

## Positive reinforcement modulates fronto-limbic systems subserving emotional interference in adolescents

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### ARTICLE INFO

#### Keywords:

Emotion  
Attentional control  
Working memory  
Reinforcement  
Functional magnetic resonance imaging (fMRI)  
Adolescence

### ABSTRACT

Fronto-limbic systems play an important role in supporting resistance to emotional distraction to promote goal-directed behavior. Despite evidence that alterations in the functioning of these systems are implicated in developmental trajectories of psychopathology, most studies have been conducted in adults. This study examined the functioning of fronto-limbic systems subserving emotional interference in adolescents and whether differential reinforcement of correct responding can modulate these neural systems in ways that could promote resistance to emotional distraction. Fourteen healthy adolescents (ages 9–15) completed an emotional delayed working memory task during fMRI with emotional distracters (none, neutral, negative) while positive reinforcement (i.e., monetary reward) was provided for correct responses under some conditions. Adolescents showed slightly reduced behavioral performance and greater activation in amygdala and prefrontal cortical regions (ventrolateral, ventromedial, dorsolateral) on correct trials with negative distracters compared to those with no or neutral distracters. Positive reinforcement yielded an overall improvement in accuracy and reaction times and counteracted the effects of negative distracters as evidenced by significant reductions in activation in key fronto-limbic regions. The present findings extend results on emotional interference from adults to adolescents and suggest that positive reinforcement could be used to potentially promote insulation from emotional distraction. A challenge for the future will be to build upon these findings for constructing reinforcement-based attention training programs that could be used to reduce emotional attention biases in anxious youth.

### 1. Introduction

The ability to resist interference from distracting emotional information while sustaining attention on goal-directed behavior is critical for adaptive behavior. According to some theories, emotional information is prioritized and mobilizes cognitive resources [1–3], as they contain signals closely linked to survival [4,5]. Such preferential access of emotional information to our cognitive system has been interpreted as a mechanism critical for the quick and effective processing of biologically relevant information rendering us better able to respond in an adaptive manner [6]. While emotional information may bolster cognitive processing and improve performance if it is goal-relevant [7], the same information could be distracting and have detrimental effects on cognitive function [8]. Some have proposed that emotional information is integrated within cognitive control processes creating a competition for information processing resources (i.e., Dual Competition Model) [9] and that such integration is supported by complex interactions between prefrontal and subcortical regions [10]. Using cognitive tasks modified to include emotional distracters, numerous studies have provided

evidence that emotional stimuli can influence many different aspects of cognition and behavior, and that they tend to “hijack” attention more easily than non-emotional stimuli [11–14] thereby resulting in disrupted cognitive goals and less optimal task performance (e.g., slower reaction times or reduced accuracy) [15].

One task that has been used to examine the functioning of fronto-limbic systems underlying attentional control in the context of emotional distracters is the emotional delayed working memory (EDWM) [15,16]. The EDWM task is a modified version of a visual delayed match-to-sample task that includes a visual probe held in working memory during a delay period and typically involves the presentation of no distracter, a neutral distracter, or an emotional distracter (e.g., negatively valenced pictures or facial expressions). Dolcos and McCarthy [23] reported one of the first neuroimaging findings demonstrating that impaired working memory performance in the presence of emotional distraction was associated with heightened activity in ventral neural regions supporting emotional processing (e.g., amygdala, ventrolateral prefrontal cortex) and reduced delay-related neural activity in dorsal brain regions implicated in attentional

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processes and active maintenance of task-relevant information in working memory (e.g., dorsolateral prefrontal cortex, lateral parietal cortex). They interpreted such a pattern of activation as an indication that dorsal regions might be temporarily driven “offline” (hijacking effect) by ventral brain regions responsible for detecting emotional salience such as the amygdala. Such an interpretation was consistent with findings of a positive correlation between amygdala activation and subjective ratings of distraction to emotional stimuli as well as positive coupling between the amygdala and ventrolateral prefrontal cortex during processing of emotional distraction [15]. Using a slightly different EDWM task, Anticevic et al. [16] replicated Dolcos and colleagues’ negative association between amygdala activation and task performance as well as heightened ventrolateral prefrontal cortex activation to correct (vs. incorrect) trials in the context of negative distracters [16]. Overall, the above findings suggest that performance of a working memory task in the context of negative distracters is linked with disruptions in behavioral performance along with patterns of elevated activation in the amygdala, reduced activation in dorsal regions of the prefrontal cortex, and negative coupling between the amygdala and prefrontal cortical regions. Most of the research regarding functioning of fronto-limbic systems subserving resisting emotional interference has been conducted in adults and as such it is unknown whether the above findings extend to adolescents and children. Replication of findings with different age groups are important basic steps needed to firmly establish the generality of emotional interference effects and presumed brain mechanisms. Replication with adolescents in particular could have important clinical implications in light of evidence suggesting that altered functioning of fronto-limbic systems may contribute to developmental trajectories of risk for affective disorders [17–20]. Accordingly, the first goal of this study was to examine the extent to which the above-described patterns of neural activation associated with emotional interference obtained with adults are also present in adolescents.

