

Supplemental Methods

Model-fitting.

A reinforcement-based learning model was fit to the choice data of the participants to determine two free parameters: the learning rate and the inverse temperature (procedures were adjusted from Averbeck et al., 2013; Costa, Tran, Turchi, & Averbeck, 2014). On every trial during the passive avoidance task, participants had the choice to either approach or avoid an object. At the start of the task, the value, V , for each stimulus, i , was set to 0. The prediction error, PE , was calculated using the feedback, F [coded 1 (\$5 reward), 0.2 (\$2), -0.2 (\$2 loss) or -1 (\$5 loss)], and the value, V , for the stimulus via the following formula:

$$PE(t) = F(t) - V_i(t)$$

where t indicates the current trial and i the stimulus. The value of the stimulus was updated using the value of the stimulus from the previous trial plus the prediction error of the previous trial multiplied by the learning rate α via the following formula:

$$V_i(t) = V_i(t - 1) + \alpha PE(t - 1)$$

Of note, participants only received feedback when they approached an object and the value, V , of a stimulus was not updated when they chose to avoid that stimulus. The free parameters of the model, the learning rate α and the inverse temperature β , were estimated through nonlinear optimization. This was done by maximizing the likelihood of the actual choices of participants to approach or avoid each stimulus. The probability, P , of approaching a stimulus i , given its value, V , was calculated using the softmax rule:

$$P_i(t) = \frac{e^{\beta V_i(t)}}{1 + e^{\beta V_i(t)}}$$

The log-likelihood was then calculated as follows:

$$LL = \sum_{t=1}^T \log[c_k(t)P_i(t) + (1 - c_k(t))(1 - P_i(t))]$$

where $c_k = 1$ when a participant approached stimulus i in trial t and $c_k = 0$ when a subject avoided stimulus i and T is the total number of trials. The negative log-likelihood was minimized using `fminsearch` in Matlab. The initial values of α were drawn from the standard uniform distribution on the open interval $(0, 1)$. The initial values of β were drawn from the standard uniform distribution. The model fit was repeated 100 times, each time with different initial values for the free parameters drawn from these distributions. The values of the free parameters were set at the value for which the iteration resulted in the minimum log-likelihood.

The overall free parameters across the group (α and β) were then calculated by taking the average across all individually estimated α and β parameters. These parameters were then used for all participants.

Supplemental Results

The group analysis of the BOLD data was performed on the un-modulated regression coefficients from individual subject analyses. The un-modulated coefficients were entered into a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (choice: approach, refuse) ANOVA in the choice-phase and a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (feedback type: reward, punishment) in the feedback-phase.

Supplemental Results 1.1: Un-modulated Choice-Phase Data

Diagnosis-by-Choice Interaction. A significant diagnosis-by-choice interaction was observed for the un-modulated choice-phase data in right superior temporal gyrus (Table S1).

Patients with Generalized Anxiety Disorder showed reduced activation relative to healthy controls when not choosing an object [$t=2.529$, $p=.014$], but the groups did not differ when choosing objects [$t=1.597$, $p=.114$].

Main Effect of Diagnosis. A significant main effect of diagnosis was observed in left culmen (Table S1). Patients with Generalized Anxiety Disorder showed greater activation relative to healthy controls.

Main Effect of Choice. Significant main effects of choice were observed in regions including dorsomedial frontal cortex, right superior frontal gyrus, two regions of rostral anterior cingulate gyrus, superior temporal gyrus, left middle temporal gyrus and left inferior parietal cortex (Table S1). In left inferior parietal cortex, dorsomedial frontal cortex and both regions of rostral anterior cingulate cortex, greater activation was observed when choosing relative to not choosing objects. In right superior frontal gyrus, superior temporal gyrus and left middle temporal gyrus, greater activation was observed when not choosing relative to choosing objects.

Supplemental Results 1.2: Un-Modulated Feedback Data

Diagnosis-by-Feedback Type Interaction. No regions showed a significant diagnosis-by-feedback type interaction.

Main Effect of Diagnosis. A significant main effect of diagnosis was observed in regions including left medial frontal gyrus, left inferior frontal gyrus, bilateral putamen, left posterior cingulate cortex, right cingulate gyrus, right middle temporal gyrus, two regions of left middle temporal gyrus and left supramarginal gyrus (Table S2). In all regions, patients with Generalized Anxiety Disorder showed greater activation relative to healthy controls.

