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Self-regulatory depletion increases emotional reactivity in the amygdala

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The ability to self-regulate can become impaired when people are required to engage in successive acts of effortful self-control, even when self-control occurs in different domains. Here, we used functional neuroimaging to test whether engaging in effortful inhibition in the cognitive domain would lead to putative dysfunction in the emotional domain. Forty-eight participants viewed images of emotional scenes during functional magnetic resonance imaging in two sessions that were separated by a challenging attention control task that required effortful inhibition (depletion group) or not (control group). Compared to the control group, depleted participants showed increased activity in the left amygdala to negative but not to positive or neutral scenes. Moreover, whereas the control group showed reduced amygdala activity to all scene types (i.e. habituation), the depletion group showed increased amygdala activity relative to their pre-depletion baseline; however this was only significant for negative scenes. Finally, depleted participants showed reduced functional connectivity between the left amygdala and ventromedial prefrontal cortex during negative scene processing. These findings demonstrate that consuming self-regulatory resources leads to an exaggerated neural response to emotional material that appears specific to negatively valenced stimuli and further suggests a failure to recruit top–down prefrontal regions involved in emotion regulation.

Keywords: amygdala; emotion; self-regulation; emotion regulation; fMRI; depletion

INTRODUCTION

Failure to regulate emotions is implicated in a range of psychological disorders (Gross, 2002) and is a potent catalyst for excessive eating (Heatherton *et al.*, 1992), drinking (Sinha *et al.*, 2009), smoking (Tiffany and Drobes, 1990; Kassel *et al.*, 2003) and drug use (Childress *et al.*, 1994). The extant research on emotion regulation has largely focused on investigating the behavioral and neural correlates of different emotion regulation strategies (e.g. suppression, cognitive reappraisal). However, emotion regulation does not take place in a void; often people are confronted with stressful situations requiring them to regulate not only their emotions but also their thoughts, behaviors and impulses. Contemporary research on self-regulatory failure suggests that self-regulation relies on a limited resource (Baumeister and Heatherton, 1996) and that having to juggle any one of these forms of regulation may impair the ability to effectively regulate in other domains.

Neuroscientific models of emotion suggest that the amygdala and prefrontal cortex (PFC) are central structures involved in the perception and regulation of emotion (Whalen, 1998; Ochsner *et al.*, 2002; Hariri *et al.*, 2003; Kim *et al.*, 2003; Urry *et al.*, 2006) and for the experience negative affect (Ochsner *et al.*, 2009). Although the amygdala responds to both negative and positively valenced stimuli, it is more consistently implicated in the former (e.g. Zald, 2003). Regulating negative affect is frequently associated with enhanced activity in two regions of the PFC, namely, the lateral prefrontal cortex (LPFC) (Ochsner *et al.*, 2002; Hariri *et al.*, 2003; Ochsner *et al.*, 2004) and the ventromedial prefrontal (VMPFC) (Urry *et al.*, 2006; Johnstone *et al.*, 2007; Passamonti *et al.*, 2008). In patients suffering from disorders of emotional regulation [e.g. borderline personality disorder, major depressive disorder (MDD), post-traumatic stress disorder], the amygdala frequently shows a maladaptive or exaggerated response to negative emotional material in conjunction with a failure to appropriately recruit the lateral PFC and/or VMPFC (Rauch *et al.*, 2000; Shin *et al.*, 2005; Johnstone *et al.*, 2007). Moreover, amygdala reactivity to negative emotional material in healthy populations is associated with individual differences in daily use of emotion regulation strategies (Drabant *et al.*, 2009). Considered together, these findings suggest that an exaggerated amygdala response to negative emotional material in the healthy population along with a failure to recruit prefrontal regions involved in top–down control may serve as a potential neural marker of self-regulatory failure in the emotional domain.

Do self- and emotion-regulation rely on a common resource?

One of the most influential models of self-regulation to emerge in recent years is the limited resource model, or the 'strength' model of self-regulation (Baumeister and Heatherton, 1996). This theory of self-regulation and its failure has marshaled considerable evidence showing that effortful acts of self-regulation can temporarily deplete people's capacity to further regulate in seemingly unrelated domains (Muraven *et al.*, 1998; Vohs and Heatherton, 2000; Richeson and Shelton, 2003; Gailliot *et al.*, 2007; for a recent meta-analysis, see Hagger *et al.*, 2010). Although emotion regulation has traditionally been studied apart from self-regulation, there is evidence that both rely on the same limited resource. For example, one of the most common techniques for exhausting self-regulatory resources is having participants engage in an emotional inhibition task (Baumeister *et al.*, 1998; Muraven *et al.*, 1998; Vohs and Heatherton, 2000; Schmeichel *et al.*, 2003; Gailliot *et al.*, 2007). This research shows that when participants are required to inhibit their emotions during an emotionally provocative film, they are subsequently impaired at regulating their behavior on tasks in other domains, such as solving difficult anagrams (Baumeister *et al.*, 1998) or avoiding tempting foods (Vohs and Heatherton, 2000).

