

ORIGINAL ARTICLE

Brain Activity and Network Interactions in the Impact of Internal Emotional Distraction

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Abstract

Emotional distraction may come from the external world and from our mind, as internal distraction. Although external emotional distraction has been extensively investigated, less is known about the mechanisms associated with the impact of internal emotional distraction on cognitive performance, and those involved in coping with such distraction. These issues were investigated using a working memory task with emotional distraction, where recollected unpleasant autobiographical memories served as internal emotional distraction. Emotion regulation was manipulated by instructing participants to focus their attention either on or away from the emotional aspects of their memories. Behaviorally, focusing away from emotion was associated with better working memory performance than focusing on the recollected emotions. Functional MRI data showed reduced response in brain regions associated with the salience network, coupled with greater recruitment of executive prefrontal and memory-related temporoparietal regions, and with increased frontoparietal connectivity, when subjects focused on nonemotional contextual details of their memories. Finally, temporal dissociations were also identified between regions involved in self-referential (showing faster responses) versus context-related processing (showing delayed responses). These findings demonstrate that focused attention is an effective regulation strategy in coping with internal distraction, and are relevant for understanding clinical conditions where coping with distressing memories is dysfunctional.

Key words: dorsolateral prefrontal cortex/dlPFC, emotion regulation, emotional interference, frontoparietal control network/FPCN, rumination

Introduction

Emotional distractions that interfere with our goal-oriented performance can be elicited by external stimuli (external distraction), but they can also originate from within (internal distraction). Regarding the latter, for instance, we might find it difficult to focus at work after witnessing a traffic accident during our commute, because images of the crash scene and thoughts about the victims may keep intruding into our mind. Such internal distractions are typically generated by spontaneous cognitions (i.e., memories, thoughts, and representations that may rise into our awareness involuntarily), and they are

often negatively valenced (Krans et al. 2015). Although previous investigations have identified the mechanisms associated with the impact of external emotional distractions (reviewed in Dolcos et al. 2011; Jordan, Dolcos, and Dolcos 2013), the mechanisms associated with the response to and regulation of internal emotional distraction are not clear. The present study investigated the impact of such distractions, elicited by recollection of memories for unpleasant personal events (i.e., negative autobiographical memories, AMs), in response to memory cues presented during the delay-interval of a working memory (WM) task. In addition, the effect of engaging a specific

emotional regulation strategy to reduce the detrimental impact of internal emotional distractions, on both the subjective emotional experience and the objective cognitive performance, was also investigated. Clarification of these issues is important because distracting phenomena such as intrusive memories, rumination, and mind-wandering have been linked to symptoms of affective dysregulation (McNally 2006; Gotlib and Joermann 2010), and the ability to successfully regulate them has been associated with increased resilience against such disturbances (Southwick and Charney 2012).

A critical aspect regarding the way emotional distraction ultimately influences our cognition and behavior is the ability to engage cognitive control mechanisms, in order to cope with it. Although much progress has recently been made in understanding the mechanisms of cognitive control of emotion, or emotion regulation (ER), in general (Ochsner et al. 2012), and of coping with external emotional distraction (Jordan, Dolcos, and Dolcos 2013), the effects of engaging specific ER strategies to cope with internal emotional distraction are unclear. A recent investigation from our group (Denkova et al. 2015) validated the effectiveness of using focused attention (FA) during emotional autobiographical recollection, in healthy participants (see parenthesis below). This ER strategy involves shifting attention away from the emotional aspects of stimuli and events, by changing the focus of memories or thoughts, in order to alter the emotional responses (Gross 2008). The results of our previous investigation showed that instructing subjects to focus away from emotion and onto other nonemotional contextual aspects (e.g., “when/where the event happened”, “who else was involved”) during AM recollection was linked to reduced subjective emotional experience associated with the recollected memories (Denkova et al. 2015). However, it is not known whether similar beneficial effects would be observed on objective measures of cognitive performance, if for instance AM recollection is triggered concurrently with performance in an ongoing cognitive task. Hence, the first main goal of the present investigation was to determine how internal emotional distraction impacts cognitive performance, and whether instructed use of FA as an ER strategy diminishes its impact. Using FA to investigate ER effects in the context of emotional distraction is well suited, because it can be more promptly engaged than other ER strategies, such as reappraisal (Hajcak et al. 2009; Thiruchselvam et al. 2011). (Research testimonials and our current scientific projects also provide strong support for the effectiveness of this ER strategy. Below, we present an excerpt from a very powerful testimonial received from a person who used it effectively, after reading about our findings disseminated through various media outlets, following the publication of our research article (Denkova et al. 2015). “I began to look back at the same memory that I have not been able to shake for 6 years now, and I felt like a lightbulb went off in my head. The simple switch from thinking about the amount of sadness I felt that day [...] changed everything. It is really remarkable the difference it made. I immediately felt an unfamiliar sense of balance and calmness. The tension in my shoulders went away and I started to cry happy tears that I have not cried in a long time”; shared with permission).

Turning to the neural level, there is abundant evidence regarding the brain mechanisms mediating the impact of external emotional distraction. Brain imaging studies in which emotional pictures were presented as task-irrelevant stimuli during WM tasks (Dolcos and McCarthy 2006; Dolcos et al. 2006, 2008, 2013; Anticevic et al. 2010; Denkova et al. 2010; Diaz et al. 2011; Oei et al. 2012; Jordan, Dolcos, Denkova et al. 2013; Jordan and

Dolcos 2017) showed that the impairing effect of negative distraction originating from the external environment was linked to opposing patterns of activity in 2 large neural systems: a dorsal executive system (DES) involved in cognitive/executive processing (showing decreased/disrupted activity) and a ventral affective system (VAS) involved in emotion processing (showing increased activity) (reviewed in Dolcos et al. 2011; Jordan, Dolcos, and Dolcos 2013). More specifically, DES includes brain regions typically associated with cognitive control and maintenance of goal-relevant information (dorsolateral prefrontal cortex, dlPFC, and lateral parietal cortex, LPC), which are also part of the frontoparietal control network (FPCN) (Fuster 1997; Smith and Jonides 1999; D’Esposito et al. 2006; Koenigs et al. 2009; Nee et al. 2012; Niendam et al. 2012). On the other hand, VAS comprises regions involved in basic emotion processing (amygdala, AMY) and emotion integration and regulation (ventrolateral prefrontal cortex, vlPFC), as well as regions involved in self-referential processing (medial prefrontal cortex, mPFC), which are also part of the salience (SN) (Seeley et al. 2007; Corbetta et al. 2008; Bressler and Menon 2010) and default-mode (DMN) networks (Raichle et al. 2001; Greicius et al. 2003; Fox et al. 2005; Buckner et al. 2008), respectively. Thus, in general, the impact of external emotional distraction on ongoing WM processing has been associated with an increased bottom-up effect, consistent with the idea that greater recruitment of VAS regions by emotional distraction (relative to control conditions) temporarily “takes off-line” DES regions and results in cognitive impairment (Dolcos and McCarthy 2006; Dolcos et al. 2011; Jordan, Dolcos, Dolcos et al. 2013). Notably, while we do not treat DES and VAS as equal to brain networks, we would like to point to considerable overlaps between these larger neural systems, sensitive to task-irrelevant emotional distraction, and the large-scale functional networks (Jordan and Dolcos 2017). Specifically, the task-induced dorsoventral dissociation between DES and VAS overlaps with the resting-state dissociation between FPCN/central-executive network and SN/ventral-attentional network, respectively (Dosenbach et al. 2007, 2008; Power et al. 2011; Seeley et al. 2007; Yeo et al. 2011).

