SUPPLEMENTARY ONLINE MATERIALS

Anterior cingulate cortex responds differentially to expectancy violation and social rejection

L. H. Somerville, T. F. Heatherton, & W. M. Kelley

Nature Neuroscience

Subjects. Forty-two subjects between the ages of 18 and 24 were recruited from the local Dartmouth community. Twenty subjects participated in Study 1 (10 male, mean age = 20), and 22 subjects participated in Study 2 (10 male, mean age = 19). Subjects reported no significant abnormal neurological history, were native speakers of English, had normal or corrected-to-normal visual acuity, and were strongly right-handed as measured by the Edinburgh Handedness Inventory. Subjects received course credit or were paid for their participation and gave informed consent in accordance with the guidelines set by the Committee for the Protection of Human Subjects at Dartmouth College.

Pre-scan Session. Approximately two weeks prior to fMRI sessions, subjects attended a brief informational session in the lab. First, they were screened to verify their eligibility for the study and ability to enter the fMRI scanning environment. They were then given a detailed cover story outlining the purpose of the study. Subjects were told that this was a multi-university study on how individuals make first impressions. They were instructed that during the scanning session, they would be rating the faces of subjects from the other participating institutions, and in turn, these same individuals would be rating their face in the interim. To ensure believability, we took a photograph of each subject, which they believed would be sent to the other universities, and rated by the 'participants' between that date and their scanning session. Following this session, their

photographs were deleted and all ratings and face stimuli were created and compiled randomly by experimenters.

Functional Imaging. Anatomical and functional whole-brain imaging was performed on a 1.5 T GE Signa Scanner (General Electric Medical Systems, Milwaukee, WI). Anatomical images were acquired using a high-resolution 3-D spoiled gradient sequence (SPGR; 124 sagittal slices, TE = 6 ms, TR = 25 ms, flip angle = 25°, 1 x 1 x 1.2 mm voxels). Functional images were collected in four functional runs of 338 time points each, using a gradient spin-echo, echo-planar sequence sensitive to blood-oxygen level-dependent contrast (T2*) (20 axial slices per whole-brain volume, 3.75-mm in-plane resolution, 5-mm thickness, 1-mm skip, TR = 2000 ms, TE = 35 ms, flip angle = 90°).

Procedure. Prior to functional scanning, subjects were reminded that they were participating in a multi-university study and that they would be making judgments about individuals from other universities. In Study 1, for each face subjects were instructed to answer the question, "*Do you think you would like this person?*" In Study 2, the judgment was changed to "*Do you think this person would like you?*" All other parameters across the two studies were identical. In both studies, subjects were further instructed that some of the individuals from other universities had made similar likeability judgments about the subject and that when such information was available, subjects would receive feedback indicating how the individual had rated the subject. As such, each trial consisted of one to three components: (1) a cue-judgment component where subjects rated each face, (2) a variable-length delay period, and (3) a feedback component where subjects learned whether they were accepted or rejected and whether this feedback was congruent or incongruent with their judgments (see **Fig. 1** in main text**)**.

A portion of these trials terminated after the cue period (20%) or the delay period (20%). The remaining 60% of trials ran to completion. In total, each subject completed 160 partial and 240 complete trials. Partial trials were included so that unique estimates of the hemodynamic response function could be computed for each subcomponent of the trial[1]. To the subject, trials either terminated prematurely or ran to completion depending on whether the target individual had completed a rating of the subject or not. Partial and complete trials were randomly intermixed with periods of fixation during which subjects simply fixated a cross hair.

Faces were counterbalanced across subjects so that for half of the faces in complete trials, subjects received positive feedback, and for the remaining half, subjects received negative feedback. Because subject responses dictated whether the trial would be subsequently coded as 'congruent' or 'incongruent', the number of trials per condition varied across subjects. The mean numbers of trials per condition were as follows: Congruent Accepted – 65 trials; Congruent Rejected – 52 trials; Incongruent Accepted – 52; Incongruent Rejected – 64 trials, with an average of 7 trials not responded to in the time allotted.

Visual stimuli were generated using PsyScope software[2] and presented using an LCD projector (Epson model ELP-7000), viewable by an angled mirror mounted on top of the head coil. Stimuli were presented centrally on an otherwise black screen. Two fiber-optic key presses, one held in each hand, were used to collect subjects' 'like' and 'dislike' responses, which were recorded through the PsyScope button box (New Micros, Dallas, TX).

Following the fMRI scanning session, subjects were given an exit questionnaire, and no subject reported that they did not believe the cover story. Moreover, when debriefed, all subjects expressed surprise when they were told the cover story was a ruse.