In light of the role of emotional interference in affective disorders, an equally important yet unexplored area of research concerns identifying variables or procedures that can be used to prevent interference and associated declines in goal-directed behavior. Some evidence suggests emotional distraction can be mitigated by top-down interventions from attentional control regions, engaged to regulate emotional responses and cope with emotional distraction [15,21–27]. Given evidence that attentional biases to emotional stimuli are an important clinical characteristic of affective disorders [28–31] and that such biases have been interpreted in terms of deficits in attentional control [28,32,33], there is thus a need to find ways to promote attentional control of emotion. A number of animal and human neuroimaging studies have shown that positive reinforcement (i.e., receipt of a reward following a specific response) boosts behavioral performance on cognitive control tasks such as working memory [34–38] and that such improvement in performance is associated with increased neural activation in dorsal and lateral prefrontal cortical regions [38–42]. In particular, according to the dual mechanisms of control framework [43], the use of positive reinforcement would increase proactive control – that is, preparatory control that is aimed at preventing conflict and optimizing task performance through sustained activation of task-relevant information. Such findings suggest that positive reinforcement for correct responding on the EDWM task could boost behavioral performance by counteracting the effects of emotional interference. There are a number of potential routes through which positive reinforcement may exert influence. These include reduced activation in subcortical limbic regions (ventral frontal), increased activation in attentional control regions (dorsal prefrontal), or both. Accordingly, the second goal of this study was to test the extent to which providing positive reinforcement (i.e., monetary rewards for correct responses) would improve task performance and modulate prefrontal cortical and subcortical regions involved in emotional interference. Specifically, we hypothesized that positive reinforcement would be associated with

reduced activation in ventral neural regions (i.e., amygdala, ventrolateral prefrontal cortex), and increased activation in dorsal and lateral regions of the prefrontal cortex.

## 2. Material and methods

### 2.1. Participants

Sixteen right-handed adolescents without any medical or psychiatric disorders participated. Two were excluded due to data loss (i.e., excessive motion) yielding a sample of 14 adolescents (age  $M = 13.4$  years,  $SD = 1.8$ ; 8 males). All participants had normal vision, as assessed using a Snellen chart, were right handed, as assessed using the Edinburgh Handedness Inventory [44], and were free of current *DSM-IV* Axis I psychiatric diagnoses, as assessed using the Stony Brook Symptom Inventory [45]. Exclusion criteria included: history of head trauma, neurological disorder, use of drug and alcohol, presence of metal objects in their body, and pregnancy. The study was approved by the Institutional Review Board for the Protection of Human Subjects at the University of Pittsburgh. To participate, children and their parents were required to sign assent and consent forms, respectively.

### 2.2. Neuroimaging task design

Participants performed an adapted version of the emotional delayed working memory (EDWM) task [16] (Fig. 1). The task included 80 trials of a version of a delayed match-to-sample task [46] with two geometric shapes and two potential distracter types presented during the delay or the maintenance period of the task: emotionally negative images and visually complex neutral images. Prior to the start of the experiment, each participant was presented with instructions explaining the task and completed a practice session. They were instructed to try to remember two shapes presented on the screen and to keep their eyes looking at the center of the screen and to not respond once the shapes disappeared. They were also told that a single shape would then be presented for a brief time and to press a button with their index finger (yes) if this shape matched one of the shapes previously presented and to press a button with their middle finger (no) if this shape did not match any of the shapes. They were also informed that at some point during the task, graphic images would be presented. In order to examine the influence of positive reinforcement on performance of the EDWM task, each block was repeated but it included instructions at the beginning of the block indicating to the participants that they would receive a monetary reward (\$1) for each correct response. As illustrated in Fig. 1, trials began with the presentation of the memoranda (3 s) followed by a fixation cross (1 s), a delay period (fixation cross (10 s) or distracter (3 s) and fixation cross (7 s)), the probe (2.5 s), inter-trial stimulus (in blocks without positive reinforcement: fixation cross (6.5 s); in blocks with positive reinforcement: feedback (0.5 s): “Correct: win \$1” written in green following correct responses or “Wrong: no money” written in red following incorrect responses or “No response” written in white following omissions and fixation cross (7 s)). A PC running E-prime software (Psychology Software Tools (PST), Pittsburgh, PA) controlled stimulus display. A color high-resolution LCD projector projected visual stimuli onto a rear screen at the head of the scanner bore, viewable via a mirror attached to the head coil. Responses were recorded using a PST glove.

The 80 trials of the EDWM task were divided according to distracter type: 30 negative distracter trials, 30 neutral distracter trials, and 20 no distracter trials, which were blank trials with a fixation cross used to estimate distracter-free maintenance activity. The trials were grouped into 8 blocks of 10 trials each. The first two blocks included trials with no distracters (block 1 without positive reinforcement and block 2 with positive reinforcement). The following 6 blocks included 30 neutral and 30 negative trials presented in a fixed random order within each block. Three blocks were presented without positive reinforcement (blocks 3,