Regarding the neural mechanisms of AM, retrieval of personal memories has been linked to activity in a host of brain regions generally associated with self-referential processing and memory, which substantially overlap with DMN (Addis et al. 2004; Greenberg et al. 2005; Svoboda et al. 2006; Buckner and Carroll 2007; Cabeza and St Jacques 2007; Daselaar et al. 2008; Spreng et al. 2009; Hoescheidt et al. 2010; Andrews-Hanna et al. 2014; Denkova et al. 2015). Also, more recent investigations point to several DMN subcomponents (e.g., ventral vs. dorsal, anterior vs. posterior) that are putatively associated with distinct functions and may also operate at different time scales during AM recollection (Daselaar et al. 2008; Zabelina and Andrews-Hanna 2016; Tailby et al. 2017). Namely, specific DMN subcomponents have been linked with functions such as episodic retrieval and prospective construction, self-referential processing, as well as more abstract forms of reflection (Uddin et al. 2009; Andrews-Hanna et al. 2010; Leech et al. 2011; Kim 2012; Qin et al. 2012; Zabelina and Andrews-Hanna 2016; Tailby et al. 2017). Regarding timing, differences in the modulation of activity during AM recollection have been reported between regions associated with initial accessing (e.g., medial temporal lobe regions—amygdala and hippocampus—and “core” midline cortical regions—mPFC and posterior cingulate cortex, PCC) versus later elaboration of AM content (e.g., precuneus and left PFC) (Daselaar et al. 2008; Inman et al. 2018; Tailby et al. 2017).

Available evidence regarding the engagement of FA as an ER strategy generally points to the engagement of cognitive/executive control regions (prefrontal and parietal cortices), to down-regulate activity in emotion-sensitive brain regions (AMY), similar to other ER strategies, such as reappraisal, putatively reflecting top-down effects (Ochsner et al. 2004; Wager et al. 2008; McRae et al. 2010; Kanske et al. 2011). In addition, focusing on context during AMs recollection has been linked with increased activity in medial temporal lobe (parahippocampal cortex, PHC) and parietal (inferior parietal lobule, IPL) regions (Denkova et al. 2015), which are memory-related brain regions implicated in the retrieval of visuospatial/situational contextual details (Hassabis and Maguire 2007; Ranganath and Ritchey 2012), and potentially also involved in attending to such information during retrieval (Cabeza et al. 2008; Vilberg and Rugg 2008), respectively. It is not known, however, whether similar mechanisms are engaged when negative AMs are recollected as emotional distraction, in the context of a concurrent cognitive task. Thus, the second main goal of the present study was to clarify the neural correlates of engaging a specific ER strategy (FA), to cope with internal emotional distraction, presented concurrently with performance in a cognitive task.

These issues were addressed here by using a dual WM task with internal emotional distraction, in which personalized cues presented during the delay interval triggered the retrieval of unpleasant AMs as internal distraction. The task also involved explicit manipulation of the attentional/retrieval focus (away from the emotional content of the recollected AMs), to diminish the negative impact of AM recollection on both subjective (emotional ratings) and objective (WM performance) measures of performance. Brain activity was recorded using event-related fMRI. To clarify potential interactions between regions associated with the major brain networks, analyses of basic differences in brain activity were complemented by functional connectivity analyses investigating task-induced dissociations in functional coupling between these regions. Overall, based on the extant evidence, we expected a general pattern of brain responses in which increased detrimental impact of emotional distraction would be linked with increased bottom-up effects, and reduced impact of distraction due to ER engagement would be linked to increased top-down response and reduced bottom-up effects. We also made the following 4 specific predictions. First, regarding the behavioral results, we expected that focusing attention away from the emotional content and on the non-emotional contextual aspects would be reflected in both reduced emotional ratings and reduced detrimental impact of recollecting goal-irrelevant negative AMs on WM performance. Second, at the neural level, we expected that internal emotional distraction would be overall associated with similar responses as those produced by external emotional distraction (decreased vs. increased activity in DES vs. VAS regions, respectively), while also engaging mechanisms specific to AM recollection (increased response in DMN regions). Third, regarding the ER manipulation, we expected that focusing away from the emotional content would be reflected in reduced activity in VAS regions and increased engagement of executive regions, as well as in areas typically involved in the retrieval of contextual information. In addition, we also explored the possibility of temporal dissociations within DMN, as a result of the ER manipulation, possibly reflecting earlier responses to the emotional content of AMs versus later retrieval of their nonemotional contextual aspects. Finally, we also expected greater functional coupling between independently identified executive regions

and regions involved in context retrieval, under the nonemotional focus.

Materials and Methods

Participants

A total of 40 healthy, young (18–39 years of age, 14 males) adults participated in this investigation. Overall, 33 subjects (11 males) participated in the main behavioral study, out of whom 19 (5 males) right-handed subjects were also part of the fMRI sample. The rest of 7 (3 males) right-handed subjects participated in a pilot study conducted to validate the time window employed for fMRI analyses (see Supplementary Methods). All subjects were screened for neurological and/or psychiatric disorders using a questionnaire developed in consultation with trained clinicians, which was employed for inclusion/exclusion criteria. Additionally, the fMRI subjects were also screened for baseline WM performance using the Delayed Matching to Sample (DMS) test, part of the Cambridge Automated Neuropsychological Testing Battery (CANTAB) (Cambridge-Cognition). Data from 2 participants in the behavioral sample were excluded due to inability to perform the task and data from 2 participants in the fMRI sample were excluded due to response box malfunction and low performance on the DMS test (accuracy 3 SD below group mean for the 12 s delay), respectively. Hence, behavioral and fMRI results are reported on 29 (11 males) and 17 (5 males) participants, respectively. The experimental protocol was approved by the Internal Review Board of the University of Illinois at Urbana-Champaign, and all subjects provided written informed consent.

Experimental Tasks

The experimental session consisted of a dual WM-AM recollection task (comprising a “main” WM task and a “secondary” AM recollection task), which also included manipulation of attentional/retrieval focus as a manipulation of emotion regulation/control. The impact of AM recollection as internal emotional distraction and of the emotional control manipulation was assessed using both subjective (emotional ratings) and objective (WM performance) measures. Before performing the dual task, participants were given detailed instructions and performed a practice session, to ensure that they understood the instructions and to get familiarized with the tasks.

The Main WM Task

Participants performed a delayed match-to-sample WM task for shapes, adapted after Dolcos and McCarthy (2006), with cues for AMs presented as distractors during the delay interval between the memoranda and the probes (Fig. 1). The memoranda consisted of pairs of polygons (Arnout and Attneave 1956) randomly generated using a MATLAB script (Collin and McMullen 2002), which allows control over the similarity and complexity of stimuli. These geometric figures are also less susceptible to other possible confounds (e.g., due to verbalization), compared with other stimuli (e.g., faces) used as memoranda in previous studies. Equal numbers of trials (i.e., 40) involved AM recollection and a control condition (see below). The pool of trials was divided into 8 equal sets (counterbalanced across distractor-type categories), which were randomly assigned to 8 experimental blocks/runs. To avoid induction of longer-lasting effects, the trials within each block were pseudo-randomized, so that no more than 2 consecutive trials of the same type were

