Data Supplement for Pinkham et al., Abnormal Modulation of Amygdala Activity in Schizophrenia in Response to Direct- and Averted-Gaze Threat-Related Facial Expressions, American Journal of Psychiatry (doi: 10.1176/appi.ajp.2010.10060832)

## **Supplemental Data**

**Participants** 

Direct comparison of the 11 patients who were excluded from the analyses due to poor image quality and motion artifact and the 35 who were included in the analyses showed no significant differences in gender, handedness, ethnicity, parental education, positive or negative symptom severity, or CPZ equivalent (p>.25 for all comparisons). Similarly, these two groups did not significantly differ in age or education (p=.147 and p=.134, respectively).

Imaging Stimuli and Task

A novel stimulus set was created from a larger database of 3D emotional facial displays (see reference 24 in the article) that allowed for manipulations of horizontal head tilt resulting in both direct and averted gaze facial expressions. Prior to inclusion in the task, candidate images were pilot tested for recognition accuracy of target emotion, and only stimuli correctly identified as expressing the target emotion by at least 80% of raters were considered for inclusion.

Figure S1 shows the visual format of the task and response options. This study used a customized scroll-wheel device that allows both cursor movements in one axis (rotating wheel) and response selection (depressing wheel) (fORP; Current Designs, Inc.; Philadelphia, PA). Participants therefore rotated the wheel to move the selection box up and down to highlight their potential response and then pressed the wheel to select their answer. Prior to scanning, participants completed a practice task of basic emotion recognition to familiarize themselves with task pacing and use of the response device.

## Behavioral Performance

A repeated-measures ANOVA was utilized to assess response time. Stimulus emotion (anger vs. fear) and gaze (direct vs. averted) were entered as within-subjects factors and participant group (control vs. patient) was entered as the between-subject factor. Both the emotion by gaze interaction (F(1,68)=4.72, p=.033) and the gaze by group interaction (F(1,68)=4.06, p=.048) were significant. Across both groups, directed fear (mean: 2.04 sec) was identified more quickly than averted fear (mean: 2.14 sec), and both directed and averted anger were recognized equally fast (means: 2.25 sec and 2.20 sec, respectively). The group by gaze interaction demonstrated that control participants showed relatively equal response times for direct (mean: 2.11 sec) and averted (mean: 2.09 sec) expressions, but that patients showed faster response times to direct (mean: 2.15 sec), relative to averted (mean: 2.25), expressions.

## Voxelwise Comparisons Across the Acquisition Slab

A main effect of gaze was evident in several occipital regions, left precentral gyrus and bilateral middle temporal gyrus. All regions showed greater activity in response to direct vs. averted gaze expressions. Further, a main effect of emotion revealed several regions in which fear expressions elicited greater activation than anger expressions and two regions in which the opposite pattern was seen. Among regions showing a greater response to fear were bilateral middle frontal gyrus, left inferior frontal gyrus, left superior frontal gyrus, and left fusiform gyrus. In contrast, the visual areas of left anterior lingual gyrus and right posterior lingual gyrus showed greater responses to anger expressions relative to fear expressions (Figure S3).

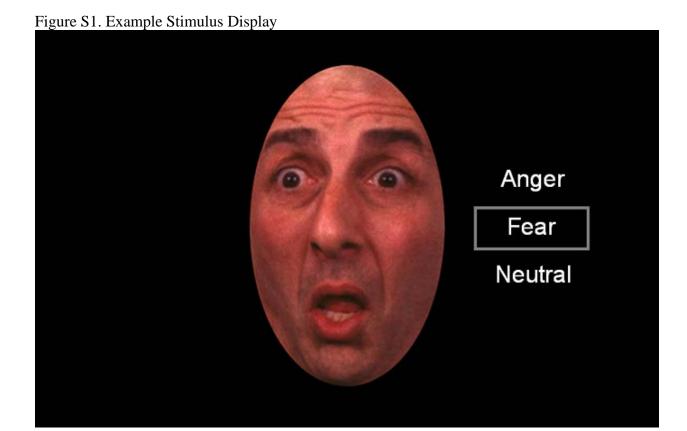
Regions demonstrating an interaction between gaze and emotion were also identified in this voxelwise analysis (Figure S4). These regions included bilateral thalamus, left inferior

occipital gyrus and right lingual gyrus. The pattern in each of these regions generally conformed to directed anger and averted fear eliciting greater responses than averted anger and directed fear (a contrast of 1, -1, -1, 1 for directed anger, averted anger, directed fear, and averted fear).

