundary because both category boundaries were spanned in different-category stimuli.

To address the possibility that SM's normal performance resulted from her over-exposure to the Ekman face set or from her use of specific features for neutral-fear morphs, we performed control experiments in SM and three age and gender-matched controls using morphs between fearful and either happy, sad, or calm expressions of six individuals from the Karolinska directed faces (KDEF) dataset[7]. Set size and morphing distance were fixed to 3 and 0.33, respectively. The stimuli were selected based on a pilot search on normal subjects in a way that the effect was maximized. For each trial one distractor was shown first at the center of the screen as a non-target. Subjects were told to move the mouse over it (so they always centered the mouse before search started). They were also told to look for a face that is different from this face. Then the distractor was removed and 3 faces (one target and two distractors) were shown in the periphery. Subjects were instructed to click on the location of the target. SM performed 508 trials and the controls performed 648 trials. The results were analyzed as described above. In all conditions, SM performed with >99% accuracy, ruling out speed-accuracy trade-offs as an explanation.

Stimuli and Task for Experiment 3

Subjects sat in front of a mirror set, composed of 4 mirrors, to view the CRT display (the eye-to-display distance was 30 cm). Because of the mirror arrangement, subjects saw only the left part of the display with the left eye and only the right part with the right eye. Each trial started upon a mouse click. Continuous flash suppression was implemented as described previously[8]. We flashed random Mondrian patterns (visual angle of 16x16 deg), composed of colorful circles, to the left eye at the rate of 10Hz, and gradually introduced an emotional face (visual angle of 8x8 deg) in one of the four quadrants (See **Supplementary Fig. 4**). The contrast of the Mondrian patterns started at 60% and gradually ramped down at the rate of 20% per second from 1s to 4s. The contrast of the face started at 0% and gradually ramped up to reach 100% at the initial 1 s and remained at 100% until response. Subjects were instructed to click a mouse as soon as they detected any part of the face. After the detection response, both Mondrians and the face were removed from the display and subjects clicked the location of the face via another mouse click. Only the trials with correct localization were analyzed (98.5% of trials).

In each session, 5 or 6 identities of faces (12 faces were from the NimStim faces, 11 faces were from the Ekman faces) were used. Each face was shown 12 times (4 quadrants X 3 emotions (fear, happy and neutral)), resulting in 60 or 72 trials per session. To estimate the effect of fearful expressions, we calculated an index that describes how much reaction time improves if the target was a fearful face than when it was a happy face, as Normalized RT difference = ((RThappy)-(RTfear))/RThappy, which is positive if RTfear is shorter than RThappy. The analysis we presented in **Fig. 1c** shows the results from 7 faces out of 23 faces, for which 7 control subjects showed significantly faster reaction times for fear than happy (for each face, $p<0.05$ with two-

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tailed t-tests across 7 controls). For the results using all 23 faces, SM also showed the fear advantage (SM's Normalized RT difference was 0.079; the controls' mean (S.D.) Normalized RT difference was 0.046 (0.056)).