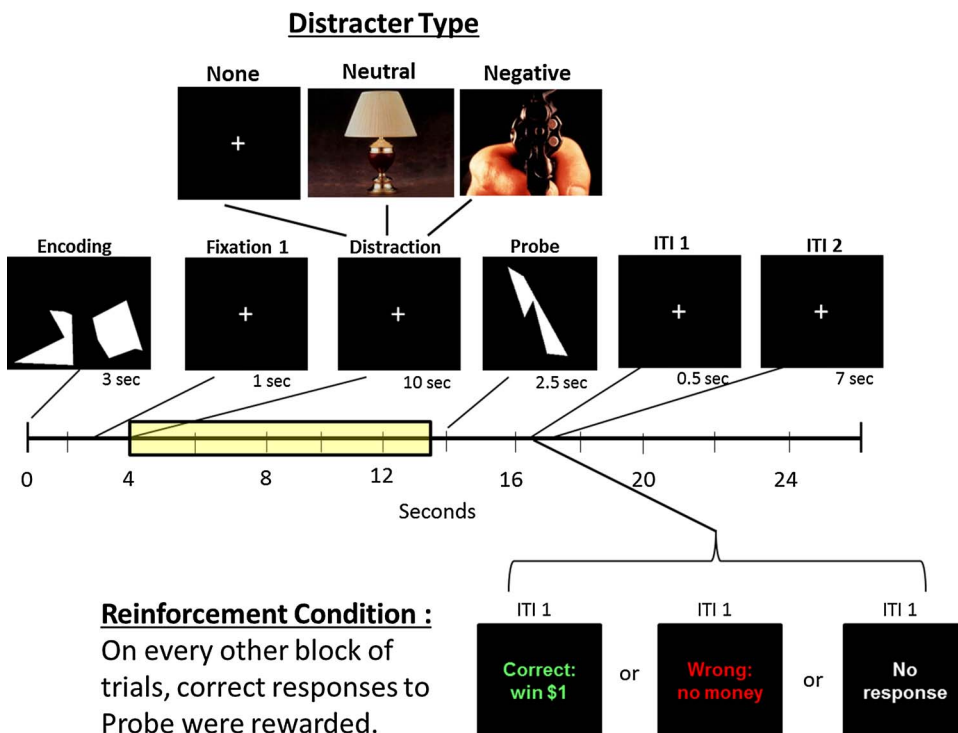


Fig. 1. Illustration of the adapted version of the Emotional Delayed Working Memory (EDWM) task [16] with and without positive reinforcement for correct responding on trials with no, neutral or negative distracters.

5, 7) and three blocks included positive reinforcement (blocks 4, 6, 8). The even-numbered blocks included the same trials and timing as the odd-number blocks but with the added instructions and feedback pertaining to reinforcement. Each trial lasted 24 s with each block lasting 4.3 min. As in Anticevic et al. [16], the memory sets were constructed from complex geometric shapes [47] created using a MATLAB algorithm designed to generate geometric shapes that were not easily described and encoded verbally [48]. The negative and neutral distracters were a subset of digitized slides from the International affective picture system (IAPS) stimulus set [49] selected for use with children and adolescents [50]. All distracters were presented at the center of the screen, with a visual angle of 8.5°. At the end of the scan, participants were informed that the monetary reward received was to be added to their participant payment card.

### 2.3. Manipulation check: post-scan valence and arousal rating task

In order to account for the possibility that the emotional distracters were not perceived as emotionally salient, participants performed a computerized valence and arousal rating task immediately following exiting the scanner. The task consisted of viewing a series of 80 IAPS pictures (40 negative and 40 neutral) that were presented in a random order and included pictures used as emotional distracters in the EDWM task (65%) and pictures that were randomly selected from the IAPS series (35%). Participants were asked to use the Self-Assessment Manikin (SAM) [51] rating scale, which is a non-verbal pictorial assessment technique, to rate their affective reactions to the pictures in terms of valence (1 = positive to 9 = negative) and arousal (1 = excited and 9 = calm).

### 2.4. fMRI data acquisition

Mean blood-oxygenation-level-dependent (BOLD) images were acquired on a 3T Siemens Tim Trio with a standard circularity-polarized head coil at the Magnetic Resonance Research Center, University of Pittsburgh Medical Center Health System, USA. Structural images were acquired first using a sagittal magnetization-prepared rapid gradient-echo (MPRAGE) T1-weighted sequence parallel to the anterior-

posterior commissure line (echo time [TE] = 3.43 msec, repetition time [TR] = 2300 msec, field of view [FOV] = 256 mm, flip = 9°, field of view: 200 × 200 mm, slice thickness: 0.8 mm, image matrix: 256 × 256, 208 slices, voxel size = 1 × 1 × 1 mm, acquisition time: 4 min 25 s.). Functional images were acquired using an echo-planar sequences sensitive to BOLD contrast (T2\*) (TR = 2000 msec, TE = 29 msec, FOV = 205 mm, flip = 90°, voxel size = 3.2 × 3.2 × 3.1 mm, ascending interleaved acquisition). A total of 39 axial sections per volume were acquired, with wholebrain coverage. To minimize T1 equilibrium effects, the first four echo-planar image (EPI) volumes for each acquisition were discarded.

### 2.5. Procedure

Prior to scanning, participants completed a practice session in a simulator scanner. During the practice session, participants were familiarized with the MRI environment and trained to remain as still. They also practiced a brief version of the EDWM task with memory sets and distracters not used in the main task to demonstrate various trial combinations. Following the practice session, participants were positioned into the scanner to complete the structural and functional scanning protocols.

### 2.6. Data analyses

#### 2.6.1. Behavioral data

Accuracy (% correct hits) and correct-trial reaction times were computed for each condition for each participant. Data were analyzed using a repeated measures analysis of variance in SPSS v.23., with emotional distracter type (no distracter, neutral, negative) and reinforcement condition (with, without) as within-subject factors and an alpha criterion set at  $p < 0.05$ . Post hoc comparisons were performed using Bonferroni corrections.