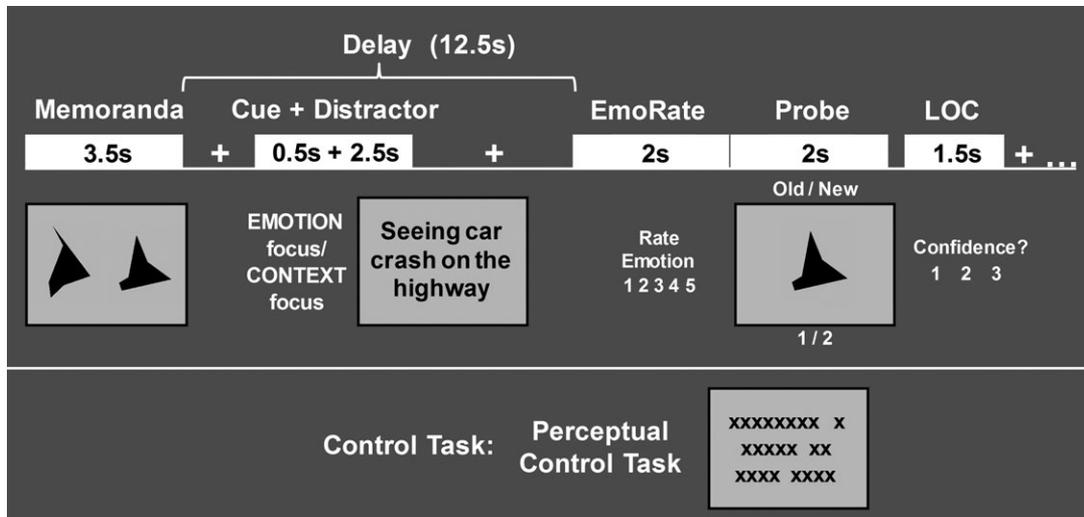


Figure 1. Diagram of the combined working memory-emotion regulation (WM-ER) task. Functional magnetic resonance imaging (fMRI) data were recorded while subjects performed a WM task for geometric shapes. Personalized cues for negative autobiographical memories (AMs) were presented during the delay interval between the memoranda and the probes. Preceding the AM cue, a retrieval instruction cue prompted participants to focus either on emotional (Emotion focus) or nonemotional contextual (Context focus) details of their recollected AMs. Recollection of AMs was followed by subjective (emotional ratings) and objective (WM performance) assessments of their impact, using a 5-point rating scale (1 = Least and 5 = Most negative) and a recognition memory task, respectively. The latter involved 2 steps: first, participants indicated by pushing a button whether single-shape probes were part of the memoranda or not (Old = 1, New = 2), and then they indicated the level of confidence (LOC) in their responses by pushing 1 of 3 buttons (1 = Low, 2 = Medium, 3 = High).

presented. To prevent possible biases from using the same run order, participants were assigned different run orders. All stimuli were presented using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA).

As illustrated in Figure 1, each trial started with the presentation of shape memoranda (3.5 s), which subjects were instructed to encode and maintain in WM during the delay interval between the offset of the memoranda and the onset of the memory probe (12.5 s). Participants were instructed to maintain focus on the main WM task, while performing the secondary task as instructed (see below), and then when the single-shape probes appeared they had to indicate by a button press whether they were part of the current memorandum (Old) or not (New); 50% of the probes were Old and 50% were New. Subjects were instructed to make quick and accurate responses while the probes were on the screen. Then, participants also rated the level of confidence (LOC) in their responses, using a 3-point Likert scale (1 = lowest, 3 = highest), but these ratings were not used in the present analyses. The WM-related responses were followed by a 10.5 s intertrial interval (ITI), to allow the hemodynamic response to return to baseline. During this time, participants were instructed to relax and refrain from doing anything systematically that could potentially affect the intertrial baseline signal (e.g., counting).

The Secondary AM Retrieval Task With Emotion Control: Emotion Versus Context Focus

During the delay interval between the memoranda and the probes, participants were presented with personalized cues for their memories collected prior to the fMRI session (see Supplementary Methods), and instructed to retrieve them either by focusing on emotional (“Emotion” condition) or on nonemotional contextual (“Context” condition) details (Fig. 1). Presentation of the AM cues started 3 s after the offset of the memoranda, and lasted for 2.5 s. For the Emotion condition, participants were instructed to focus on the emotional aspects

of their memories, including sensations and feelings that they may have triggered (e.g., “butterflies” or “burning” sensations in the stomach). For the Context condition, participants were instructed to focus on other (nonemotional) contextual aspects of their memories, by retrieving as many details as possible (e.g., about where and when the event occurred and who/what was present during the event, how they/others were dressed, what was the weather like). Each memory cue was preceded by an instruction cue (“Emotion Focus” or “Context Focus,” corresponding to the Emotion and Context conditions, respectively). Following the presentation of the memory cues, participants continued remembering their AMs until cued again to rate the subjective emotional response elicited by each recollection, on a 5-point Likert scale (1 = not at all negative and 5 = very negative). Participants were instructed to make quick and accurate responses and to use the whole scale. Finally, the task also employed a minimal-distraction control condition involving watching random strings of letters “X,” mimicking the structure of sentences used as AM cues. The control stimuli were preceded by the instruction “Look,” and subjects were instructed to look at the screen and maintain focus on the WM task. For consistency with the AM conditions, each control trial was also rated for negativity.

Imaging Protocol

Scanning was conducted on a 3 T Siemens Trio scanner, hosted at the Beckman Institute’s Biomedical Imaging Center. After the sagittal localizer and the 3D MPRAGE anatomical images (TR = 1800 ms; TE = 2.26 ms; flip angle = 9°; FOV = 256 × 256 mm²; matrix size = 256 × 256 mm²; slice thickness = 1 mm; volume size = 192 slices; voxel size = 1 × 1 × 1 mm³), 8 blocks of full-brain EPI functional images were acquired axially, coplanar with the AC-PC (TR = 2000 ms; TE = 40 ms; flip angle = 90°; FOV = 256 × 256 mm²; matrix size = 64 × 64 mm²; slice thickness = 4 mm, no gap; volume size = 28 slices; voxel size = 4 × 4 × 4 mm³).

Behavioral Data Analyses

Responses in the WM task were classified in 1 of the 4 categories derived from signal detection theory (Macmillian and Creelman 2005): 1) Hits, corresponding to memorandum shapes correctly classified as Old; 2) Misses, corresponding to memorandum shapes incorrectly classified as New; 3) Correct Rejections (CRs), corresponding to new shapes correctly classified as New; and 4) False Alarms (FAs), corresponding to new shapes incorrectly classified as Old. Average percentages of probes correctly identified as being Old or New were also calculated for each participant [$\%WM\ Accuracy = (\%Hits + \%CR)/2$]. It should be noted that $\%WM\ Accuracy$ is mathematically equivalent to $\%Corrected\ Recognition$ ($\%Hits - \%False\ Alarms$) and related to d' $z(H) - z(F)$, where H and F are the proportions of hits and false alarms, respectively (Macmillian and Creelman 2005). In general, $\%WM\ Accuracy$ is used in WM studies with an fMRI component to capitalize on all possible trials, and is consistent with fMRI analyses that employ both Old and New trials. This is particularly important if delay/maintenance brain activity is targeted, because it allows combination of both types of correct responses (Hits and CRs). To check for consistency, we repeated our calculations using d' and the results were similar (see Results). WM performance scores provided assessments of the objective impact of internal emotional distraction and of the effects of engaging ER on online cognitive performance, which complemented the ratings of negative experience associated with AM recollection that provided subjective indices of the effectiveness of the ER manipulation on (re)experiencing the associated emotions (Denkova et al. 2015). Differences in WM performance and negativity ratings among the trial types were assessed using repeated-measures ANOVAs and follow-up t tests, using SPSS.

fMRI Data Analyses

Statistical analyses were preceded by the following preprocessing steps (performed with SPM12—Statistical Parametric Mapping): slice timing correction, realignment, coregistration, normalization, and smoothing (8 mm kernel). For the data analysis, we used in-house custom MATLAB scripts involving whole-brain voxel-wise analyses (Dolcos and McCarthy 2006; Jordan, Dolcos, Denkova et al. 2013; Jordan and Dolcos 2017), to compare the brain activity associated with the conditions of interest (e.g., trials with Context vs. Emotion focus). For subject-level analyses, the fMRI signal was selectively averaged in each subject's data as a function of trial type (e.g., Context focus, Emotion focus, and Control) and time point (one prestimulus and 14 poststimulus onset time points). Pair-wise t statistics for the contrasts of interest were calculated for each subject. No assumption was made about the shape of the hemodynamic response function, because this method allows finer comparisons of the MR signal on a TR-by-TR basis and has been proven effective in dissociating responses produced by the WM task with emotional distraction (Dolcos and McCarthy 2006; Dolcos et al. 2008; Denkova et al. 2010; Jordan and Dolcos 2017; Jordan, Dolcos, Denkova et al. 2013; Morey et al. 2009). The individual analysis produced whole-brain average and activation t maps for each condition, contrast of interest, and TR/time point.