Main Effect of Feedback Type. Regions showing a significant main effect of feedback type included dorsomedial frontal cortex, bilateral medial frontal gyrus, bilateral lateral frontal

cortex, left orbitofrontal cortex, bilateral ventral striatum, bilateral anterior insula cortex, right insula cortex, left posterior cingulate cortex, left middle temporal gyrus, left temporal pole and right inferior parietal lobule (Table S2). Greater activation to reward relative to punishment was observed in bilateral lateral frontal cortex, left orbitofrontal cortex, bilateral ventral striatum, right insula cortex, left posterior cingulate cortex, left middle temporal gyrus and right inferior parietal lobule. Greater activation to punishment relative to reward was observed in dorsomedial frontal cortex, bilateral medial frontal gyrus, bilateral anterior insula cortex and left temporal pole.

Supplemental Results 2.0: Modulated Choice-Phase Data-Supplemental Analysis.

The group analysis of the BOLD data was performed on the modulated regression coefficients from individual subject analyses. The modulated coefficients were entered into a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (choice: approach, refuse) ANOVA in the choice-phase and a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (feedback type: reward, punishment) in the feedback-phase.

Given our a priori hypotheses regarding ventromedial prefrontal cortex and striatum, an additional analysis at a more lenient threshold ($p=.02$) was conducted examining these regions. This revealed a significant main effect of diagnosis within ventromedial prefrontal cortex (see Table S3) where patients with Generalized Anxiety Disorder showed reduced BOLD response modulated by EV relative to HCs. Furthermore, significant diagnosis-by-choice interactions were observed within ventromedial prefrontal cortex, ventral striatum and caudate. In ventromedial prefrontal cortex, patients with Generalized Anxiety Disorder failed to show the typical drop in activation modulated by EV when not choosing objects [$t=2.713$, $p=.008$], though the groups did not significantly differ in modulated activation when choosing objects [$t=.465$, $p=.643$]. In

striatum and caudate, patients with Generalized Anxiety Disorder showed reduced activation modulated by EV when not choosing objects [$t= 2.400$ & 3.181 respectively, $p<.019$], though significant differences were not observed when choosing objects [$t= 1.168$ & $.543$ respectively, $p>.247$].

Supplemental Results 3.1: Choice-Phase Data Modulated by Expectancies of Reinforcement

The group analysis of the BOLD data was performed on the modulated regression coefficients from individual subject analyses. The modulated coefficients were entered into a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (choice: approach, refuse) ANOVA in the choice-phase and a 2 (diagnosis: Generalized Anxiety Disorder, healthy controls) by 2 (feedback type: reward, punishment) in the feedback-phase.

Main Effect of Choice. Significant main effects of choice were observed in regions including bilateral anterior insula cortex, dorsomedial prefrontal cortex/dorsal anterior cingulate cortex and bilateral visual cortex (Table S4). Significantly greater modulated activation was observed when choosing relative to refusing an object in bilateral visual cortex. Significantly greater modulated activation was seen when refusing an object relative to choosing an object in all other regions.

Supplemental Results 3.2: Feedback Data Modulated by PE

Main Effect of Feedback Type. Regions showing a significant main effect of feedback type included bilateral anterior insula cortex /inferior frontal gyrus and thalamus (Table S4). All regions showed increased modulated activation to reward relative to punishment feedback.

Supplemental Results 4.0: Examining impairment in individuals with Generalized Anxiety Disorder and individuals with Generalized Anxiety Disorder+Social Anxiety Disorder separately relative to healthy individuals

To ensure that the group differences detailed above of individuals with Generalized Anxiety Disorder relative to healthy comparison adults was not driven only by individuals who only presented with Generalized Anxiety Disorder or only those individuals who were comorbid for Generalized Anxiety Disorder and Social Anxiety Disorder, we conducted two further ANOVAs: one 2(diagnosis: Generalized Anxiety Disorder only, healthy controls) by 2(feedback type: reward, punishment) and one 2(diagnosis: Generalized Anxiety Disorder+Social Anxiety Disorder, healthy controls) by 2(feedback type: reward, punishment). These revealed very similar results whether the performance of healthy individuals was contrasted against individuals with Generalized Anxiety Disorder or individuals with Generalized Anxiety Disorder+Social Anxiety Disorder. The analysis contrasting healthy controls and participants with Generalized Anxiety Disorder+Social Anxiety Disorder replicated the findings from the original analysis in the diagnosis-by-feedback type interaction and in the main effect of diagnosis in all regions at the FWE corrected threshold. When the analysis was conducted comparing healthy controls and participants with Generalized Anxiety Disorder, the findings from the original analysis were replicated in the main effect of diagnosis in all regions at the FWE corrected threshold with the exception of the ventral striatum. However, this result was significant at only a slightly less stringent threshold ($p=.006$). With respect to the diagnosis-by-feedback type interaction, the lentiform nucleus/putamen results were also present though at a less stringent threshold (left lentiform/putamen, $p=.015$, right lentiform/putamen, $p=.034$).