The results of two prior experiments indicate that this 'depletion' effect also works in the opposite direction. That is, engaging in effortful self-regulation can subsequently lead to emotion dysregulation. In the first experiment of its kind, Muraven *et al.* (1998) found that participants who completed a thought suppression task were subsequently

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impaired at inhibiting their emotions compared to control participant. Similarly, Schmeichel (2007) showed that inducing self-regulatory depletion via a complex working memory task led to emotion regulation failure as measured by participants' ability to suppress facial expressions of emotion when viewing a highly aversive video segment. Importantly, both studies show that the effect of self-regulatory exertion on emotion regulation is not mediated by any changes in mood brought about by the depletion task itself (Muraven *et al.*, 1998; Schmeichel, 2007). Finally, we note that this work is distinct from research on the role of cognitive load in emotional reactivity that shows that a concurrent cognitive demand (e.g. working memory load) during the perception of emotional stimuli reduces amygdala reactivity (Pessoa *et al.*, 2002). Rather, in work on self-regulatory depletion, it is subsequent rather than concurrent attempts at self-regulation that are impaired.

The current study

The results of the aforementioned behavioral studies suggest that engaging in effortful self-regulation may impair subsequent attempts at emotional control. Given the recognized importance of emotion regulation to psychological well being, understanding the neural mechanisms behind common failures of emotion regulation in otherwise healthy participants may help shed light on how life's many stressors can impair self-control. Specifically, assessing the relative contribution of the amygdala and PFC to an emotional challenge following self-regulatory depletion may inform our knowledge of how the brain supports successful emotion regulation and what happens when regulation fails.

In the present study, we employed a commonly used self-regulatory depletion paradigm followed by a task designed to assess naturally occurring neural responses to emotional material (similar to Drabant *et al.* 2009). Participants were not explicitly instructed to engage in any specific emotion regulation strategy (e.g. reappraisal, suppression, distraction) but rather it was expected that participants would engage in spontaneous emotion regulation (e.g. Egloff *et al.*, 2006; Richards and Gross, 2006; Berkman and Lieberman, 2009; Schmeichel and Demaree, 2010) that would be disrupted following self-regulatory depletion. Participants ($n = 48$) were randomly assigned to one of two groups, both of which underwent functional neuroimaging while viewing a series of negative, neutral and positively valenced emotional scenes. This was followed by a difficult attention control task in which participants had to pay attention to a film while ignoring a series of distractor words that appeared on the screen (Gilbert *et al.*, 1988; Schmeichel *et al.*, 2003; Gailliot *et al.*, 2007). Half of the participants were required to regulate their attention and inhibit reading any of the distractor words (depletion group), whereas participants in the control group could freely read the distractors. Finally, in order to assess the effects of exerting self-regulatory effort on the subsequent neural response to emotional material, participants viewed another series of emotional scenes. We hypothesized that, compared to the control group, participants in the depleted group would show exaggerated amygdala activity to negative emotional material following self-regulatory depletion in conjunction with reduced recruitment of—and functional coupling with—lateral and ventromedial regions of the PFC involved in emotion regulation.

METHODS

Participants

Participants were 56 right-handed volunteers who reported no abnormal neurological history and were not currently using any psychiatric medication. Participants were randomly assigned to either the depletion or the control group. Eight participants (four in the depletion condition and four in the control condition) were excluded from further analysis due to excessive movement (more than two incidences of >2 mm movement) in either the pre- or post-depletion sessions. This left 24 participants (13 women, mean age: 20.3) in the depletion group and 24 participants in the control group (14 women, mean age 20.6). Participants in both groups slept equal number of hours on the evening prior to scanning (Depletion group $M = 7.0$ h; Control group $M = 7.3$ h). In addition, all participants completed a 36-item measure of trait Self-Control (Tangney *et al.*, 2004) as part of a previous mass testing session. All participants gave informed consent in accordance with the guidelines set by the Committee for the Protection of Human Subjects at Dartmouth College.

Stimuli

Stimuli consisted of 180 emotional scenes from the International Affective Picture System (IAPS; Lang *et al.*, 2005) and were chosen based on normative valence and arousal ratings such that the emotionally negative category was both unpleasant and arousing (valence $M = 2.8$; arousal $M = 5.1$), the positive category was pleasant and arousing (valence $M = 7.2$; arousal $M = 5.0$) and the neutral category was neither pleasant or unpleasant and of low arousal (valence rating $M = 5.4$; arousal rating $M = 3.6$). In addition, emotional categories were matched for the presence of people and faces in each scene to ensure that any differential response observed between categories was not due to a preponderance of faces in any one category. Finally, images were split into two matched sets of 90 images each (30 images per emotional category) to be used before and after self-regulatory depletion (see 'Procedure' section). The presentation order of these two sets was counterbalanced across participants.