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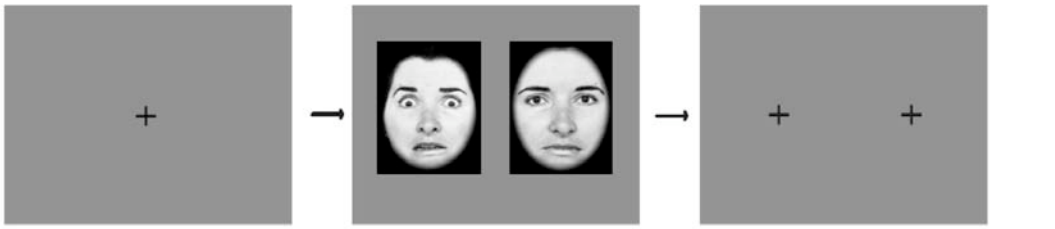
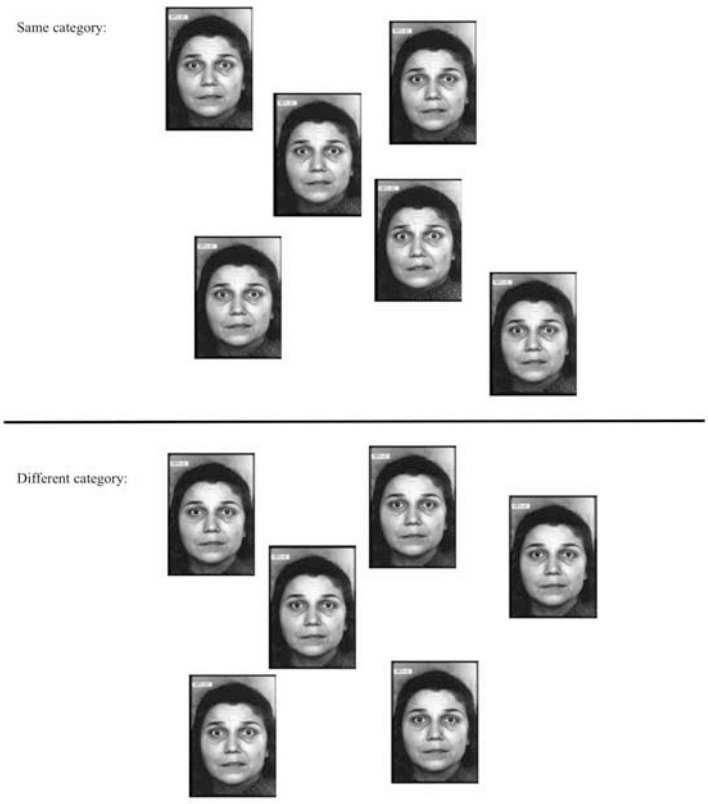
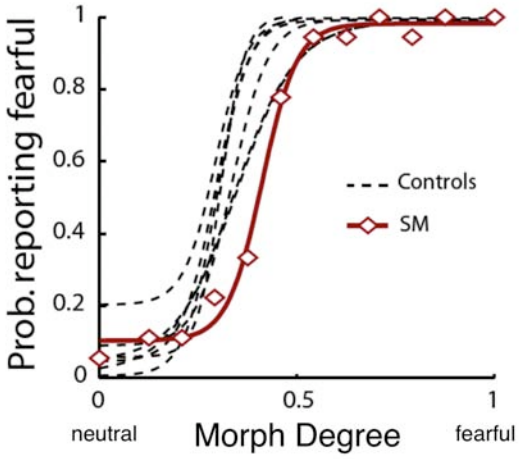


Supplementary Figure 1
Paradigm and stimuli for Experiment 1.

Nature Neuroscience: doi:10.1038/nn.2380

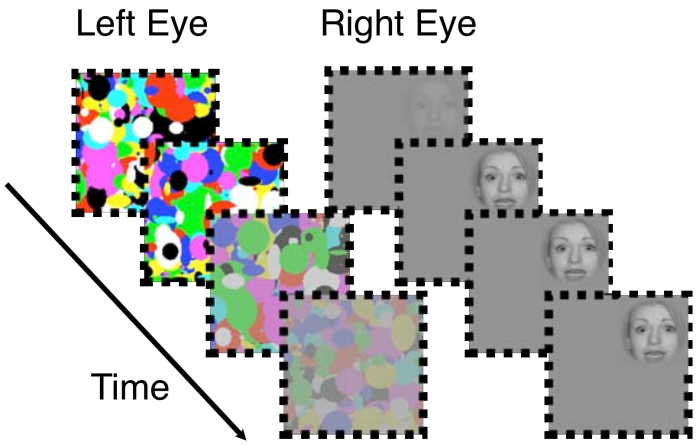


Supplementary Figure 2
Paradigm and stimuli for Experiment 2



Supplementary Figure 3
Results of the categorization task using morph stimuli

Nature Neuroscience: doi:10.1038/nn.2380



Supplementary Figure 4
Paradigm and stimuli for Experiment 3

		d' for SM	z(SM)	Mean d' for controls	Std for d' across controls
Experiment 1A: Ekman faces (fear vs. neutral, happy, sad intermixed)		1.94	-0.79	2.83	1.13
Experiment 1B: NimStim faces		0.88	-0.86	1.75	0.97
	fear vs. neutral	1.01	-0.77	1.69	0.81
	fear vs. happy	1.14	-0.62	1.72	1.05
	fear vs. sad	0.49	-1.18	1.84	1.05

Supplementary Table 1
Breakdown of the performance for Experiment 1A and 1B.

Nature Neuroscience: doi:10.1038/nn.2380