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Dissociable roles of ventromedial prefrontal cortex (vmPFC) and rostral anterior cingulate cortex (rACC) in value representation and optimistic bias

Karina S. Blair *, Marcela Otero, Cindy Teng, Madeline Jacobs, Stephanie Odenheimer, Daniel S. Pine, R.J.R. Blair

National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA

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ABSTRACT

Optimistic bias (OB) is seen when individuals underestimate their probability of experiencing negative life events and overestimate their probability of experiencing positive life events. A reduced OB has been linked with increased depression symptoms. However, given the relevance of this information to mood and anxiety disorders, little is currently known regarding the neurobiology of OB. In the current study, we examine the neural basis of OB in healthy individuals (n = 33) during probability estimation of future positive and negative events occurring to themselves relative to other, comparable individuals. In line with previous work, subjects showed significant OB; they considered themselves significantly *more* likely to experience future positive and significantly *less* likely to experience future negative events relative to comparable others. Positive, relative to negative events, un-modulated by subjects' probability estimates, were associated with significantly greater activity within the ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC). Moreover, responses within both regions to positive events negatively related to the healthy subjects' self reports of depression symptoms. However, there was no significant modulation of activity in either region by the subject's OB, objectified as the level to which they thought the event was more likely [positive events] or less likely [negative events] to occur to them relative to comparable others. In contrast, activity within the rostral anterior cingulate cortex (rACC) was positively modulated by OB for positive events and activity within the anterior insula and dorsomedial prefrontal cortex (dmPFC) was negatively modulated by OB for negative events. However, there was no significant relationship between responsiveness within these regions and self reports of depression symptoms. The data are discussed with reference to current models of vmPFC, rACC and anterior insula functioning.

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Introduction

Optimistic bias (OB) is the tendency to believe that negative events are less likely, and positive events more likely, to happen to oneself than to others (Weinstein, 1980). It can lead to serious underestimations of health and economic risks. Biases can be resistant to change and contribute to an unwillingness to take preventative action. Significantly, reduced OB is seen in patients with depression where the extent of reduction is related to symptom severity (Strunk et al., 2006). Thus, an understanding of the neuro-cognitive systems mediating OB is important.

Very little work has considered the neural systems mediating OB/optimism (Sharot et al., 2007, 2011, 2012). However, two potentially separable functional systems have been implicated. Sharot et al. (2007) asked subjects to think about events that had occurred in the past or might occur in the future (e.g., 'winning an award' or 'the end of a romantic relationship') and the blood oxygen level dependent (BOLD) response to positive and negative events was contrasted. Within both the amygdala and ventromedial prefrontal cortex (vmPFC including subcallosal anterior cingulate cortex; sACC), BOLD responses were reduced when subjects imagined future negative relative to future positive events. Moreover, the degree of this difference in BOLD response within sACC correlated positively to a self-report measure of trait optimism. Sharot et al. (2011) examined BOLD responses to information updating the individual's probability estimates of potential future negative events occurring to the self. They reported that estimation errors calling for a positive update (i.e., the undesirable event was less likely to occur than the subject's estimate) were tracked within a rather more rostral and bilateral region of the medial prefrontal cortex (as well as the left inferior frontal cortex and right cerebellum). In contrast, a region of the right inferior frontal cortex extending into the insula tracked estimation errors calling for a negative update (i.e., the undesirable event was more likely to occur than the subject's estimate). In Sharot et al. (2011), more optimistic individuals showed reduced negative (but not positive) update tracking relative to less optimistic individuals. Finally, Sharot et al. (2012) reported that transcranial

* Corresponding author at: National Institute of Mental Health, 15K North Drive, MSC 2670, Bethesda, MD 20892, USA.
E-mail address: peschark@mail.nih.gov (K.S. Blair).

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magnetic stimulation (TMS) of the left, but not right, inferior frontal cortex (IFG) increased updating of the probability of negative events following information that the event was more likely than expected. TMS of either left or right IFG had a significant impact on updating subject estimations on the probability of negative events following information that the event was less likely than expected.

In the current study, we examined subjects' BOLD responses when they estimated the probability that a positive/negative event would occur to them in the future *relative to a similar other individual*. Moreover, we examined BOLD responses to positive and negative events with and without parametric *modulation by the subjects' estimate of the likelihood of that action occurring to them in the future* (i.e., their level of OB). Our aim was to address three issues.

First, what are the systems mediating the OB? We predicted that those regions related to optimism for future events (i.e., vmPFC; Sharot et al., 2007) and/or tracking estimation errors calling for positive or negative updates (i.e., rostral medical frontal cortex (rMFC) and inferior frontal gyrus (IFG)/insula; Sharot et al., 2011) would be modulated by the subjects' OB.