#### 2.6.2. fMRI data

Preprocessing and analyses were performed with Statistical Parametric Mapping software (SPM8; Wellcome Trust Centre for Neuroimaging, UK). Preprocessing of functional data for each subject

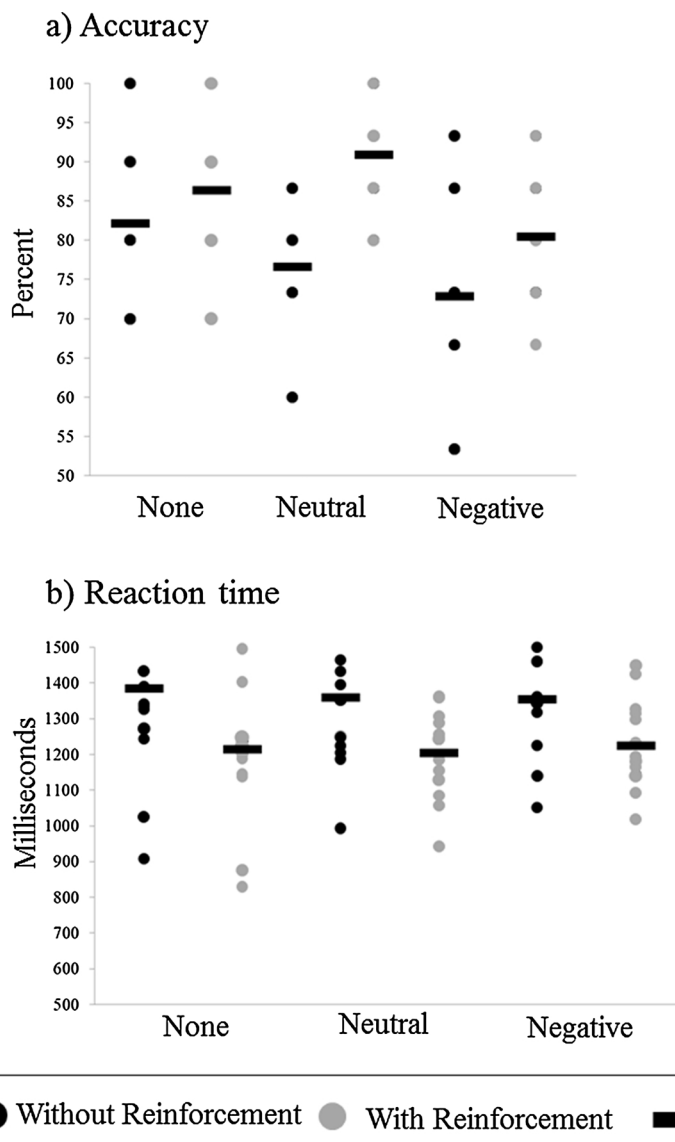


Fig. 2. Scatter plots of individual and mean percent accuracy (hits) and mean correct reaction times on the Emotional Delayed Working Memory task.

included slice acquisition time correction, coregistration, within-subject realignment, spatial normalization to the standard Montreal Neurological Institute EPI template with resampling to  $2 \times 2 \times 2$  mm voxel sizes, and spatial smoothing using a Gaussian kernel (6 mm full width at half-maximum). High pass filtering (1/128 Hz) was applied to the time series of echo-planar images to remove any low frequency drift in the signal. Data were not included in the group analyses if participants showed movement in the translational or rotational planes that exceeded 3 mm or  $3^\circ$ , respectively.

Functional imaging analyses proceeded through two stages: 1) examine neural activation associated with performing the delayed working memory task as a function of the distracter type (none, neutral, negative), with a focus on regions-of-interest (ROIs) previously reported in studies with adults [16], 2) repeated measures analyses limited to the post-distracter period (8–16 s) of the negative distracters to examine the effects of positive reinforcement on emotional distraction.

For the first level analysis, individual effects were estimated using the general linear model (GLM) approach implemented in SPM8. Individual subject time series data were analyzed using a Finite Impulse Response (FIR) model and a 2 s sampling rate across the 24 s working memory trial (12 TRs). Events of interest modeled included each distracter type with and without positive reinforcement (referred to as *conditions* throughout). Only trials with correct responses were used in

analyses (see Supplemental Table S1). Participant-specific head movement parameters were also modeled as a covariate of no interest to control for signal change related to motion.

First level images were then carried to a second-level for group analyses. A priori planned comparisons focused on fronto-limbic regions using an anatomically-based ROI mask created with the Automated Anatomic Labeling atlas [AAL; 52] of the WFU Pickatlas toolbox [53]. Specifically, the ROI mask included the following neural regions: bilateral amygdala and bilateral prefrontal cortical regions including ventromedial (BA 10 and 11), ventrolateral (BA 45 and 47) and dorsolateral (BA 9 and 46). Consequently, second-level analyses were restricted to the regions included in this ROI mask. To correct for multiple comparisons correction, the significance level was corrected using  $q < 0.05$  false discovery rate [FDR correction; see [54,55–57] and 50 contiguous voxels. To address our first question pertaining to the effects of emotional distracters on fronto-limbic activation in adolescents, a full factorial GLM focusing on distracter type (none, neutral, negative – without reinforcement) by time (12 TRs) interaction was performed. Peak voxel parameters estimates were extracted (based on the significant clusters from the interaction maps) for each subject for all conditions. Using SPSS, we probed the significant distracter by time interaction for each of these significant clusters by comparing the mean peak voxel parameter estimates averaged during the post-distracter

period (8–16 s) using a priori contrasts (negative > neutral and negative > baseline distracters) ( $p < 0.05$ , Bonferroni corrected). To address our second question pertaining to the effects of positive reinforcement on fronto-limbic activation during the negative distracter trials, we extracted the peak voxel parameter estimates for the negative distracters with and without positive reinforcement. We then performed a repeated measures ANOVA in SPSS to examine the reinforcement condition (with vs. without) by time (12 TRs) interaction for negative distracters ( $p < 0.05$ , Bonferroni corrected). Greenhouse-Geisser correction was applied upon any violations of the assumption of sphericity. We probed the significant interactions using paired  $t$ -tests ( $p < 0.05$ , Bonferroni corrected) to compare the mean peak voxel parameter estimates averaged across the 8–16 s post-distracter.