TABLE S1. Brain Regions Demonstrating Differential Un-Modulated BOLD Response During the Choice-Phase of a Passive Avoidance Task in 32 Healthy Comparison Individuals and 46 Patients with Generalized Anxiety Disorder

Region ^a	Coordinates of Peak Activation ^b						F	p	Voxels
	Left/Right	BA	x	y	z				
<u>Diagnosis-by-Choice Interaction</u>									
superior temporal gyrus	Right	38	43.5	22.5	-15.5	13.45	.0005	20	
<u>Main Effect of Diagnosis</u>									
culmen	Left		-1.5	-52.5	-9.5	12.22	.0008	21	
<u>Main Effect of Choice</u>									
mid-line structures			-16.5	-49.5	-21.5	100.0	<.0001	7527	
<i>striatum/thalamus*</i>	Left		-7.5	-19.5	5.5	100.0	<.0001	2890	
<i>cingulate gyrus*</i>	Left		-1.5	1.5	35.5	73.38	<.0001	372	
<i>culmen*</i>	Left		-16.5	-49.5	-21.5	100.0	<.0001	372	
<i>culmen*</i>	Right		22.5	-55.5	-21.5	43.04	<.0001	97	
<i>culmen*</i>	Right		19.5	-52.5	-6.5	34.34	<.0001	43	
dorsomedial frontal cortex	Right	8	7.5	34.5	38.5	16.83	.0001	27	
superior frontal gyrus	Right	8	31.5	22.5	50.5	23.27	.0001	157	
rostral anterior cingulate gyrus	Right	32	10.5	28.5	20.5	16.03	.0001	60	
rostral anterior cingulate gyrus	Right	32	1.5	40.5	8.5	13.15	.0005	20	
superior temporal gyrus	Right	22	61.5	-28.5	5.5	28.98	<.0001	348	
middle temporal gyrus	Left	39	-43.5	-70.5	11.5	13.52	.0004	38	
inferior parietal	Left	40	-46.5	-31.5	41.5	100.1	<.0001	1115	
middle occipital gyrus	Right	18	28.5	-82.5	-9.5	40.64	<.0001	207	
middle occipital gyrus	Left	19	-25.5	-82.5	-9.5	38.24	<.0001	99	
culmen/parahippocampal	Right	19	19.5	-52.5	-6.5	34.34	<.0001	133	
paracentral lobule	Left	6	-7.5	-31.5	53.5	28.00	<.0001	116	
cuneus	Right	18	7.5	-73.5	20.5	15.72	.0002	53	
culmen	Left	19	-13.5	-61.5	-3.5	16.12	.0001	25	

^a According to the Talairach Daemon Atlas (<http://www.nitrc.org/projects/tal-daemon/>).

^b Based on the Tournoux & Talairach standard brain template, BA= Brodmann's Area

* indicates local maxima at $p=.0001$

TABLE S2. Brain Regions Demonstrating Differential Un-Modulated BOLD Response During the Feedback-Phase of a Passive Avoidance Task in 32 Healthy Comparison Individuals and 46 Patients with Generalized Anxiety Disorder

Region ^a	Coordinates of Peak Activation ^b						F	p	Voxels
	Left/Right	BA	x	y	z				
<u>Main Effect of Diagnosis</u>									
medial frontal gyrus	Left	6	-7.5	43.5	35.5	18.25	<.0001	41	
inferior frontal gyrus	Left	46	-49.5	28.5	14.5	15.61	.0002	30	
putamen	Left		-34.5	-28.5	8.5	20.84	<.0001	439	
putamen	Right		28.5	4.5	-0.5	16.30	.0001	133	
posterior cingulate cortex	Left	29	-7.5	-46.5	17.5	16.83	.0001	60	
cingulate gyrus	Right	31	7.5	-22.5	41.5	15.61	.0002	34	
middle temporal gyrus	Right	21	55.5	1.5	-6.5	16.08	.0001	54	
middle temporal gyrus	Left	38	-49.5	1.5	-15.5	19.15	<.0001	46	
middle temporal gyrus	Left	21	-49.5	-43.5	5.5	13.35	.0005	27	
supramarginal gyrus	Left	40	-55.5	-46.5	26.5	14.39	.0003	37	
precentral gyrus	Right	4	40.5	-13.5	38.5	15.34	.0002	22	
postcentral gyrus	Left	43	-55.5	-7.5	14.5	12.80	.0006	18	
paracentral lobule	Left	5	-22.5	-40.5	47.5	11.11	.0013	22	
lingual gyrus	Right	17	7.5	-91.5	-0.5	12.39	.0007	20	
precuneus	Right	7	4.5	-37.5	47.5	13.05	.0005	76	
<u>Main Effect of Feedback Type</u>									
dorsomedial frontal cortex	Left	9	-7.5	40.5	26.5	100.0	<.0001	28	
medial frontal gyrus	Right	6	10.5	1.5	59.5	100.0	<.0001	446	
medial frontal gyrus	Left	9	-22.5	34.5	26.5	100.0	<.0001	53	
lateral frontal cortex	Right	11	40.5	46.5	6.5	100.0	<.0001	26	
lateral frontal cortex	Left	46	-40.5	46.5	5.5	100.0	<.0001	18	
orbitofrontal cortex	Left	11	-19.5	43.5	-9.5	100.0	<.0001	19	
ventral striatum	Right		16.5	13.5	-3.5	100.0	<.0001	173	
ventral striatum	Left		-10.5	13.5	-3.5	100.0	<.0001	137	
anterior insula cortex	Right	44/13	40.5	7.5	5.5	100.0	<.0001	109	
anterior insula cortex	Left	13	-37.5	7.5	8.5	100.0	<.0001	85	
insula cortex	Right	13	34.5	-4.5	14.5	100.0	<.0001	24	