The outputs of subject-level analyses were used as inputs for second-level random-effects within-group analyses. The main analyses focused on effects recorded in a 2-time point window (i.e., covering the 14–18 s period after the memoranda

onset: TRs 9–10), a priori selected based on previous investigations regarding the effects of external emotional distractors (Dolcos and McCarthy 2006; Denkova et al. 2010; Jordan, Dolcos, Denkova et al. 2013; Jordan and Dolcos 2017) and previous evidence indicating timing differences between components of AM recollection (Daselaar et al. 2008). Moreover, the selected time window was further validated by a pilot study with an independent sample (see Supplementary Methods and Supplementary Fig. S1). Each random-effects t statistic map was thresholded and corrected for multiple comparisons. Unless specified otherwise, the maps were thresholded at $P_{FWE} < 0.05$, corrected for multiple comparisons using a cluster defining threshold of $P < 0.001$ (one-tailed) and 10 000 Monte Carlo simulations (Slotnick et al. 2003; Slotnick 2017), in conjunction with a gray matter mask derived from the corresponding tissue probability map part of SPM12 (The IXI Dataset, <http://www.braindevelopment.org>), liberally thresholded at $P = 0.2$ to ensure that effects were more likely to be located in gray matter (Heinzel et al. 2016).

Identification of Brain Regions Involved in the Response to, and Coping With, Internal Emotional Distraction

First, to identify brain regions involved in the overall response to internal emotional distraction, both Emotion and Context focus trials were collapsed into a single AM condition. Because the focus of this analysis was on identifying mechanisms shared by internal distractors regardless on their impact on WM performance, all trials were included. Specifically, to identify brain regions whose activity was sensitive to internal emotional distraction, we directly compared brain activity related to AM recollection and control. Similar to the procedures used in studies with external emotional distraction (Dolcos and McCarthy 2006; Dolcos et al. 2006, 2008, 2013; Anticevic et al. 2010; Denkova et al. 2010; Diaz et al. 2011; Oei et al. 2012; Jordan, Dolcos, Denkova et al. 2013; Jordan and Dolcos 2017) (reviewed in Jordan, Dolcos, and Dolcos 2013), responses to internal emotional distraction were identified by deactivations (see parenthesis below) in DES regions (AM < Ctrl) and increased activity in VAS regions (AM > Ctrl) for the AM recollection condition versus control. Notably, given the nature of distraction involved here, increased activity was also expected in DMN regions in response to AM recollection. Second, to identify brain regions involved in the regulation of internal emotional distraction, we directly compared brain activity related to the Emotion versus Context focus manipulation (i.e., Emotion > Context and Context > Emotion, respectively), which was expected to influence both the subjective emotional (re)experience of the recollected negative AMs and their objective impact on WM performance. Because these analyses target differences in WM performance linked to ER manipulation (see Results), they were performed on correct trials only (Hits and CR collapsed). This more stringent approach ensured that only instances where subjects were actually performing the task were included in the analyses. However, because this approach may have rendered the analysis relatively less sensitive to effects of WM impairment, which could be due to distraction but also due to other factors, such as unsuccessful encoding or lapses of attention, we also performed a supplementary analysis that eliminated the correctness criterion. (We use the term “deactivation” because, in general, the observed response to emotional distraction has indeed been one of deactivation below the intertrial baseline (Dolcos and McCarthy 2006). Although this may not always be the case, the expected pattern is still one of

“deactivation” relative to both peak activation during maintenance and the Control condition, similar to previous investigations (Dolcos et al. 2008; Denkova et al. 2010; Jordan, Dolcos, Denkova et al. 2013; Jordan and Dolcos 2017)).

Temporal Dissociation Analyses

To test for possible temporal dissociations (see parenthesis below) of activity within DMN, as a result of the ER manipulation, activity for the “earliest” and “latest” time frames was compared across “dorsal” and “ventral” subcomponents of DMN (Daselaar et al. 2008; Andrews-Hanna et al. 2010; Shirer et al. 2012). The “dorsal” and “ventral” DMN subcomponents were identified by 2 a priori defined ROIs, part of a commonly employed functional brain parcellation derived based on using independent component analyses performed on resting-state data (Shirer et al. 2012), and included DMN regions associated with initial accessing and processing of self-relevant content (e.g., hippocampus and midline cortical structures—mPFC and PCC) versus regions associated with the construction of mental scenes based on memory (e.g., PHC, precuneus, and lateral frontal regions). Importantly, because the ROIs were defined independently from the current dataset, the analysis was not circular (Kriegeskorte et al. 2009). To test for a temporal dissociation, brain activity within each ROI was averaged separately for Emotion and Context trials, for the “earliest” and “latest” time points, defined by extending our initially targeted time window (TRs 9–10) by one time point “before” (TR 8) and one time point “after” (TR 11). Of note, this extension was based on inspecting the shape of the hemodynamic response, which suggested that certain peaks might have been shifted by 1 TR, and for this reason the temporal dissociation analysis was deemed exploratory (see Supplementary Methods). To maximize the differences in time, the temporal analysis compared these 2 “extreme” time points. The data were then exported to SPSS and analyzed with a repeated-measures ANOVA with the following within-subject factors: DMN Subcomponent (Dorsal vs. Ventral), ER manipulation (Emotion vs. Context), and Time (Earlier vs. Later). (Of note, fMRI is not the best modality for investigating temporal dissociations, due to its relatively low temporal resolution, and other modalities such as magnetoencephalography (Garcia-Pacios et al. 2015) may be more suitable. Nevertheless, such temporal dissociations have been previously proposed based on BOLD fMRI (Daselaar et al. 2008; Tailby et al. 2017; Inman et al. 2018), and thus we also explored this aspect.)

Functional Connectivity Analyses

To test whether Context focus was associated with greater functional coupling between executive regions and regions involved in context retrieval, we examined functional connectivity between dlPFC and other regions associated with cognitive control, and between dlPFC and regions associated with context retrieval, using a procedure previously employed and validated by us (Dolcos et al. 2006; Jordan and Dolcos 2017). This approach is similar to the “beta-series correlations” procedure described by Rissman et al. (2004), but uses the baseline-subtracted MR signal instead of beta values. For these analyses, at the first level, within-subject voxel-wise correlations were performed on a trial-by-trial basis, using activity extracted from 2 a priori defined seed ROIs and targeting activity in one a priori defined ROI (i.e., the binary map). The seed ROIs were two 6 mm radius spheres identifying the left and right dlPFC (MNI/Talairach coordinates [x, y, z]: -40, 24, 34/-38, 18, 36 [left ROI] and 44, 26, 42/39, 19, 45 [right ROI]), independently derived