### 3. Results

#### 3.1. Distracter ratings

Our manipulation check of distracter type revealed important differences in subject's ratings of distracters. Comparison of the mean rating scores for valence and arousal indicated that participants had significantly higher scores on the SAM valence scale (Mean = 6.5, SD = 1.1,  $t(14) = -5.9$ ,  $p < 0.001$ ) and significantly lower score on the SAM arousal scale (Mean = 4.8, SD = 2.0,  $t(14) = 5.2$ ,  $p < 0.001$ ) for the negative distracters compared to the neutral distracters (valence: Mean = 4.7, SD = 0.8; arousal: Mean = 8.0, SD = 1.5), indicating that subjects rated the negative distracters as more negatively valenced and arousing than the neutral distracters (see Supplemental Table S2).

#### 3.2. Task performance

Fig. 2 shows mean percent accuracy and reaction times for each distracter type with and without positive reinforcement for correct responding. Repeated measures ANOVA performed on percent correct responses revealed a significant main effect of distracter type, [ $F(2, 12) = 4.75$ ,  $p = 0.03$ ], a significant main effect of positive reinforcement, [ $F(1, 13) = 12.6$ ,  $p = 0.004$ ], and no significant interaction [ $F(2, 12) = 2.46$ ,  $p = 0.13$ , n.s.] (Fig. 2a). Post hoc comparisons showed that overall accuracy was significantly higher for trials with no (84%) or neutral (83%) distracters than those with negative distracters (77%),  $p < 0.05$ , and that it was also higher for trials with (86%) than without (77%) positive reinforcement,  $p < 0.05$ . Repeated measures ANOVA performed on reaction times revealed a significant main effect of positive reinforcement, [ $F(1, 13) = 17.97$ ,  $p = 0.001$ ], indicating that reaction times were faster for trials with (1215.18 msec) than without (1366.72 msec) reinforcement,  $p < 0.05$ . There was no significant main effect of distracter type [ $F(2, 12) = 0.11$ ,  $p = 0.89$ , n.s.] or interaction [ $F(2, 12) = 0.16$ ,  $p = 0.86$ , n.s.] (Fig. 2b).

#### 3.3. Neuroimaging

In support of our first hypothesis regarding the effects of emotional distracters on fronto-limbic systems in adolescents, results indicated a significant distracter type by time interaction in the amygdala as well as ventromedial and lateral prefrontal cortical regions (see Table 1). Fig. 3 depicts the statistical activation maps and the mean peak voxel time courses for the significant clusters in key regions, which have previously been shown to be implicated in emotional distraction [16]. Plotted are time courses over the trial for baseline and neutral and negative distracter conditions. Results show a substantial increase in activation during the presentation of negative distracters as compared to baseline and neutral conditions. A priori contrasts comparing mean neural activation post-distracter (8–16 s period) (i.e., negative > neutral and negative > none) confirmed that neural activation was significantly greater to negative compared to neutral or no distracters

**Table 1**

Comparisons of BOLD signal during correct trials of the Emotional Delayed Working Memory Task: Effect of distracter type x time.

Region	Brodmann's Area	x	y	z	Cluster	Z	F
L VLPFC	47	-50	24	-6	449	4.93	3.43
R vmPFC	11	2	58	-14	52	4.89	3.39
L Precentral gyrus	73	-44	4	24	73	4.73	3.38
R DLPFC	9	10	50	44	497	4.69	3.25
R Inferior frontal gyrus	45	56	26	2	158	4.07	2.84
R VLPFC	47	42	24	-14	243	4.01	2.80
R Amygdala	-	28	0	-18	61	3.62	2.56
L Medial frontal gyrus	6	-2	12	50	187	3.61	2.56
R Medial frontal gyrus	6	2	-4	52	54	3.55	2.52
L vmPFC	10	-2	60	10	172	3.29	2.37

Note: Coordinates for each cluster's center-of-mass are presented in Montreal Neurological Institute (MNI) space. Table shows local maxima more than 8.0 mm apart. All findings are from ROI analysis with correction for multiple comparisons using FDR  $p < 0.05$  and extent threshold  $k = 50$  voxels. Degrees of freedom = 22, 468. BOLD = blood-oxygen-level dependent; L = Left; R = Right; VLPFC = ventrolateral prefrontal cortex; vmPFC = ventromedial prefrontal cortex; DLPFC = dorsolateral prefrontal cortex.

( $p < 0.05$ , Bonferroni corrected).