**Table S1. Neural Regions Showing Specified Effects** 

Region Regions Showing	Cluster size	Coordinates			
		X	У	Z	Peak Z
Main Effect of Gaze (Direct > Averted)					
L inferior occipital gyrus (BA17)	163	-26	-98	-6	4.24
L lingual gyrus (BA18)	143	-2	-80	-4	3.70
L precentral gyrus (BA 44)	90	-56	18	2	3.70
L middle temporal gyrus	57	-44	-44	-4	4.01
R middle temporal gyrus	57	50	-40	-8	3.38
R middle temporal gyrus	54	58	-22	-12	3.05
Main Effect of Emotion (Fear > Anger)					
L middle frontal gyrus (BA46)	258	-38	54	-2	4.58
L inferior frontal gyrus (BA45)	100	-50	26	14	3.08
R middle frontal gyrus (BA10)	98	32	62	2	3.36
L posterior lingual gyrus (BA17)	93	-10	-90	-4	3.66
L superior frontal gyrus (BA10)	85	-24	58	10	3.09
L fusiform gyrus (BA37)	69	-58	-52	-18	3.73
Main Effect of Emotion (Anger > Fear)					
L anterior lingual gyrus (BA18)	219	-8	-80	-10	5.09
R posterior lingual gyrus (BA17)	77	10	-88	10	3.94
Emotion by Gaze Interaction (DA and AF > AA and DF)					
R thalamus	134	12	-10	14	3.87
L inferior occipital gyrus (BA18)	80	-38	-84	-12	3.56
L thalamus	75	-10	-14	12	3.59
R lingual gyrus (BA 17)	49	6	-94	4	3.21

L=Left, R=Right, DA=directed anger, AF=averted fear, AA=averted anger, DF=directed fear. Anatomical labels and brodmann areas, where appropriate, were assigned according to Talairach and Tournoux (reference 40 in the article). All clusters significant at p<0.01, corrected.



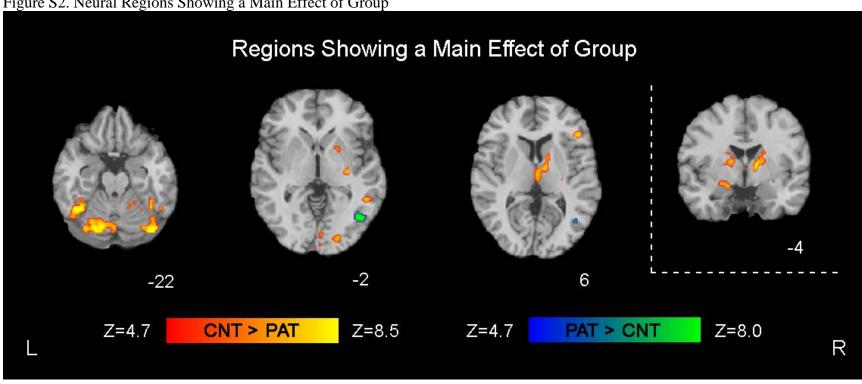
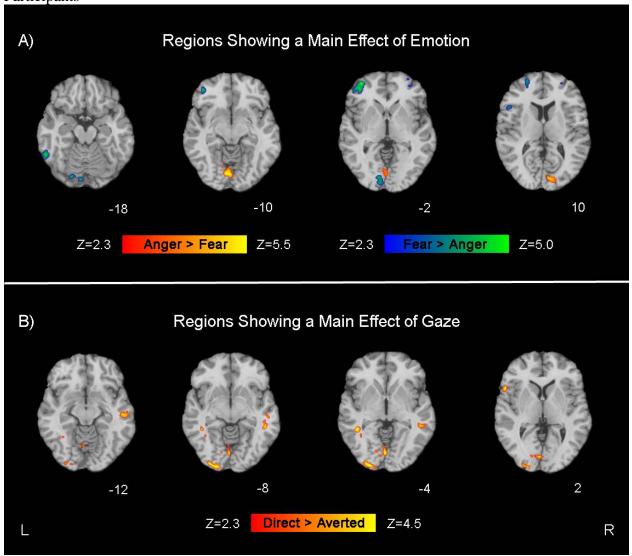


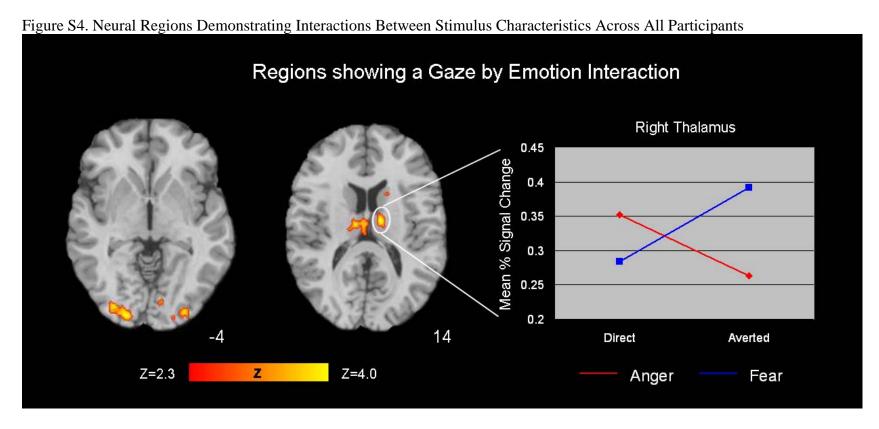
Figure S2. Neural Regions Showing a Main Effect of Group

Images displayed at p<0.05 (FWE corrected, cluster >50). Insert showing area of greater activation for control participants relative to patients in left amygdala displayed at a cluster level correction of p<0.0001.

Figure S3. Neural Regions Demonstrating Main Effects of Stimulus Characteristics Across All Participants



A) Main effect of emotion. B) Main effect of gaze. Images cluster level corrected at p<0.01.



Mean percent signal change extracted from the peak voxel within right thalamus cluster to demonstrate the direction of the interaction. Images cluster level corrected at p<0.01.