Second, is there dissociation in the regions mediating OB for positive relative to negative future events? Notably, Sharot et al. (2011) reported that estimation errors calling for a positive update were tracked within bilateral rMPFC (as well as left inferior frontal cortex and right cerebellum) while a region of right IFG/insula tracked estimation errors calling for a negative update. Moreover, disruption of left insula functioning by TMS reduced the negative updating of negative event probabilities following new information (Sharot et al., 2012). Interestingly, the insula has been implicated in the anticipation of aversive reinforcement expectancies during decision making tasks (Kuhnen and Knutson, 2005; Liu et al., 2007; Preuschoff et al., 2008; Wu et al., 2011). Given this and the findings of Sharot et al. (2011, 2012), we predicted that the IFG/insula might be relatively more involved in a subject's OB for future negative events.

Third, we also examined the relationship between OB-related BOLD responses and self-reported level of depressive symptomatology. As noted above, reduced OB is seen in patients with depression where the extent of reduction is related to symptom severity (Strunk et al., 2006). As optimism can, in some respects, be considered the inverse of depression, we predicted, following Sharot et al. (2007) that self-reported depression symptomatology might be related to value representations within vmPFC. The current study tests these predictions.

Material and methods

Subjects

Thirty-three right-handed subjects (eighteen males, fifteen females; aged 22–48, mean age = 29.15) volunteered for the study and were paid for their participation. Subjects were in good physical health as confirmed by a complete physical exam, with no history of any psychiatric illness as assessed by the DSM-IV (1994) criteria based on the Structural Clinical interview for DSM-IV Axis I disorders (SCID) (First et al., 1997). All subjects gave written informed assent/consent to participate in the study, which was approved by the National Institute of Mental Health Institutional Review Board.

Optimistic bias (OB) task

The stimuli consisted of 40 high negative (e.g., having a heart attack; being sentenced to jail), 40 low negative (e.g., getting seasick; losing your spot in a long line), 40 high positive (e.g., finding the cure for AIDS; living past 80) and 40 low positive (e.g., getting a hug; having a perfect hair day) possible future events. These 160 stimuli were selected from a larger set of stimuli given to a different group of 35 healthy adults who were asked to rate potential future events according to their pleasantness/unpleasantness. The high pleasant and unpleasant items and low pleasant and unpleasant items were matched according to their level of differentiation from neutral (though in opposite directions). In addition, the four different future event types were matched on number of letters and words.

Prior to scanning, subjects were told that they would read different possible future events. For each event, they were told to rate the likely probability of the event happening to them across their lifetime, compared to other people of their same gender and age. The subjects rated their likelihood according to a 4 point scale where 1 = much below average; 2 = below average; 3 = above average; or 4 = much above average, using the second and third digits of both hands. Each event was presented for 5500 ms following a 500 ms fixation point. In addition, for each experimental run, 48 3000 ms fixation points were presented between the stimuli (4 at the beginning of the run, 4 at the end of the run and 40 randomized throughout the run), serving as an implicit baseline. The fMRI scan acquisition followed an event-related design, and consisted of four runs.

Following EPI acquisition, subjects rated each of the 160 events on a 5-point Likert scale according to how much experience they had with each event, where 1 = don't know anybody this has happened to and 5 = it has happened to me. The paradigm was programmed in E-Studio. Stimuli were presented on a computer display that was projected onto a mirror in the MRI scanner. Subjects were placed in a light head restraint within the scanner to limit movement during acquisition.

Inventory of Depressive Symptomatology (IDS)

Because we were interested in the relationship between OB and depressive symptoms, subjects also completed the Inventory of Depressive Symptomatology (IDS) (Rush et al., 1986). This scale assesses the level of depressive symptomatology by means of 30 items that each describes a symptom of depression. Two sets of symptoms are mutually exclusive (weight loss/gain and appetite loss/gain), resulting in 28 scored items. Each item is scored according to best fit (0 through 3).

MRI parameters

Whole-brain blood oxygen level dependent (BOLD) fMRI data were acquired using a 1.5 Tesla GE MRI scanner. Following sagittal localization, functional T2* weighted images were acquired using an echo-planar single-shot gradient echo pulse sequence (matrix = 64 × 64 mm, repetition time (TR) = 3000 ms, echo time (TE) = 30 ms, field-of-view (FOV) = 240 mm (3.75 × 3.75 × 4 mm voxels). Images were acquired in 31 contiguous 4 mm axial slices per brain volume, with each run lasting 6 min 24 s. In the same session, a high-resolution T1-weighed anatomical image was acquired to aid with spatial normalization (three-dimensional Spoiled GRASS; TR = 8.1 ms; TE = 3.2 ms, flip angle = 20°; FOV = 240 mm, 124 axial slices, thickness = 1.0 mm; 256 × 256 acquisition matrix).

Imaging data preprocessing

Data were analyzed within the framework of the general linear model using Analysis of Functional Neuroimages (AFNI) (Cox, 1996). Both individual and group-level analyses were conducted. The first four volumes in each scan series, collected before equilibrium magnetization was reached, were discarded. Motion correction was performed by registering all volumes in the EPI dataset to a volume collected close to acquisition of the high resolution anatomical dataset.

The EPI datasets for each subject were spatially smoothed (isotropic 6 mm kernel) to reduce variability among individuals and generate group maps. Next, the time series data were normalized by dividing the signal intensity of a voxel at each time point by the mean signal intensity of that voxel for each run and multiplying the result by 100, producing regression coefficients representing percent-signal change.