Tasks

Participants completed three functional runs consisting of two tasks that were: an emotional scene categorization task (runs 1 and 3) and the attention control task (run 2). Both versions of the emotional scenes task consisted of making 'indoor or outdoor' judgments on scenes (30 per valence category) in a rapid event-related design. Null event trials consisting of a white fixation cross against a black background were added to introduce 'jitter' into the blood-oxygen-level-dependent (BOLD) time series in order to allow for efficient estimation of tasks effects. The attention control task was modeled after a task widely used in studies of self-regulatory depletion (e.g. Schmeichel *et al.*, 2003; Gailliot *et al.*, 2007) requiring participants to engage in effortful self-control over an extended period of time. The task consisted of viewing 7 min of a silent nature documentary on Canadian Bighorn mountain sheep (Brind & Schmalz, 1970) that was chosen for being emotionally neutral and has been used previously to induce a neutral mood (Heatherton *et al.*, 1993). During the video, a series of brightly colored one- or two-syllable distractor words (80 words total) appeared first at the bottom of the screen and slowly moved to the center, over the course of 3 s, before disappearing. The words encompassed approximately one-sixth the height of the video and were presented in a bold yellow font, with a two-pixel red outline to ensure visibility over the film (Figure 1). Task instructions for participants in the depletion and control conditions differed in only one important respect: participants in the depletion condition were instructed to inhibit reading the words, whereas participants in the control condition were told that they needed only to pay attention to the video and could freely read the words or not.

Procedure

In order to reduce suspicion, participants were informed that they would be taking part in two separate studies, one involving the categorization of visual scenes and another involving understanding the

Fig. 1 Schematic of the study design. Participants were randomly assigned to either a depletion ($n = 24$) or control ($n = 24$) group. Both groups completed a single functional run of the emotional scenes task followed by either the attention control task (depletion group) or passive viewing (control group) which were identical in instruction save for the requirement that the depletion group inhibit reading a series of words that appeared on screen (see 'Methods' section). Finally, participants completed another functional run of the emotional scenes task, in this way the first functional run served as a pre-depletion measure of baseline emotional reactivity.

gist of a movie. For the emotional scenes task, participants were explicitly instructed to maintain fixation on the images at all times, even if they found them upsetting, and to indicate via button press whether the image took place indoors or outdoors.

Prior to performing the depletion task, all participants underwent a bogus eye tracking calibration session designed to convince participants that the location of their gaze was being monitored and thereby ensure that participants in the depletion condition exert maximum effort. In this bogus task, participants were instructed to fixate their gaze on a series of sequentially presented white squares spanning the four corners of the display, and were told that when the eye tracker had determined the location of their gaze, the square would turn red. In reality, the squares changed color after a variable amount of delay (between 1.5 and 5 s).

Following scanning, participants completed a questionnaire to assess suspicion, along with ratings of difficulty for the depletion task and questions assessing how rested they were prior to scanning and whether they managed to maintain fixation on the negatively valenced scenes. None of the participants reported suspecting a link between the self-regulatory depletion task and the emotional scenes task. Participants in the depletion condition rated the attention control task as more difficult (on a scale of 1–7 with 1 being 'very easy' and 7 being 'extremely difficult') than did participants in the control condition [Depleted = 5.4; Control = 2.1, $t(46) = 8.34$, $P < 0.001$] and participants in both groups indicated that they had managed to maintain their gaze on the screen during the presentation of negatively valenced images.

Image acquisition

Magnetic resonance imaging was conducted with a Philips Achieva 3.0 Tesla scanner using an eight-channel phased array coil. Structural images were acquired using a T1-weighted MP-RAGE protocol (160 sagittal slices; TR: 9.9 ms; TE: 4.6 ms; flip angle: 8°; $1 \times 1 \times 1$ mm voxels). Functional images were acquired using a T2*-weighted echo-planar sequence (TR: 2200 ms; TE: 35 ms; flip angle: 90°; field of view: 24 cm). For each participant, two runs of 268 whole-brain volumes (36 axial slices per whole-brain volume, 3 mm isotropic voxels were collected.

Image pre-processing and analysis

FMRI data were analyzed using the general linear model (GLM) in SPM8 (Wellcome Department of Cognitive Neurology, London, UK). For each functional run, data were pre-processed to remove sources of noise and artifact. Images were corrected for differences in acquisition time between slices and realigned within and across runs via a rigid body transformation in order to correct for head movement. Images were then unwarped to reduce residual movement-related image distortions not corrected by realignment. Functional data were normalized into a standard stereotaxic space (3-mm isotropic voxels) based on the SPM8 EPI template that conforms to the ICBM 152 brain template space [Montreal Neurological Institute (MNI)] and approximates the Talairach and Tournoux atlas space. Finally, normalized images were spatially smoothed (6-mm full-width-at-half-maximum) using a Gaussian kernel to increase the signal to noise ratio and to reduce the impact of anatomical variability not corrected for by stereotaxic normalization.