Data Analysis. fMRI data were analyzed using the general linear model for event-related designs in SPM99 (Wellcome Department of Cognitive Neurology, London, UK). For each functional run, data were preprocessed to remove sources of noise and artifact. Functional data were corrected for differences in acquisition time between slices for each whole-brain volume, realigned within and across runs to correct for head movement, and coregistered with each participant's anatomical data. Functional data were then transformed into a standard anatomical space (3-mm isotropic voxels) based on the ICBM 152 brain template (Montreal Neurological Institute), which approximates the Talairach and Tournoux[3] atlas space. Normalized data were then spatially smoothed (6 mm full-width-at-half-maximum [FWHM]) using a Gaussian kernel. Analyses took place at two levels: formation of statistical images and regional analysis of hemodynamic responses.

For each participant, a general linear model incorporating six task effects (cue, delay and four types of feedback which comprised four cells of the 2 x 2 repeated measures ANOVA: congruent and positive feedback [CP], congruent and negative feedback [CN], incongruent and positive feedback [IP], and incongruent and negative feedback [IN]) and covariates of no interest (a session mean, a linear trend, and six movement parameters derived from realignment corrections) were used to compute parameter estimates (β) and contrast images (containing weighted parameter estimates) for each comparison at each voxel and for each subject. Of interest was the neural activity that accompanied the feedback portion of trials. Contrast images for each subject comparing each feedback condition to the baseline control (fixation) were then submitted to a second-level whole-brain voxel-wise ANOVA which yielded F-statistical maps for both main effects (expectancy violation and feedback type) and the interaction.

Functional ROIs were derived from the main effect maps and included voxels activated at a threshold of $P < 0.001$ (uncorrected) within 6mm of the peak activated voxel. In the expectancy violation main effect map, a ROI was identified in the dorsal anterior cingulate (dACC; BA32) containing 13 voxels (Talairach coordinates: xyz = -6, 28, 32). In the feedback main effect map, a ROI was identified in ventral anterior cingulate (vACC; BA32/10) at the confluence of the cingulate gyrus and middle frontal gyrus (16 voxels; Talairach coordinates: xyz = -6, 49, -13). Other regions demonstrating main effects of expectancy violation or feedback type at this threshold are listed in Table 1.

Mean signal change values for each subject and each condition were extracted for the dACC and vACC regions and submitted to an offline ANOVA to explicitly test the hypothesis that (1) dACC and vACC yielded dissociable patterns of activation, and (2) the dissociation was present in both studies. This was accomplished by performing a 2 x 2 x 2 x 2 ANOVA with three repeated factors (expectancy violation x feedback type x ACC region) and one between-subject factor (Study 1 versus Study 2). The results of the expectancy violation x region interaction and the feedback type x region interaction are depicted in the main manuscript. These interactions are significant in both Studies 1 and 2 when examined independently (**Supplementary Fig. 1**).

References

1. Ollinger, J. M., Corbetta, M., Shulman. G. L. Separating processes within a trial in event-related functional MRI. *Neuroimage*, **13**, 218-29 (2001).
2. Cohen, J. D., MacWhinney, B., Flatt, M., & Provost, J. Psyscope: A new graphic interactive environment for designing psychology experiments. *Behavioral Research Methods, Instruments, and Computers,* **25,** 257-271 (1993).