Our second goal was to examine the effects of positive reinforcement on neural activation to negative distracters in fronto-limbic regions. Specifically, whether positive reinforcement contingent upon correct responding would attenuate increases in activation in ventral regions associated with negative distracter presentation and increase activation in dorsal and lateral regions of the prefrontal cortex. As depicted through the hashed red line for negative distracters in the positive reinforcement condition on the plots in Fig. 3, our hypothesis was partially supported. The level of activation in ventral regions to the negative distracters with reinforcement was substantially reduced compared to the negative distracters without reinforcement but there were no corresponding significant increases in activation in dorsal and lateral regions of the prefrontal cortex. Repeated measures ANOVA, with Bonferroni correction, performed for each of the 6 regions depicted in Fig. 3 revealed a significant reinforcement condition by time interaction for the negative distracters in the right VLPFC ( $F(3, 11) = 2.80$ ,  $p = 0.04$ ) and right vmPFC ( $F(3, 11) = 2.61$ ,  $p = 0.005$ ) regions but this interaction was not significant for left VLPFC ( $F(3, 11) = 1.81$ ,  $p = 0.17$ ), right DLPFC ( $F(3, 11) = 1.30$ ,  $p = 0.23$ ), left vmPFC ( $F(3, 11) = 2.18$ ,  $p = 0.08$ ), and the amygdala ( $F(3, 11) = 1.32$ ,  $p = 0.22$ ). Also, there was a significant main effect of reinforcement for left VLPFC ( $F(1, 13) = 8.45$ ,  $p = 0.01$ ). Fig. 4 shows differences in parameter estimates for the post-distracter period in the right VLPFC, right vmPFC, and left VLPFC. Post-hoc paired  $t$ -tests revealed that neural activation in these regions was significantly reduced when participants received positive reinforcement for correct responding during negative distracters (R VLPFC:  $t(13) = 4.74$ ,  $p < 0.001$ ; R vmPFC:  $t(13) = 3.92$ ,  $p = 0.002$ ; L VLPFC:  $t(13) = 2.96$ ,  $p = 0.01$ ). Secondary analyses indicated no differences between reinforcement conditions for the no distracter or neutral distracters (Supplemental Fig. S1).

### 4. Discussion

The first goal of this study was to examine the extent to which emotional interference from negative distracters differentially modulates activation in fronto-limbic regions in adolescents. A secondary goal was to assess whether differential reinforcement of correct responding could modulate activation in these fronto-limbic regions. Findings from this preliminary study suggest that typically developing adolescents exhibit somewhat similar patterns of neural activity as those documented in healthy adults performing the emotional delayed

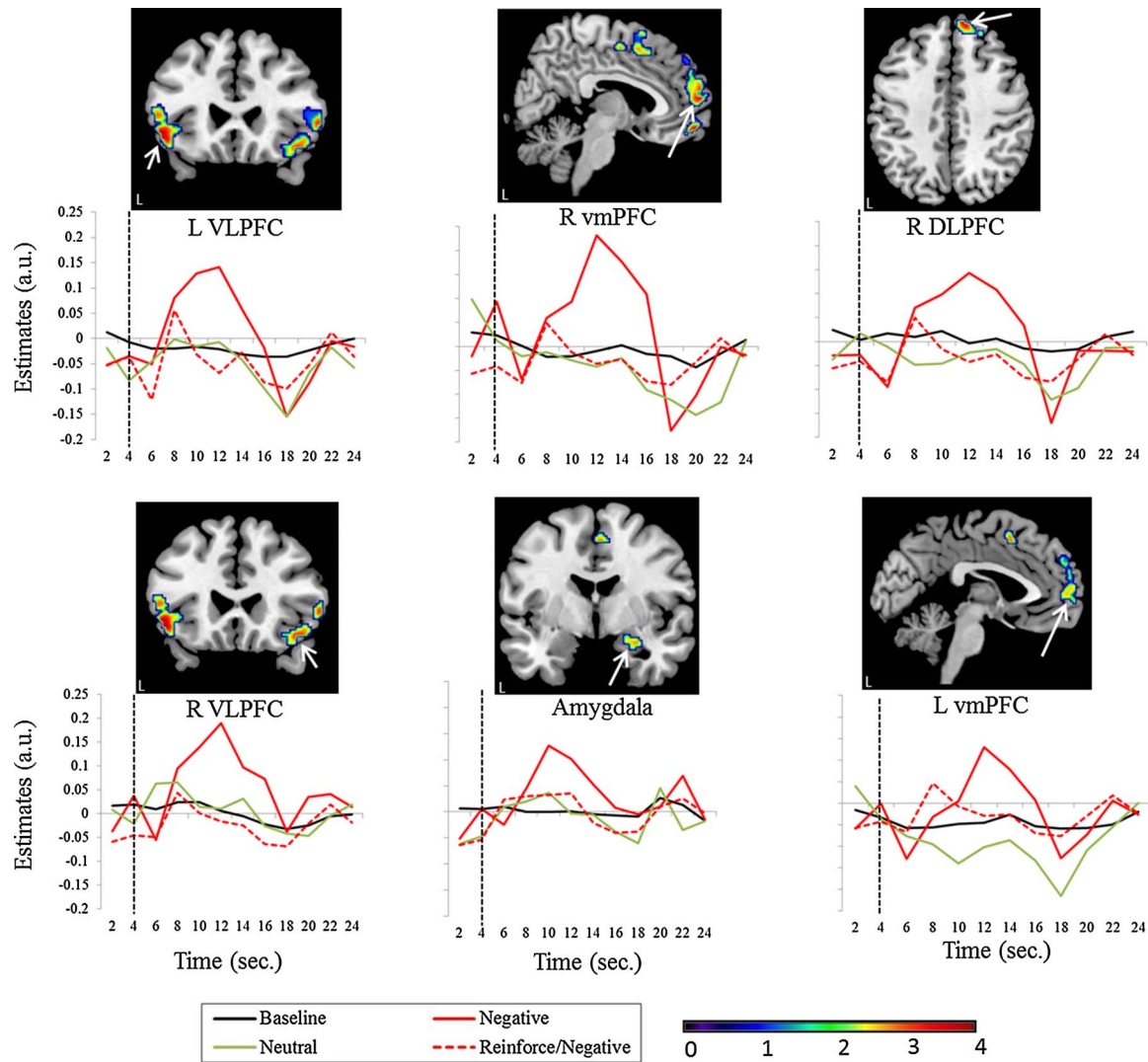


Fig. 3. Task-evoked time courses for the amygdala and prefrontal cortical regions on correct trials. Event-related time courses are shown based on the distracter type (none, neutral, emotional) x time (12 volumes) interaction regions-of-interest analysis. Activation maps highlight significant interactions ( $q < 0.05$  false discovery rate and an extent threshold of 50 contiguous voxels) overlaid on the skull stripped Colin brain (ch2better.nii). Plots show changes in mean parameter estimates for peak voxels for the baseline/no distracter (black), neutral distracter (green), negative distracter (solid red) and negative distracter with positive reinforcement (hashed red line) conditions across a trial (24 sec). Distracter onset is marked by a black hashed vertical line. L = Left; R = Right; vmPFC = ventromedial prefrontal cortex; VLPFC = ventrolateral prefrontal cortex; DLPFC = dorsolateral prefrontal cortex. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