In order to estimate emotional scene category specific brain activity, a GLM was constructed for each participant. This GLM included six task effects (three for each valence category before and following the controlled attention task) and covariates of no interest (a session mean, a linear trend to account for low-frequency drift and six movement parameters derived from realignment correction). Contrast images for each participant, comparing the response to each emotional scene category with baseline (i.e. null events), were then submitted to a second-level repeated measures analysis of variance (ANOVA). This analysis generated a statistical parametric map of *F*-values for the main effect of emotional scene category (i.e. negative, neutral, positive) identifying brain regions that responded to at least one of the emotional scene categories across all participants and both time points (i.e. before and after the attention control task). Monte Carlo simulations using AFNI's AlphaSim were used to calculate the minimum cluster size at an uncorrected threshold of $P < 0.001$ required for a whole-brain correction of $P < 0.05$. Simulations (10 000 iterations) were performed using smoothness estimated from the residuals obtained from the GLM and resulting in a minimum cluster size of 39 contiguous voxels. This map was used to define regions-of-interest (ROI) which were subsequently interrogated for an effect of depletion. Specifically, ROIs (10-mm spherical ROI centered on peak voxels) were used to extract parameter estimates for each emotional scene category both before and after the controlled attention task. As both groups contribute equally to the ROI-defining statistical map, these ROIs are considered unbiased with regards to group effects. Finally, an *a priori* anatomical ROI for the amygdala, created with the SPM Anatomy toolbox (Eickhoff *et al.*, 2005), was also used.

Psychophysiological interaction (PPI) analyses (Friston *et al.*, 1997) were employed in order to assess whether depleted and control participants show differential connectivity between the amygdala and PFC. Specifically, a functionally defined left amygdala ROI was used as a seed region to investigate valence-dependent changes in functional connectivity between the left amygdala and other regions of the brain. Six millimeter spherical ROIs centered on the left amygdala ROI identified in the group GLM analysis (MNI coordinates: −21, −6, −21) were used to extract the first eigenvariate of the individual voxel time-series within the ROI. This representative time-series was deconvolved from the hemodynamic response function (HRF) to generate an estimated neuronal time-series (Gitelman *et al.*, 2003). The product of this estimated neuronal time-series and vectors representing each of the onsets for the three different valence types prior to and following depletion was computed. These six interaction terms were then reconvolved with the HRF and entered into a new GLM along with the vectors for the onsets for each valence type (i.e. the psychological vectors), the original eigenvariate time-series and covariates of no interest (i.e. a session mean, a linear trend to account for low-frequency drift and six movement parameters derived from realignment corrections). This 'generalized' form of PPI analysis differs from standard PPI analyses in that it allows for the simultaneous modeling of context-dependent connectivity for all conditions while also showing increased sensitivity and specificity compared to traditional PPI analyses (McLaren *et al.*, 2012).

In order to examine whether depleted and non-depleted participants exhibited differential connectivity with the left amygdala, we followed the same analysis procedure as with the analysis of BOLD responses to emotional scenes. Specifically, the contrast images of the PPI interaction term for all valence types and for each participant were submitted to a repeated measures ANOVA which resulted in a main effect of valence map identifying regions which show differential connectivity with the left amygdala seed as a function of valence type. Statistical thresholding and subsequent ROI analysis of this statistical map was carried out using the same criteria as the above analysis.

Table 1 Brain regions showing a main effect of emotional scene valence across all participants and sessions

Brain region	Side	BA	*F*-value	Coordinates of peak activation *x*	*y*	*z*
Amygdala	L	–	19.27	−21	−6	−21
Lateral prefrontal cortex (IFG)	L	45	22.92	−48	24	6
Lateral prefrontal cortex (IFG)	R	45	19.44	48	24	18
Dorsal anterior cingulate cortex	R	24	19.97	9	12	42
Dorsal medial prefrontal cortex	L	10	14.02	−9	57	21
Orbitofrontal cortex	R	11	13.91	−42	57	−9
Postcentral gyrus	R	3	56.10	39	−24	48
Insula	R	13	26.87	48	−21	15
Insula	L	13	22.37	−45	−36	18
Middle temporal gyrus	L	20	24.72	−51	−6	−24
Middle temporal gyrus	R	21	21.38	51	6	−36
Superior temporal gyrus	L	38	18.68	−36	15	−30
Supramarginal gyrus	L	40	21.57	−63	−30	33
Inferior occipital gyrus	L	19	39.34	−42	−81	−9
Periaqueductal gray	–	–	35.33	−3	−33	−6
Caudate	R	–	11.89	9	3	9

Note: Brain areas are listed along with the best estimate of their location. Coordinates are in MNI stereotaxic space. BA = approximate Brodmann's area; IFG = Inferior Frontal Gyrus