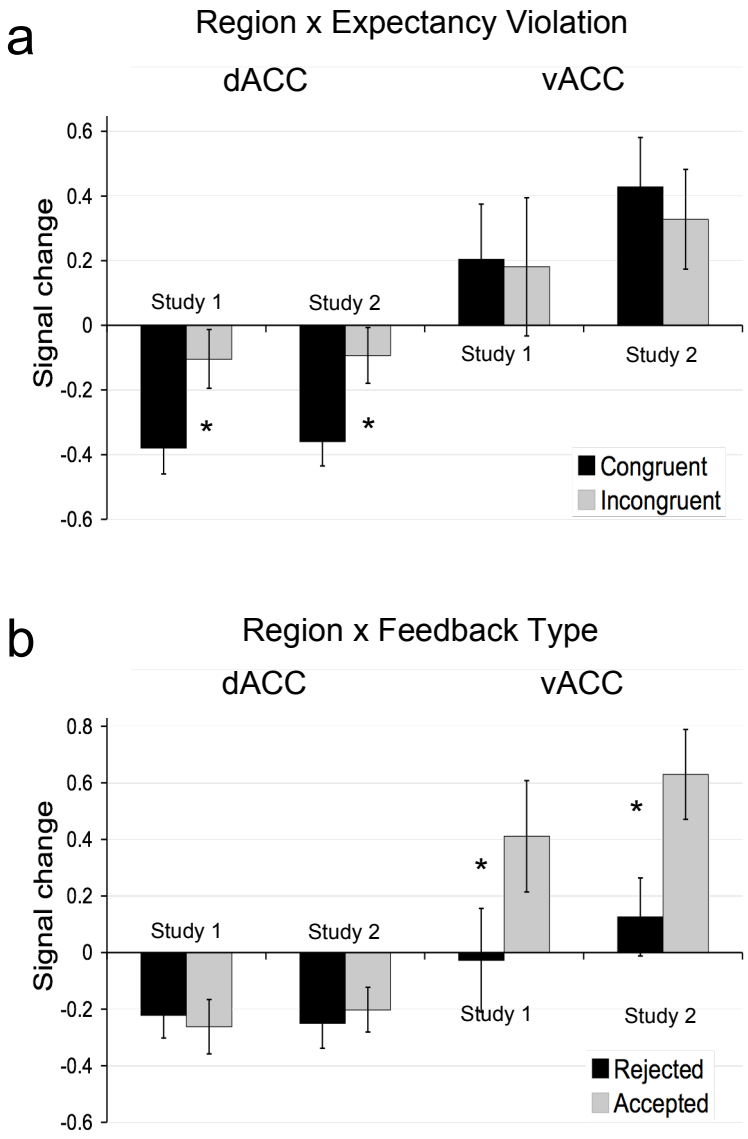
3. Talairach, J., & Tournoux, P. *Co-planar stereotaxic atlas of the human brain.* (M. Rayport, Trans.). New York, NY: Thieme Medical Publishers.

Table 1. Identification of BOLD signal changes associated with the main effects of expectancy violation and feedback type.

Brain Region		***F***	***x***	***y***	***z***
Main Effect of Expectancy Violation					
BA6	R Superior Frontal Gyrus	33.16	12	23	60
	R Putamen	32.92	-12	8	-16
BA10	R Superior Frontal Gyrus	26.90	21	62	13
	R Putamen	23.82	15	14	-13
	Thalamus	19.38	-9	23	-1
	Thalamus	18.30	-6	-32	7
BA21	R Middle Temporal Gyrus	17.63	48	-24	-6
	Thalamus	14.93	0	-5	9
BA40	R Inferior Parietal Lobule	14.92	59	-54	28
Main Effect of Feedback Type					
BA21	R Middle Temporal Gyrus	32.95	48	-24	-9
BA47	L Inferior Frontal Gyrus	29.60	-39	29	-1
BA8	L Middle Frontal Gyrus	24.45	-24	37	42
	Left Cerebellum	22.79	-3	-74	-14
	Left Cerebellum	22.38	-30	-49	-38
BA8	R Middle Frontal Gyrus	22.05	33	19	29
BA6	L Middle Frontal Gyrus	21.71	-24	-4	39
BA18	L Middle Occipital Gyrus	21.46	-21	-84	4
	R Insula	20.84	48	12	2
BA22	L Superior Temporal Gyrus	19.98	-42	-46	11
BA6	R Middle Frontal Gyrus	19.35	30	-7	36
BA18	R Middle Occipital Gyrus	16.75	30	-76	4
BA18	R Cuneus	16.11	9	-89	27
BA7	L Superior Parietal Lobule	16.02	-18	-44	46
	Right Cerebellum	15.50	12	-80	-21
BA6	L Superior Frontal Gyrus	15.24	-18	50	6
BA6	L Superior Frontal Gyrus	14.89	-18	3	52

Activations determined to be significant ($p < 0.001$, uncorrected) are listed along with the best estimate of their location. BA = approximate Brodmann's area location. Coordinates are from the Talairach & Tournoux atlas[3]. Locations of the activations are determined based on the functional responses superimposed on averaged anatomical MRI images and are referenced to the Talairach atlas.

Supplementary Figure 1.



Supplementary Figure 1. The Region x Expectancy Violation and Region x Feedback Type interactions reported in Figure 1 were independently present in each study. **(a)** Voxels in the dACC (BA32: -6, 28, 32; 13 voxels) demonstrated a significant main effect of expectancy violation (incongruent > congruent; Study 1: $p < 0.03$; Study 2: $p < 0.001$). **(b)** Voxels in the vACC (BA32/10: -6, 49, -13; 16 voxels) demonstrated a significant main effect of feedback type (accepted > rejected; Study 1: $p < 0.02$; Study 2: $p < 0.001$).