Human Amygdala Responsivity to Masked Fearful Eye Whites

Paul J. Whalen,[1]* Jerome Kagan,[2] Robert G. Cook,[3] F. Caroline Davis,[1] Hackjin Kim,[1] Sara Polis,[1] Donald G. McLaren,[1] Leah H. Somerville,[4] Ashly A. McLean,[1] Jeffrey S. Maxwell,[1] Tom Johnstone[1]

The human amygdala has been shown to be activated robustly by fearful facial expressions in neuroimaging studies, even when expressions are presented with backward masking techniques that decrease the temporal availability of facial expression information and mitigate subjective awareness of their presence (*1*). This efficiency in information processing could be consistent with the proposal that the amygdala can respond to crude representations of stimuli (*2*). On the basis of data showing that the eye region of the face is one of the key regions where expression information is extracted (*3*–*6*) and data showing that the amygdala is responsive to the "wide-eyed" expressions of both fear and surprise (*7*, *8*), we hypothesized that the larger size of fearful eye whites (i.e., sclera) would be sufficient to modulate amygdala responsivity.

To test this possibility, we modified standardized fearful and happy face stimuli (*9*) by removing all information from the face but the eye whites (Fig. 1). Because presentation of eye whites alone represents a noncanonical stimulus, we presented these stimuli in a backward masking paradigm to decrease subject's awareness of their presence and, in turn, of their aberrant nature. Grayscale neutral faces were thresholded to create black and white line drawings for use as masks for the eye stimuli (fig. S1C). During functional magnetic resonance imaging, 20 subjects (*10*) viewed neutral face mask presentations, half of which were preceded by fearful eye whites (larger) and half of which were preceded by happy eye whites (smaller).

In separate scans, subjects viewed presentations of "eye blacks" (fig. S1B), inverse, "negative" images of the fearful and happy eye-white stimuli, masked in the same fashion. Because "edge" information was identical in the eye-white and eye-black conditions, the eye-black condition tested whether it was the eye outline that determined amygdala response or the size of the white scleral field. Thus, eye-black stimuli of an identical size, shape, and positioning were presented within-subject to show that the size of the more ecologically valid eye whites is a basic and important stimulus of interest to the amygdala.

Figure 1 shows that signal intensity within the ventral amygdala was greater to fearful than to happy eye whites ($x = -15$, $y = -4$, $z = -19$; $P = 0.0000004$, uncorrected) and also shows the predicted expression by sclera color interaction [$F(1, 19) = 10.69$, $P = 0.004$]. All subjects reported being unaware of the presence of the masked eye stimuli (*11*). No other area of the amygdala was differentially responsive to the fearful versus happy eye-black stimuli ($P > 0.05$). The ventral locus observed here is compelling because in the human, the ventral amygdala comprises the basolateral complex (*12*) where the majority of subcortical and cortical inputs to the amygdaloid system converge (*2*, *7*, *8*). Responsivity here to eye whites, but not to eye blacks, appears to be driven by the size of the white scleral field and not by the outline of the eye, a finding that may be consistent with data showing that the amygdala is more responsive to low than to high spatial frequency information (*13*). Future studies could determine if this is a response to fearful eyes per se or indicates a more general mechanism (e.g., size or intensity). In the interim, this finding augments data showing that the top half of a fearful face is sufficient to produce amygdala response (*4*) by specifically implicating the sclera. Finally, backward masking is shown here to be a useful strategy for examining component processing of faces (*11*).

Facial expressions of emotion are complex configural stimuli. Although there are holistic messages to be discerned (e.g., "that person is afraid of something"), this demonstration offers one example of a simpler rule that a subset of neuronal systems could use to prime additional circuits that will decode more detailed facial information and/or ready response systems for the potential outcomes predicted by this rule (fig. S2).

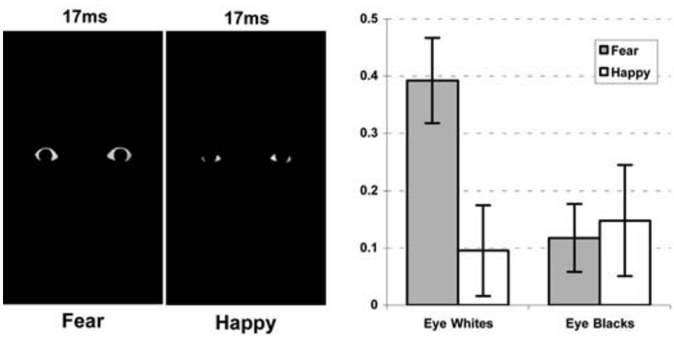

Fig. 1. (**Left**) Examples of the eye-white stimuli. (**Right**) Greater signal increases in the left ventral amygdala occurred to fearful eye whites than to happy eye whites, fearful eye blacks, and happy eye blacks (fig. S1) (*11*). The *y* axis shows the percent signal change from fixation.

References and Notes

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10. We studied healthy, right-handed, male subjects (mean age 21.9 ± 1.34 years) for consistency with our previous study (*1*) and to minimize between-subject signal heterogeneity related to handedness and/or gender differences. We scanned 27 subjects and excluded data from seven for excessive movement (>1.5 mm, 4 subjects), brain or visual abnormalities (2 subjects), or post-scan Beck Depression Inventory scores > 10 (1 subject).
11. Materials and methods are available as supporting material on *Science* Online.
12. We used an imaging protocol focused on the amygdala (*7*) that provides excellent coverage even in ventral and medial regions. The mean signal-to-noise ratio after spatial filtering (full width at half maximum, 6 mm) at the ventral amygdala locus reported here was more than 100 to 1.
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Supporting Online Material
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Materials and Methods
Figs. S1 and S2
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[1]Departments of Psychiatry and Psychology and The Waisman Center, W. M. Keck Laboratory for Brain Imaging and Behavior, University of Wisconsin, Madison, WI, USA. [2]Department of Psychology, Harvard University, Cambridge, MA, USA. [3]Department of Psychology, Tufts University, Medford, MA, USA. [4]Department of Psychological and Brain Sciences, Dartmouth College, Hanover, NH, USA.

*To whom correspondence should be addressed. E-mail: pwhalen@wisc.edu