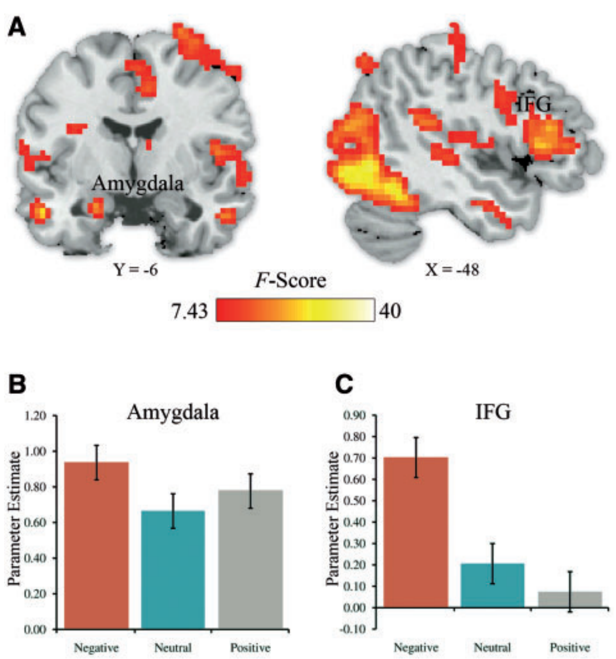

Fig. 2 (**A**) Brain regions showing a main effect of emotional scene valence (negative, neutral or positive) across both depletion and control groups ($P < 0.05$ corrected). (**B**) ROI analysis of parameter estimates in the left amygdala (−21, −6, −21) and (**C**) left LPFC (inferior frontal gyrus; −48,24,6) (B) demonstrate that these regions responded primarily to negatively valenced emotional scenes. Error bars indicate SEM based on the mean squared error term for within subjects comparisons. Coordinates (*x*, *y*, *z*) are in Montreal Neurological Institute stereotaxic space. IFG = Inferior Frontal Gyrus.

RESULTS

Reaction times for scene categorization

Participants in the depleted and control groups showed similar response latencies during the categorization of emotional scenes both prior to [Depletion = 1032 ms; Control = 1078 ms, $t(46) = 1.4$, $P = 0.16$] and following the controlled attention task [Depletion = 1013 ms, Control = 1049 ms, $t(46) = 1.04$, $P = 0.3$]. This was also the case when reaction times were broken down according to the valence category of the emotional scenes (all $P > 0.14$).

Brain regions sensitive to emotional valence across both groups

A repeated measures ANOVA across all participants and both sessions identified regions showing a main effect of emotional scene valence in a number of regions commonly implicated in the processing emotional stimuli and regulating emotional responses (Table 1 and Figure 2a). Specifically, the amygdala (MNI coordinates: −21, −6, −21) and LPFC showed a main effect of emotional scene type characterized by having the largest response to negative scenes, followed by neutral and positive scenes (Figure 2b).

Brain regions differentiating between depleted and control participants

In order to test for an effect of self-regulatory depletion we subtracted each participant's BOLD response prior to the attention control task from their response following the task in functionally defined ROIs and in two anatomically defined amygdala ROIs. In this way each participant's response prior to the attention control task serves as a subject specific baseline for emotional reactivity. Analysis of these change scores revealed that, following the attention control task, depleted participants showed increased activity in the left amygdala to negative emotional scenes, $t(23) = 2.1$, $P = 0.047$, whereas control participants showed no change, $t(23) = 1.2$, $P = 0.242$. Moreover, this difference was significant between groups, $t(46) = 2.38$, $P = 0.021$ (Figure 3). This was also true when using an anatomically defined left amygdala ROI [depleted: $t(23) = 2.12$, $P = 0.045$; control: $t(23) = 0.586$, $P = 0.563$] and the difference was significant between groups, $t(46) = 2.09$, $P = 0.042$. The same analyses for the anatomically defined right amygdala were all non-significant (all $P > 0.1$).

This effect appears to be specific to negative scenes as the left amygdala ROI showed no evidence of a change in response for neutral [depleted: $t(23) = 1.17$, $P = 0.25$; control: $t(23) = 1.58$, $P = 0.13$] or positive scenes [depleted: $t(23) = 1.34$, $P = 0.2$; control: $t(23) = 0.7$,

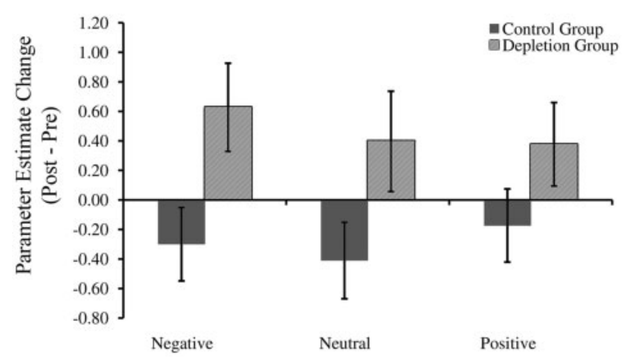

Fig. 3 Compared to control participants, depleted participants exhibited greater left amygdala (−21, −6, −21) reactivity to negative emotional material following depletion [$t(46) = 2.38$, $P = 0.021$]. Within groups, depleted participants exhibited increased amygdala activity to negative emotional material compared to their pre-depletion baseline [$t(23) = 2.1$, $P = 0.047$] whereas control participants did not [$t(23) = 1.2$, $P = 0.242$]. This was also true of an anatomically defined left amygdala ROI (see text). Error bars indicate SEM.