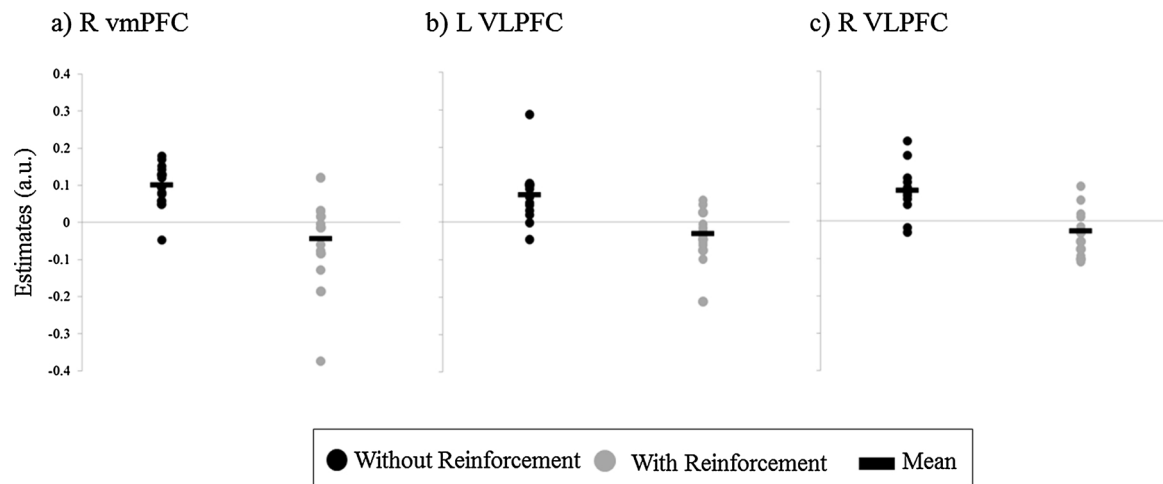


Fig. 4. Effects of positive reinforcement on regional activation during presentation of negative distracters. Scatter plots of individual and mean regional activation depicting significant reductions in regional activation for trials when correct responses were positively reinforced (gray) compared to trials when reinforcement was not provided for correct responses (black). L = Left; R = Right; vmPFC = ventromedial prefrontal cortex; VLPFC = ventrolateral prefrontal cortex.

working memory task [15,16]. Specifically, results showed an emotional distracter effect characterized by a decrease in response accuracy and greater activation in ventrolateral and medial prefrontal cortical and amygdalar regions when negative compared to neutral distracters were presented during delay period of the working memory task. Another important aspect of our findings is positive reinforcement for correct responding produced higher accuracy and faster reaction times across all trial types. Regional activation to negative emotional distracters was also found to decrease significantly when positive reinforcement was provided for correct responding, suggesting positive reinforcement could have a modulatory effect on fronto-limbic activation.

Overall, findings support our primary hypotheses of greater amygdalar and prefrontal cortical activation to negative compared to neutral or no distracters. Findings of greater amygdala activation to negative distracters are consistent with the patterns of amygdala time courses reported in Anticevic et al. [16] and Dolcos et al. [25] and with findings in studies of emotional interference in adolescents [58–60]. Because our fMRI analyses focused on correct trials, it is unclear to what extent greater amygdalar activation to negative vs. neutral distracters is associated with levels of distractibility as previously shown [15,23]. Results from the analyses of the behavioral data suggest that negative distracters did confer working memory costs, with accuracy being significantly lower in the negative distracter condition.

We also observed greater activation in ventral regions of the prefrontal cortex during the delay period to negative versus neutral or no distracters. This more ventral system is thought to play an important role in redirecting attention to behavioral salient information [61] as well as inhibiting the distracting effects of stimuli presented during the delay period [27,62]. As such, it is possible that the frontal areas of the ventral attentional system are particularly sensitive to emotional salient stimuli, which is consistent with evidence indicating that these prefrontal cortical regions, especially the medial PFC regions, are more strongly interconnected with the amygdala than the dorsal regions of the PFC [63]. These ventral and medial prefrontal cortical regions have also been reported in studies of response inhibition to emotional stimuli in adolescents [64] and other voluntary emotion regulation subprocesses [28] such as those focused on cognitive reappraisal of negative emotion in adults [65,66] and adolescents [67–69].