using spatiotemporal partial least squares performed on across-tasks activity (Spreng et al. 2013). These 2 ROIs were selected because of their reliable affiliation with FPCN in an independent investigation across multiple tasks, involving both externally and internally oriented processing (Spreng et al. 2013) (see Supplementary Methods for details). The target ROI was a composite map identifying regions involved in cognitive control (FPCN/“executive control network”) and regions involved in the retrieval of contextual information (“ventral” DMN) from Shirer et al. (2012). The composite map was created using a logical “OR” conjunction between the maps identifying each of the 2 targeted networks, thus limiting our results to an a priori defined ROI (2083 voxels; see Supplementary Fig. S2). Again, because both the seeds and the targeted ROI were defined independently from the present data, the analyses were not circular (Kriegeskorte et al. 2009). Consistent with our temporal dissociation hypothesis, we expected greater coupling between executive and context-retrieval regions under ER during the “later” time window. Thus, the trial-based analyses were performed for the “later” time point when the maximal effect of ER was also observed in DES regions (i.e., TP 10 for the Context > Emotion contrast in the main analyses), in each participant, for the 2 targeted trial types (i.e., associated with Emotion and Context focus). The resulting correlation maps were normalized using Fisher’s z transformation. At the second level, across subject random-effects t comparisons of the individual correlation maps were performed, to identify regions systematically showing greater functional connectivity with the seed regions, for one condition relative to the other (e.g., Context > Emotion). A voxel-wise false discovery rate (FDR) (Benjamini and Hochberg 1995; Genovese et al. 2002) correction for multiple comparisons ($q_{FDR} < 0.05$, 5 contiguous voxels) was employed for this analysis, instead of simulation-based cluster extent thresholding, because the binary map isolating the targeted brain regions (i.e., FPCN and DMN regions) included multiple regions that varied in size and location, and it was noncontiguous (Woo et al. 2014).

Brain–Behavior Interaction Analyses

Finally, we also performed brain–behavior analyses that correlated fMRI signals in response to emotional distraction with ratings of negative experience and WM performance (see Supplementary Methods).

Results

Behavioral Results

Reduced Negative Experience and WM Interference for Context Focus
Analyses of the behavioral data showed both reduced negative experience and WM interference of AM retrieval when focusing away from the emotional content of negative memories (i.e., Context compared with Emotion focus) (Fig. 2 and Supplementary Table S1). Confirming these, the results of a one-way repeated measures ANOVA (Attention Focus: Emotion, Context, Control) on negativity ratings yielded a significant effect ($F_{(2,56)} = 220.49$, $P < 0.001$), and planned comparisons showed significantly lower experienced negativity when subjects were focusing on context compared with emotion ($t_{(28)} = 6.58$, $P < 0.001$). Second, the results of a one-way repeated measures ANOVA (Attention Focus: Emotion, Context, Control) on WM performance yielded a significant effect ($F_{(2,56)} = 5.11$, $P = 0.009$), and planned comparisons showed significantly better WM performance under Context than Emotion focus ($t_{(28)} = 2.75$, $P = 0.01$). Similar results were also

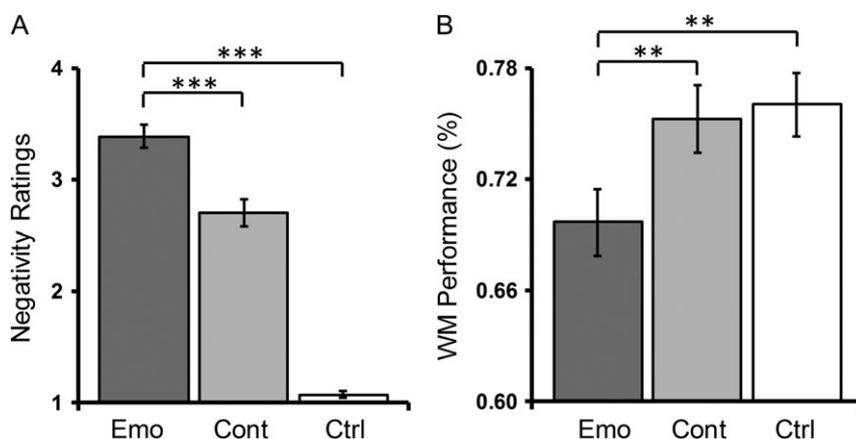


Figure 2. Diminished experienced emotion and working memory interference under emotion regulation. Focusing on context and away from emotional aspects during recollection of task-irrelevant emotional AMs reduced both (A) subjective negativity ratings and (B) objective WM interference. Working memory performance reflects overall accuracy (average of Hits and CRs) in the Old/New responses. Emo, Emotion Focus; Cont, Context Focus; Ctrl, Control Condition. Error bars represent standard errors of means. ** $P \leq 0.01$, *** $P < 0.001$.

observed in the fMRI subsample (Supplementary Table S1). Specifically, a one-way repeated measures ANOVA on negativity ratings yielded a significant effect ($F_{(2,32)} = 193.47$, $P < 0.001$), and planned comparisons showed significantly lower experienced negativity when subjects were focusing on context compared with emotion ($t_{(16)} = 5.07$, $P < 0.001$). Similarly, the results of a one-way repeated measures ANOVA on WM performance yielded a significant effect ($F_{(2,32)} = 3.48$, $P = 0.043$), and planned comparisons showed significantly better WM performance under Context than Emotion focus ($t_{(16)} = 2.32$, $P = 0.034$). Finally, we repeated our calculations using d' instead of %WM accuracy, and the results were similar. Specifically, d' WM performance was better under Context compared with Emotion focus in both the full sample ($t_{(28)} = 2.64$, $P = 0.013$) and the fMRI subsample ($t_{(16)} = 2.37$, $P = 0.031$). There were no differences in d' WM performance between Context focus and Control, in either the full sample ($t_{(28)} = 0.56$, $P > 0.5$) or the fMRI subsample ($t_{(16)} = 0.15$, $P > 0.8$). Together, the present behavioral results suggest that the instructed use of FA as an ER strategy to cope with internal emotional distraction is associated with both reduced “subjective” emotional experience and reduced “objective” interference on WM performance.

fMRI Results

Analyses of fMRI data investigated both the general brain response to internal emotional distraction, irrespective of WM performance, and brain activity specifically linked to instructed manipulation of ER (Emotion vs. Context focus). Overall, these analyses yielded evidence consistent with both similar responses to AM recollection as internal emotional distraction, independent of the ER manipulation, and ER-related dissociations in DES, VAS, and DMN regions. These results are presented below.

Opposing Patterns of Response to Internal Emotional Distraction in VAS and DMN Versus DES Regions

To identify brain regions involved in the response to internal emotional distraction, analyses performed on all trials compared brain activity linked to AM recollection (irrespective of attentional/retrieval focus) versus Control. As expected, recollection of negative AMs as internal emotional distraction was associated with both increased activity in VAS and DMN

regions, coupled with greater deactivation relative to Control in DES regions (Fig. 3 and Supplementary Table S2). Specifically, internal emotional distraction was associated with higher activity in basic emotion processing (AMY) and emotion integration (vlPFC) regions, part of VAS. In addition, there was also increased activity in brain regions involved in AM recollection and self-referential processing (mPFC, PCC), part of DMN. By contrast, internal emotional distraction evoked strong deactivation relative to Control in LPC (inferior parietal lobule), a brain region involved in WM and attentional processing. These findings regarding internal distraction extend previous results focusing on external distraction, and show that similar dorso-ventral mechanisms are overall engaged independent of the originating source of distraction (external or internal), while internal distraction is also specifically linked to the engagement of DMN mechanisms. Moreover, as described below, dissociations in brain activity in VAS and DES regions for Emotion versus Context focus were also identified, linked to the differences in behavioral performance associated with the ER manipulation.