$P = 0.49$]. Moreover, the difference in change scores between depleted and control groups was not significant for positive scenes, $t(46) = 1.46$, $P = 0.15$, although there was evidence of a non-significant trend for neutral scenes, $t(46) = 1.89$, $P = 0.065$ (Figure 3). Importantly, there were no differences between the control and depletion group at baseline (e.g. pre-depletion) in amygdala activity to the three emotion scene types (all $P > 0.22$; see Supplementary Figure S1).

In addition to the amygdala, we also investigated the effect of self-regulatory depletion on the responses to emotional scenes in two regions of LPFC that have been implicated in emotion regulation (i.e. the left and right LPFCs / Brodmann's Area 45). Analysis of left (MNI coordinates: −48,24,6) and right (MNI coordinates: 48,24,18) LPFC ROIs derived from the statistical map of the main effect of emotional scene type (Figure 2) showed no difference in changes scores between depleted and control participants for negative [left LPFC, $t(46) = 0.37$, $P = 0.71$; right LPFC, $t(46) = 1.46$, $P = 0.71$], neutral [left LPFC, $t(46) = 1.24$, $P = 0.22$; right LPFC, $t(46) = 1.91$, $P = 0.063$] and positive [left LPFC, $t(46) = 1.54$, $P = 0.25$; right LPFC, $t(46) = 0.72$, $P = 0.48$] emotional scenes.

Correlation of left amygdala activity to negative scenes with individual differences in self-control and a measure of depletion

Analysis of left amygdala change scores (post- minus pre-depletion) with individual differences in trait self-control showed no relationship in control participants ($r = 0.09$, $P = 0.68$) whereas there was a non-significant negative relationship between trait self-control and amygdala activity to negative scenes following depletion in the depleted group ($r = -0.28$, $P = 0.19$) such that individuals high in trait self-control show less amygdala activity to negative scenes following depletion. A moderated regression analysis failed to find evidence of participant group being a moderator for the relationship between left-amygdala activity to negative scenes and trait self-control ($\beta_{\text{Self-Control} \times \text{Group}} = 0.61$, $P = 0.16$). Analysis of individual differences in self-reported difficulty of the depletion task, showed a non-significant positive relationship between amygdala change scores with self-reported difficulty that was larger in the depleted participants ($r = 0.29$, $P = 0.17$) than the control participants ($r = 0.14$ $P = 0.51$) however a moderated regression analysis failed to evidence of participant group being a moderator ($\beta_{\text{Difficulty} \times \text{Group}} = 0.4$, $P = 0.52$).

Brain regions showing differential connectivity as a function of valence and group (PPI analysis)

A repeated measures ANOVA of regions showing functional connectivity with the left amygdala seed (MNI coordinates: −21, −6, −21) as a function of scene valence type revealed two regions: the right dorsolateral PFC (MNI coordinates: 39,27,54; BA 8) and the left VMPFC (MNI coordinates: −12,54, −15; BA 11). ROI analysis of these two regions showed that, compared to controls, depleted participants exhibited reduced coupling between the VMPFC and left amygdala during negative scene viewing [$t(46) = 2.27$, $P = 0.028$]. This effect was driven primarily by the control participants showing increased coupling between VMPFC and the left amygdala during the second session whereas coupling between these regions slightly decreased in the depleted participants (Figure 4). The same pattern was in evidence for the dorsolateral prefrontal cortex but was not significant [$t(46) = 1.25$, $P = 0.22$]. Connectivity between the left amygdala and VMPFC for positive and, separately, for neutral scenes did not differ between groups (all $P > 0.6$).