Contrary to findings in adults, we found greater activation in right DLPFC and not reduced activation in lateral and anterior prefrontal cortical regions to negative (vs. neutral) distracters. The fact that we did not observe reductions in dorsal regions of the prefrontal cortex as reported in adult studies could indicate that resisting emotional interference requires recruitment of a more widespread network of prefrontal regions (dorsal and ventral regions) to mobilize the attentional control network needed to perform the working memory task correctly in the context of emotional distracters [70]. This interpretation is consistent with findings from neuroimaging studies focused on the development of interference control in adolescents suggesting that younger adolescents tend to exhibit more widespread activation and with the maturation of prefrontal cortical networks less activation (reduced activation in less relevant regions with more fine-tuned functioning) is needed to overcome interference [71]. Though few studies have examined age-related changes in neural systems supporting resistance to emotional distraction, findings from some studies comparing neural activation in youth and adults have reported reduced activation in dorsal cortical regions in older but not younger participants. For instance, Cservenka et al. [72] reported that age was negatively correlated with left and right middle frontal gyrus activity during emotional conflict in a sample of children, adolescents, and adults [72]. Another explanation could be that younger adolescents have not yet developed the connections between prefrontal cortical regions or efficiency of brain networks [73] needed to reallocate attentional resources according to task demand [74] and resolve the cognitive-affect push-pull competition [62]. However, future work that includes an adult

comparison group is needed to determine whether the current pattern in adolescents of greater activation in right DLPFC and not reduced activation in lateral and anterior prefrontal cortical regions to negative (vs. neutral) distracters is significantly different from adults.

Another important goal of this study was to explore the extent to which using positive reinforcement for correct responding could be used to influence fronto-limbic regions associated with resisting emotional distraction. Preliminary findings from the current study are the first to show that positive reinforcement for correct responding on a cognitive-affective task is associated with reduced activation in the amygdala and ventral regions of the prefrontal cortex to negative versus neutral distracters. As depicted in Figs. 3 and 4, signals associated with negative distracters without reinforcement in key fronto-limbic regions were significantly reduced in trials with positive reinforcement. Yet, similar effects were not observed in secondary analyses (Supplemental Fig. S1) for trials with no or neutral distracters. Although we did not find a corresponding effect for behavioral performance to negative distracter trials, findings showing improved overall accuracy and faster reaction times across trial types suggest that positive reinforcement may have had the effect of more generally enhancing motivation and promoting recruitment of attentional resources to perform the main working memory task.

Indeed, our findings of increased accuracy and faster reaction times to trials with positive reinforcement are consistent with neuropsychological studies showing that working memory performance is faster [35,75] and more accurate [76] when it is rewarded than when positive reinforcement is absent or low. This enhancing effect of positive reinforcement on cognitive control is consistent with findings from numerous studies reporting faster reaction times for high relative to low reward expectation [77,78], increased spiking of frontal neurons in monkey [40,79] and increased BOLD response in caudal lateral frontal areas in humans [36,37,75,80]. Contrary to our hypothesis, however, our fMRI results indicate that positive reinforcement for correct responding was associated with reduced, not increased, activation in dorsal and lateral regions of the prefrontal cortex, which support attentional control processes. Such a reduction in neural activation could be explained by the type of proactive control being engaged through positive reinforcement. In a study examining the effects of motivation on cognitive control circuitry implicated in visual working memory, results showed that neural activation in scene-selection brain regions was significantly increased in the reward condition compared to a passive viewing condition when the scenes had to be remembered but it was significantly suppressed in the reward condition when the scenes had to be ignored [75]. As such, it is possible that the reduced activation in prefrontal cortical regions with reinforcement on correct trials may be related to successful interference control, which is needed for optimal task performance on working memory tasks [81–83]. Another interpretation could be that positively reinforcing correct performance “re-balanced” the competition for resources thereby reducing the need to “mobilize” the ventral system for negative distracters.

The current findings must be interpreted in light of certain limitations. The modest sample size reflects the preliminary nature of these findings with regard to the effects of reinforcement on emotional distraction in adolescents. As such, it is possible that some of the effects that were not or marginally statistically significant were due to the amount power. Because of this, a priori analyses were performed on neural regions that showed activation associated with emotional distraction on the EDWM in adults [16]. In contrast to the task design using in Anticevic et al. [16], however, we did not manipulate the level of difficulty or include task-related distracters as these manipulations did not yield significant findings in adults and including such experimental conditions would have considerably increased task duration. Although we investigated the effect of emotional distraction using negative emotional pictures, it would be informative to test whether using other negative emotional stimuli (e.g., verbal stimuli or threat cues) or positively valenced stimuli [84] would yield similar patterns of findings.

## 5. Conclusions

In summary, findings from this initial study provides preliminary evidence indicating that patterns of neural activation in fronto-limbic regions associated with emotional interference obtained with adults are also present in adolescents, with the exception that adolescents showed elevated, and not reduced, activation in dorsal and lateral regions of the prefrontal cortex. This study also provides a “proof of concept” that positive reinforcement (i.e., monetary rewards for correct responses) can be used to modulate fronto-limbic systems associated with resisting emotional distraction. Specifically, we show that positive reinforcement generally improves task performance and reduces activation in medial and ventrolateral prefrontal cortical regions in a group of healthy adolescents. Future studies replicating these findings and conducting amygdala-based functional connectivity analyses in a larger sample and testing interactions with age, which have been shown to be associated with changes in attentional control [71] and reward processing [85], respectively, will provide further knowledge about the possible underlying mechanisms. Such research will determine the extent to which it may be possible to harness adolescent neural response to the effects of positive reinforcement on prefrontal cortical function to counteract negative environmental influences and facilitate coping.

## Acknowledgements

This work was funded by a pilot grant from the Department of Psychiatry, University of Pittsburgh. The authors would like to thank Drs. Anticevic and Barch for allowing them to adapt the EDWM task for adolescents and for their feedback on the design of the study. They also thank the children and their families for participating in this research study.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.bbr.2017.10.019>.

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