Reduced VAS Activity and Greater Engagement of DES and Context Retrieval Regions under ER

To identify brain regions involved in the instructed ER of internal emotional distraction, analyses performed on correct trials compared brain activity linked to the attentional manipulation (i.e., comparison of Emotion vs. Context focus) (Fig. 4 and Supplementary Table S3). Consistent with the behavioral results showing reduced impact of internal distraction under Context compared with Emotion focus, brain imaging results showed that focusing on context was associated with both reduced activity in emotion processing regions (overlapping with SN) and increased activity in cognitive control regions and in regions associated with the retrieval of contextual information. Specifically, Context focus was associated with reduced activity in basic emotion processing regions (AMY) and in regions associated with integration and filtering of emotional information (dorsal anterior cingulate cortex—dACC and anterior insula—aiNS), which are also key regions of SN. Supplementary brain-behavior correlational analyses performed on all trials (see Supplementary Methods) identified a positive correlation between dACC activity and emotional ratings in response to Emotion versus Context focus (Supplementary Fig. S3). Similar effects were observed in

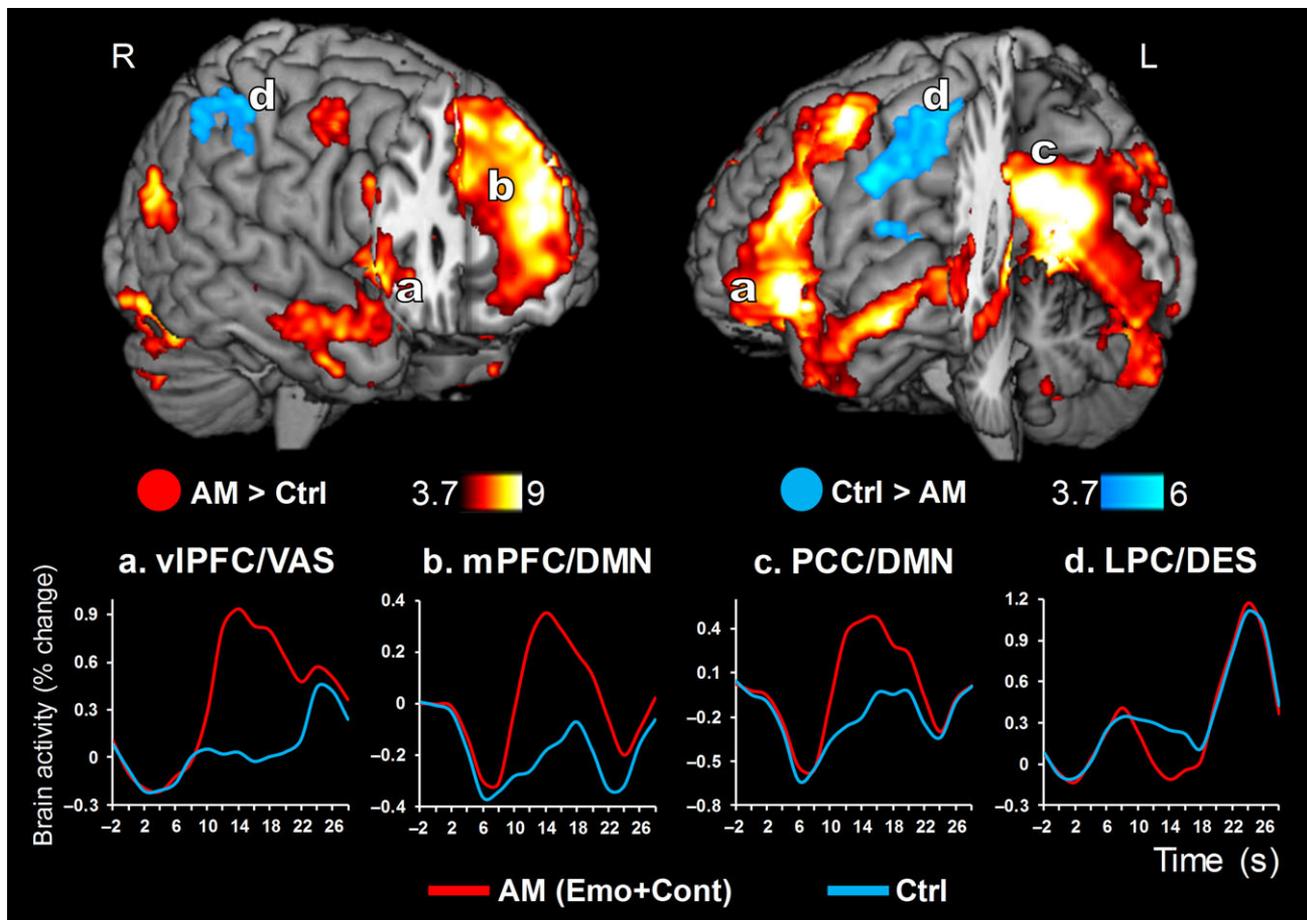


Figure 3. Opposing responses in VAS and DMN versus DES regions to internal emotional distraction. Brain responses to internal emotional distraction were characterized by increased activity in VAS (a, vIPFC) and midline regions part of DMN (b, mPFC and c, PCC) versus deactivation relative to Control in DES regions (d, LPC). The line graphs display the time courses of brain activity extracted from peak voxels of the AM versus Ctrl comparison (Talairach coordinates [x, y, z]: -42, 22, -2/47, 21, 3 [L/R vIPFC]; -8, 45, 23 [mPFC]; -9, -56, 24 [PCC]; -42, -36, 43/39, -36, 45 [L/R LPC]). The colored horizontal bars represent the gradient of the t values. The t maps are displayed at $P_{FWE} < 0.05$ (see [Materials and Methods](#)). VAS, Ventral Affective System; DMN, Default Mode Network; DES, Dorsal Executive System; vIPFC, Ventrolateral Prefrontal Cortex; mPFC, Medial PFC; PCC, Posterior Cingulate Cortex; LPC, Lateral Parietal Cortex; AM (Emo + Cont), Autobiographical Memories: Emotion and Context Focus collapsed; Ctrl, Control Condition; L, Left hemisphere; R, Right hemisphere.

several other VAS/SN regions (right frontotemporal junction, Talairach coordinates [x, y, z] = 47, 14, -8; left and right INS, Talairach coordinates [x, y, z] = -38, -16, -5 [left] and 36, -9, -3 [right]; precuneus, Talairach coordinates [x, y, z] = 17, -68, 31). These findings further suggest that greater activity in SN was linked to greater subjective experience and possibly increased conflict driven by unpleasant emotions.

Focusing on context was also associated with greater sustained activity in an executive control region (dlPFC) and in memory-related regions involved in the retrieval of contextual information (parahippocampal/fusiform cortex, and middle temporal/angular gyrus, AG), which are also part of DMN. Furthermore, results of a supplementary analysis conducted on all trials (i.e., independently of WM performance) did not identify significant dlPFC effects for the Context > Emotion comparison (not even at lower thresholds; see Supplementary Fig. S4), thus indicating that greater engagement of this executive region was characteristic of successful WM performance. Finally, Neurosynth-based (Yarkoni et al. 2011) meta-analyses confirmed that our peak coordinate (Talairach coordinates [x, y, z]: -42, 15, 27/MNI coordinates [x, y, z]: -44, 20, 24), as well as the dlPFC cluster, overlapped with regions involved in cognitive control

(see Supplementary Results and Supplementary Fig. S5). Thus, the brain imaging findings suggest that focusing away from emotion was associated with a shift in processing bias from emotion/salience regions to executive and context retrieval regions. Interestingly, the timing of the responses in emotion versus executive processing regions was slightly different (TRs 8/9 vs. 10/11, respectively) and it overlapped with the timing of responses in “dorsal” versus “ventral” DMN regions (Shirer et al. 2012), suggesting a temporal dissociation within DMN in response to the ER manipulation (see below).