DISCUSSION

Extensive behavioral evidence shows that the ability to regulate thoughts, behaviors and emotions draws upon a domain-general limited resource (Muraven *et al.*, 1998; Vohs and Heatherton, 2000; Gailliot *et al.*, 2007; Hagger *et al.*, 2010). In this study, we used functional neuroimaging to investigate the effects of engaging in effortful self-regulation on subsequent neural responses to emotional material. Drawing upon findings from affective neuroscience on the neural mechanisms involved in emotion regulation, we hypothesized that self-regulatory depletion would impair participants' ability to regulate negative affect as evidenced by an exaggerated response in the amygdala to negative emotional scenes in conjunction with reduced recruitment of prefrontal regions involved in emotion regulation. The present findings offer partial support for this conjecture in that, although depleted participants demonstrated an exaggerated response to negative emotional scenes compared to non-depleted control participants, we failed, however, to find evidence of decreased recruitment of the LPFC or VMPFC in depleted participants. Instead, we found that, compared to control participants, depleted participants showed reduced functional coupling (i.e. PPIs analysis) between the left amygdala and VMPFC that was specific to negative emotional scenes. Taken together these findings suggest that self-regulatory depletion leads to increased emotional reactivity that is largely specific to negatively valenced material (although see below for an alternative conceptualization) and that this exaggerated response may be due to a failure to engage the VMPFC in top–down control of the amygdala.

The present findings are analogous to research on patients with mood disorders. Previous work has shown that, compared to controls, patients with MDD (Johnstone *et al.*, 2007), anxiety disorder (-Somerville *et al.*, 2004), borderline personality disorder (Donegan *et al.*, 2003) and post-traumatic stress disorder (Rauch *et al.*, 2000; Shin *et al.*, 2005) show an exaggerated amygdala response to negative emotional material. In this study, participants were healthy young adults who were not suffering from mood disorders, but were nevertheless induced to experience exaggerated responses to negative emotional stimuli through a commonly used self-regulatory depletion procedure. We point out these similarities not to suggest that depleted subjects are in any way experience a clinical mood disorder, but rather to highlight the similarity in neural mechanism underlying emotion dysregulation.

With regards to the functional connectivity analysis we found that, compared to control participants, depleted subjects showed reduced coupling between VMPFC and left amygdala. This difference between depleted and control participants was driven primarily by an increased coupling between the VMPFC and left amygdala in the control participants during negative emotional scenes whereas the depleted participants showed a non-significant decrease in VMPFC and

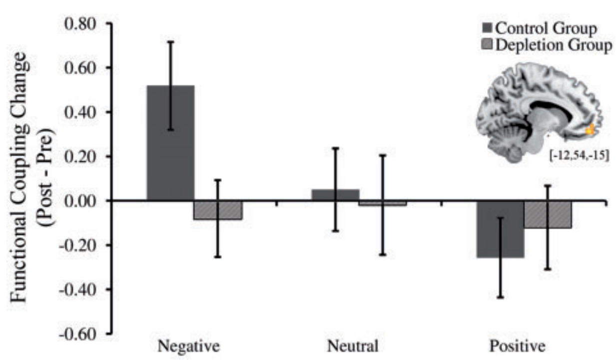

Fig. 4 ROI Analysis demonstrated that the functional coupling between the VMPFC and the left amygdala seed differed between depleted and control participants during negative scene processing [$t(46) = 2.27$, $P = 0.028$]. This difference was driven primarily by an increase in the functional coupling between amygdala and VMPFC in control subjects during the second session (positive change scores) whereas depleted participants showed reduced coupling between these regions after depletion (negative change scores). Error bars indicate SEM.

amygdala coupling following depletion. Although it was expected that control participants would show no change in functional connectivity between the VMPFC and left amygdala, we instead found that, control participants showed increased coupling between left amygdala and VMPFC concomitant with an overall reduced in amygdala responses to emotional scenes during the second session. Given prior evidence of an important role for the structural (Kim and Whalen, 2009) and functional coupling between VMPFC and amygdala for the regulation of affect (i.e. Kim *et al.*, 2003) we speculate that, in the present study the emotion heightening effects of self-regulatory depletion are superimposed upon the normal process of habituation of amygdala responses to emotional material (e.g. Breiter *et al.*, 1996; Kim *et al.*, 2004; Somerville *et al.*, 2004; Davis *et al.*, 2009) and that this failure to habituate may result from reduced amygdala–VMPFC coupling as compared to control participants.

Behavioral studies have shown evidence of spontaneous emotion regulation (e.g. Egloff *et al.*, 2006; Richards and Gross, 2006) and demonstrate that spontaneous emotion regulation occurs more frequently for negative than positive material (Volokhov and Demaree, 2010). Neuroscientific research has similarly uncovered evidence of spontaneous emotion regulation by showing that individual differences in daily use of emotion regulation strategies is correlated with reduced amygdala reactivity to negative material (Drabant *et al.*, 2009). The current findings dovetail with this research by showing that inducing self-regulatory failure through resource depletion leads to increased amygdala activity to negative emotional material but not to positive scenes. We did, however, observe a trend towards an exaggerated response to neutral emotional scenes in depleted participants compared to controls. Although speculative, this effect may be due to the fact that neutral emotional scenes are more ambiguous than clearly valenced negative and positive scenes and are therefore more susceptible to being interpreted in a negative light. Similar findings have been reported previously demonstrating a correlation between amygdala activity to neutral faces and individual differences in anxiety (Somerville *et al.*, 2004). In addition, highly anxious individuals also tend to view neutral faces as threatening (Yoon and Zinbarg, 2008). Although the findings from clinical research support our conjecture, further research is required to determine whether this trend towards increased amygdala response to neutral items following depletion does indeed reflect a shift towards viewing neutral material as being more emotionally aversive.