posterior cingulate cortex	Left	31	-1.5	-40.5	32.5	100.0	<.0001	37
middle temporal gyrus	Left	37	-55.5	-49.5	-9.5	100.0	<.0001	834
temporal pole	Left	38	-43.5	7.5	-18.5	100.0	<.0001	46
inferior parietal lobule	Right	40	40.5	-40.5	50.5	100.0	<.0001	257
middle occipital gyrus	Right	19	34.5	-61.5	8.5	100.0	<.0001	558
parahippocampal gyrus	Right	19	28.5	-40.5	-0.5	100.0	<.0001	46
paracentral lobule	Left	5	-4.5	-37.5	50.5	100.0	<.0001	26
cuneus	Right	17	16.5	-91.5	8.5	100.0	<.0001	20
precentral gyrus	Right	6	25.5	-19.5	50.5	16.12	.0001	18

^a According to the Talairach Daemon Atlas (<http://www.nitrc.org/projects/tal-daemon/>).

^b Based on the Tournoux & Talairach standard brain template, BA= Brodmann's Area

TABLE S3. Brain Regions Demonstrating Differential BOLD Response Modulated by Expected Value at $p=.02$ During a Passive Avoidance Task in 32 Healthy Comparison Individuals and 46 Patients with Generalized Anxiety Disorder

Region ^a	Coordinates of Peak Activation ^b					F	p	Voxels
	Left/Right	BA	x	y	z			
<u>Main Effect of Diagnosis</u>								
ventromedial prefrontal cortex	Right	10	10.5	49.5	-3.5	8.577	.0045	25
<u>Diagnosis-by-Choice Interaction</u>								
ventromedial prefrontal cortex	Right	10/11	7.5	40.5	-12.5	9.173	.0034	24
caudate	Right		16.5	16.5	14.5	9.173	.0034	12
ventral striatum	Left		-13.5	4.5	-3.5	10.91	.0015	15

^a According to the Talairach Daemon Atlas (<http://www.nitrc.org/projects/tal-daemon/>).

^b Based on the Tournoux & Talairach standard brain template, BA= Brodmann's Area

TABLE S4. Brain Regions Demonstrating Differential BOLD Response Modulated by Expected Value/Prediction Error During a Passive Avoidance Task in 32 Healthy Comparison Individuals and 46 Patients with Generalized Anxiety Disorder

Region ^a	Coordinates of Peak Activation ^b					F	p	Voxels
	Left/Right	BA	x	y	z			
<u>Main Effect of Choice Modulated by Expected Value</u>								
dorsomedial frontal cortex	Left	32	-7.5	7.5	44.5	23.87	<.0001	66
anterior insula cortex	Left	13	-28.5	19.5	8.5	29.10	<.0001	234
anterior insula cortex	Right	13	28.5	16.5	-3.5	19.69	<.0001	118
cuneus/lingual gyrus	Right	17	16.5	-82.5	8.5	44.58	<.0001	372
cuneus/lingual gyrus	Left	17	-10.5	-94.5	8.5	20.41	<.0001	154
<u>Main Effect of Feedback Modulated by Prediction Error</u>								
AIC/iFG	Left	47/13	-28.5	19.5	-3.5	19.69	<.0001	140
AIC/iFG	Right	13/47	31.5	19.5	-0.5	11.76	.001	32
Thalamus	Left		-1.5	-16.5	5.5	16.61	.0001	36

^a According to the Talairach Daemon Atlas (<http://www.nitrc.org/projects/tal-daemon/>).

^b Based on the Tournoux & Talairach standard brain template, BA= Brodmann's Area
AIC/iFG= anterior insula cortex/inferior frontal gyrus