Temporal Dissociation of DMN Activity, in Response to Emotion Versus Context Focus

To formally test for a temporal dissociation within DMN in response to the ER manipulation, activity in 2 independently defined ROIs identifying the “dorsal” and “ventral” DMN sub-components (Shirer et al. 2012) (see [Materials and Methods](#)) was averaged separately for trials corresponding to Emotion and Context focus, for earlier (TR 8) and later (TR 11) time points, and submitted to SPSS analyses. Results of a 3-way repeated measures ANOVA (DMN Subcomponent \times ER manipulation \times

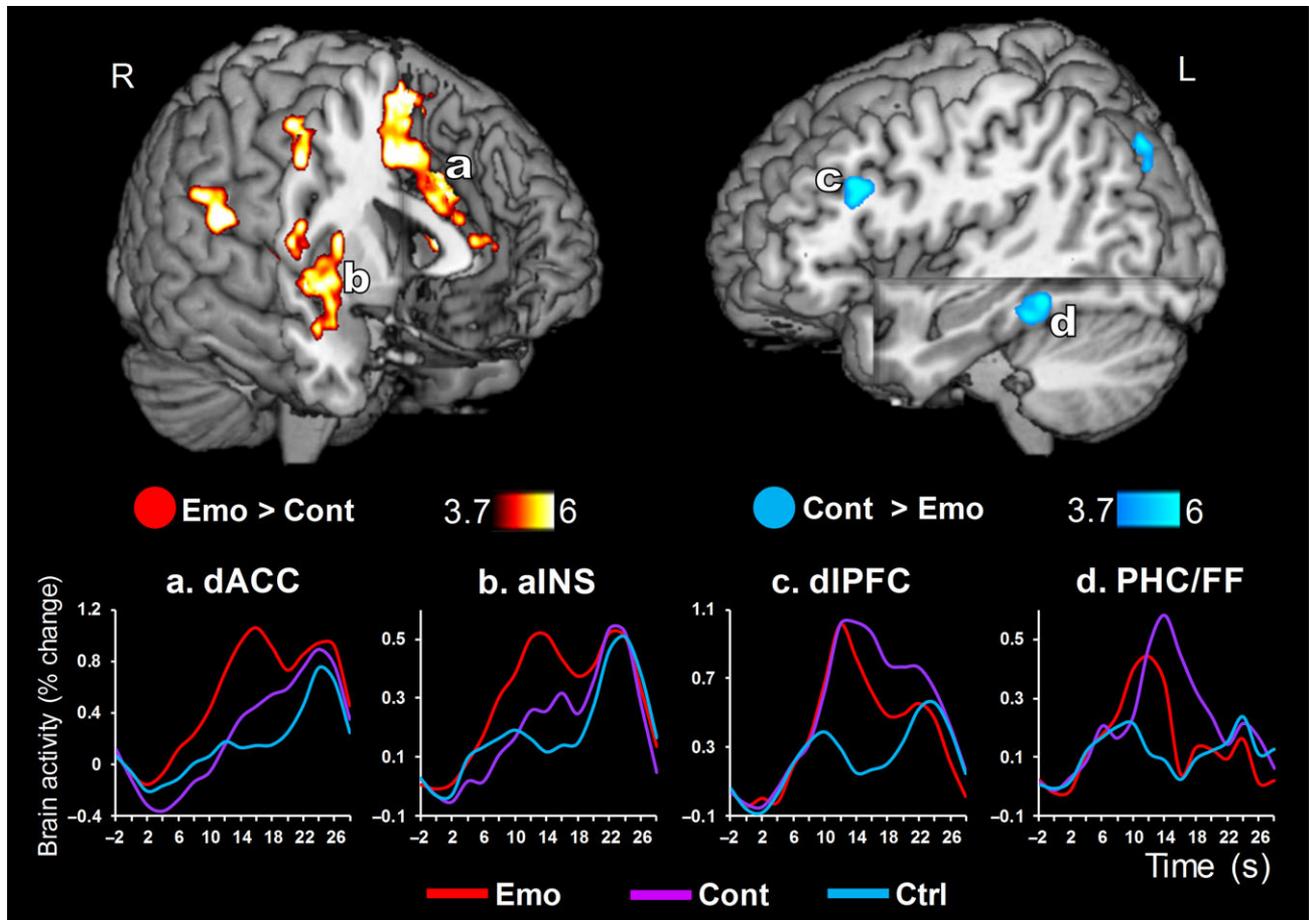


Figure 4. Reduced VAS activity and greater engagement of DES and context retrieval regions under ER. Focusing on context was associated with reduced activity in VAS regions overlapping with SN (a, dACC and b, aINS; also in AMY, see Supplementary Table S3) and increased activity in executive (c, dlPFC; also in LPC—time course not shown) and context retrieval regions (d, PHC/FF). The line graphs display the time courses of brain activity extracted from peak voxels of the Cont versus Emo comparisons (Talairach coordinates [x, y, z]: -9, 11, 30 [dACC]; 47, 10, 2 [aINS]; -42, 15, 27 [dlPFC]; -31, -37, -14 [PHC/FF]). The colored horizontal bars represent the gradient of the t values. The t maps are displayed at $P_{FWE} < 0.05$ (see Materials and Methods). dACC, Dorsal Anterior Cingulate Cortex; aINS, Anterior Insula; AMY, Amygdala; dlPFC, Dorsolateral Prefrontal Cortex; PHC/FF, Parahippocampal/Fusiform Cortex; Emo, Emotion Focus; Cont, Context Focus; Ctrl, Control Condition; L, Left hemisphere; R, Right hemisphere.

Time) yielded a DMN Subcomponent \times ER manipulation interaction ($F_{(1,16)} = 13.89$, $P = 0.002$), an ER manipulation \times Time interaction ($F_{(1,16)} = 12.6$, $P = 0.003$), and a 3-way DMN Subcomponent \times ER manipulation \times Time interaction ($F_{(1,16)} = 6.64$, $P = 0.02$) (Fig. 5). We further resolved the 3-way interaction by performing separate 2-way repeated measures ANOVAs (ER manipulation \times Time) on activity in each DMN subcomponent. Results showed significant ER manipulation \times Time interactions for both subcomponents (dorsal DMN: $F_{(1,16)} = 8.07$, $P = 0.012$; ventral DMN $F_{(1,16)} = 13.77$, $P = 0.002$). However, the patterns of activity in the 2 subcomponents were opposite: in the “dorsal” DMN, there was greater activity under Emotion focus in the earlier time window, whereas in the “ventral” DMN, there was greater activity under Context focus in the later time window. These results suggest a temporal dissociation between earlier engagement of self-referential processing regions under the Emotion focus, potentially driven by the high personal relevance of recollected emotional AMs (Daselaar et al. 2008), and later engagement of context retrieval regions under the Context focus, potentially driven by executive control processes elicited by the ER manipulation and retrieval of contextual details.

Greater Functional Connectivity Between Executive and Context Retrieval Regions Under Context Focus

As described above, results showed that focusing on context was associated with increased activity in dlPFC, part of DES/FPCN, and in regions typically associated with retrieval of contextual information, which are also part of the “ventral” DMN (Shirer et al. 2012). Because we hypothesized that Context focus would also be associated with greater functional coupling between executive and context-retrieval regions, we next targeted the dlPFC to determine whether focusing on context was associated with greater functional coupling between dlPFC and other executive regions part of FPCN, and between dlPFC and “ventral” DMN regions, compared with focusing on emotion. These analyses used 2 a priori defined ROI seeds identifying the left and the right dlPFC, respectively (Spreng et al. 2013), and targeted activity in a composite ROI identifying regions associated with the FPCN and the “ventral” DMN (Shirer et al. 2012). Consistent with the temporal dissociation described above, the analyses were performed at the “later” time point at which the maximal effect of Context focus was also identified in DES (i.e., left dlPFC, TP 10). For the left dlPFC seed, results showed greater functional connectivity with both FPCN (right dlPFC, Talairach