Throughout we have discussed the effects of self-regulatory depletion in terms of failure to appropriately engage in self control, however recent work suggests that depletion may also have the unexpected effect of increasing the strength of emotions and cravings directly. Specifically, ratings of negative and positive affect in response to emotional scenes are increased in depleted compared to non-depleted participants (Vohs *et al.*, 2012, submitted for publication). Similarly, when evaluating neutral items depleted participants demonstrate more extreme ratings of valence than non-depleted controls. Consistent with neuroscientific models of self-regulation failure (i.e. Heatherton and Wagner, 2011), what these findings suggest is that impulses and self-regulation are held in balance, such that when self-control is impaired (such as during self-regulatory depletion) then impulses and emotions increase in strength. In the present study we have focused mainly on neural responses to negative scenes, however we did observe a non-significant trend towards increased left amygdala activity to neutral scenes following depletion. Indeed, Figure 2 shows that responses to all emotional scene types increased overall in depleted subjects, even if only significant for negative scenes. Thus, the present findings do appear to support, at least in part, the recent finding that self-regulatory depletion may serve to heighten emotional reactivity across the board.

A limitation of the current study is the lack of online ratings of affect when viewing emotional scenes. Instead, participants completed a low-level categorization task that minimally interferes with natural amygdala responses (e.g. Hariri *et al.*, 2003). This specific task was chosen as prior work suggests that 'affect labeling' interferes with normal affective responses in the amygdala (Lieberman *et al.*, 2007). Whether self-regulatory depletion itself disrupts the effects of affect labeling, or indeed of other emotion regulation strategies, is a question for future study. A related issue is that eye gaze was not monitored, given recent research indicating that differences in gaze fixation patterns during emotion regulation can explain some of the variability between different emotion regulation strategies (van Reekum *et al.* 2007), a potential concern is that depleted and control participants had different gaze patterns when viewing emotional scenes. Although we did not collected eye tracking data inside the MRI environment, we explicitly collected self-reports of participants ability to fixate on the different scene types and found no differences between control and depleted participants (see 'Materials and methods' section). Regarding the attention control task itself, one possible concern is that this task may elicit a change in mood. Although we did not measure mood, we note that a number of prior studies of resource depletion, some using the same attention control task, have explicitly assessed mood following depletion and have found no difference between depleted and control participants (Muraven *et al.*, 1998; Vohs and Heatherton, 2000; Schmeichel *et al.*, 2003; Gailliot *et al.*, 2007).

CONCLUSION

Maintaining control over one's emotions is important for human social life. Failure to regulate one's mood can lead to all manner of maladaptive behaviors (Leith and Baumeister, 1996) such as breaking one's diet (Heatherton *et al.*, 1992), alcohol use (Sinha *et al.* 2009), excessive smoking (Tiffany and Drobes, 1990; Kassel *et al.*, 2003) or drug use (Childress *et al.*, 1994). In the present, study we show that engaging in an effortful self-regulation task leads to a subsequent exaggerated neural response to negative emotional scenes along with reduced functional coupling between the VMPFC and amygdala during negative scene processing when compared to non-depleted controls. Based on our findings, we hypothesize that people reflexively regulate their responses to aversive material (e.g. Berkman and Liberman, 2009) but that when this ability to regulate is temporarily depleted, the experience of negative emotion becomes exaggerated relative to normal, a result that is analogous to commonly reported findings of exaggerated amygdala activity in clinical mood disorder populations (e.g. Rauch *et al.*, 2000; Shin *et al.*, 2005; Johnstone *et al.*, 2007). Self-regulatory depletion thus may serve to shift the regulatory balance, such that prefrontal regions involved in top–down control are muted and regions involved in threat detection and vigilance are amplified (e.g. Heatherton and Wagner, 2011). That this effect is largest for negative emotional scenes may be due to the greater inherent threat that such scenes present compared to neutral or positive categories although we note that recent work by Vohs and colleagues suggests that self-regulatory depletion may serve to amplify affective responses to neutral and positive material as well (Vohs *et al.*, 2012). This last conjecture is partially supported by our finding of a marginal increase in left amygdala activity to neutral scenes in depleted compared to control participants.

Finally, the present findings offer further evidence that emotion regulation is dependent on the same limited resource as other forms of self-regulation and can similarly be impaired following depletion of those resources. Understanding how these various forms of self-control interact is vital, as failing to regulate emotions can lead to a cascade of further self-regulatory failures, such as when people drink alcohol, take drugs, or eat to reduce their anxiety or repair their mood.

SUPPLEMENTARY DATA

Supplementary data are available at *SCAN* online.

Conflict of Interest

None declared.

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