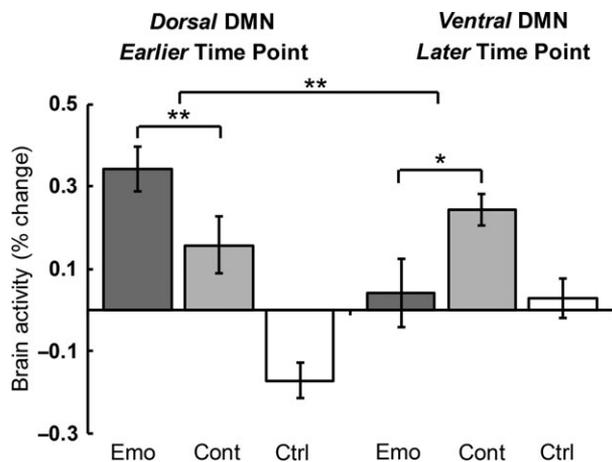


Figure 5. Temporal dissociation in DMN activity in response to Emotion versus Context focus. Emotion focus was associated with greater activity in the “dorsal” DMN subcomponent, in an earlier time window (TR 8, i.e., 6–8 s following presentation of retrieval cue), whereas Context focus was associated with greater activity in the “ventral” DMN subcomponent, in a later time window (TR 11, i.e., 12–14 s following presentation of retrieval cue). This DMN Subcomponent \times ER manipulation \times Time interaction is also visible in Figure 4, in which the response to Emotion focus in VAS regions occurs earlier than the response to Context focus in executive and context retrieval regions. The bar graphs display the average signal extracted from the “dorsal” and “ventral” DMN subcomponents as identified by Shirer et al. (2012). DMN, Default Mode Network; ER, emotion regulation; VAS, Ventral Affective System; TR = Repetition time/Time point. * $P < 0.05$; ** $P < 0.01$.

coordinates [x, y, z]: 39, 33, 33 and bilateral LPC, Talairach coordinates [x, y, z]: -39, -62, 41 [left] and 50, -50, 35 [right] and “ventral” DMN (PHC, Talairach coordinates [x, y, z]: -27, -34, -10 and PCC, Talairach coordinates [x, y, z]: -12, -63, 13 [left] and 2, -55, 13 [right]) regions, under Context compared with Emotion focus (Fig. 6). Additional regions showing greater functional connectivity with the left dlPFC seed, under Context compared with Emotion focus, were the frontopolar cortex (Talairach coordinates [x, y, z]: 29, 53, 21) and the cerebellum (Talairach coordinates [x, y, z]: -45, -61, -38). A similar pattern was obtained for the right dlPFC seed. Thus, although only select executive and context retrieval regions (e.g., left dlPFC and left PHC) dissociated between Context and Emotion focus in terms of the mean level of activity, specific FPCN and “ventral” DMN regions also showed stronger functional coupling for Context compared with the Emotion focus. Together with the results above showing greater activity in the left dlPFC for Context focus, these findings suggest both greater response in executive regions and greater connectivity with context retrieval regions, under instructed ER during AM recollection.

Discussion

The main goal of the present study was to clarify the neural mechanisms associated with the impact of autobiographical recollection as internal emotional distraction. Cued recollection of task-irrelevant negative AMs was used as internal emotional distraction during a WM task, and manipulation of FA was used as a specific ER strategy to cope with such distraction. There were 5 main findings. First, focusing away from emotion (Context focus), compared with focusing on emotion (Emotion focus), diminished both the subjective negative experience and the objective WM interference. Second, regarding the overall response to internal emotional distraction, brain imaging results identified opposing patterns of response in VAS (AMY,

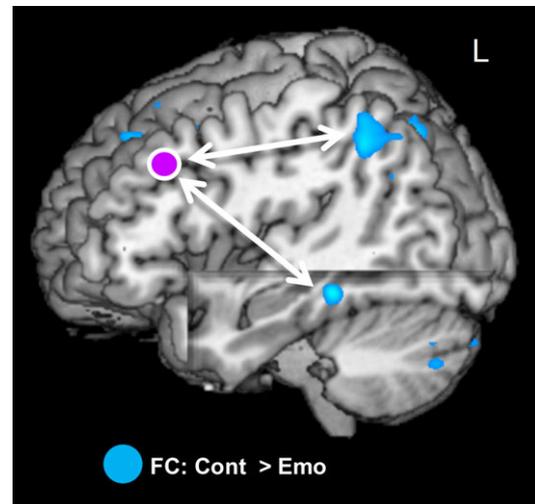


Figure 6. Increased functional connectivity between executive and context retrieval regions for Context focus. Compared with Emotion focus, Context focus was associated with greater functional connectivity between the left dlPFC (Talairach coordinates [x, y, z]: -38, 18, 36) and other regions part of the FPCN (LPC, Talairach coordinates [x, y, z]: -39, -62, 41), as well as regions associated with context retrieval, part of the “ventral” DMN (PHC, Talairach coordinates [x, y, z]: -27, -34, -10). Additional regions showing greater functional connectivity with the left dlPFC seed, under Context compared with Emotion focus, are described in the Results section. A similar pattern was also observed for the right dlPFC seed (Talairach coordinates [x, y, z]: 39, 19, 45). The t map is displayed at $P_{FDR} < 0.05$ (see Materials and Methods). Emo, Emotion Focus; Cont, Context Focus; L, Left hemisphere; FPCN, Frontoparietal Control Network; DMN, Default Mode Network; dlPFC, Dorsolateral Prefrontal Cortex; LPC, Lateral Parietal Cortex; PHC, Parahippocampal Cortex.

vlPFC) and DES (LPC) regions, similar to the responses to external distraction, which were complemented by specific activation in medial regions part of DMN (mPFC, PCC), linked to AM recollection. Third, regarding the neural mechanisms linked to the downregulation (see parenthesis below) of internal distraction, and consistent with the behavioral results, Context focus was associated with both diminished activity in VAS regions part of SN (AMY, dACC, aINS), and increased activity in executive (dlPFC) and memory-related regions involved in context retrieval (PHG, AG). Fourth, a spatiotemporal dissociation was found within the DMN, with the “dorsal” DMN showing greater activity under Emotion focus in an “earlier” time window and the “ventral” DMN showing greater activity under Context focus in a “later” time window. Finally, Context focus was also associated with increased functional connectivity between frontoparietal executive regions and regions involved in context retrieval. These findings are discussed in turn below. (It should be noted that FA can also be used to upregulate emotional responses [e.g., of pleasant feelings], but the focus here is on its effectiveness in reducing the impact of negative emotions associated with the retrieval of unpleasant AMs. As alluded to in the Introduction, focusing away from emotion and on nonemotional contextual details enables downregulation of emotional experience, while minimally taxing the cognitive system, which allows better coping with emotional distraction).

Reduced Negative Experience and WM Interference for Context Focus

To our knowledge, this is the first study providing insight into the effects of manipulating emotion regulation during internal

emotional distraction on concurrent cognitive performance. The finding that simply focusing away from emotional aspects of AMs can reduce both the subjective re-experiencing of emotion and the objective WM interference demonstrates that this is an efficient ER strategy to use when confronted with unwanted internal distractions. Although all irrelevant cognitions may be distracting to some degree, deployment of an efficient ER strategy allows better coping with distraction, even in the context of dual tasks. This is important because, typically, emotional distraction does not occur in a cognitive vacuum, but in the context of the need to maintain performance in cognitive tasks at hand. This interpretation is consistent with our model of dynamic interactions between executive and affective systems (Dolcos et al. 2011; Jordan, Dolcos, and Dolcos 2013), and is further supported by the brain imaging results discussed below. The results showing diminished negative experience for Context focus replicate and considerably extend previous findings (Denkova et al. 2015) by showing that FA is also an efficient ER strategy when AM recollection occurs in the context of a dual-task with distraction. The evidence that engaging FA allows coping with (re)experienced emotion while also facilitating cognitive performance is important because both of these aspects are important for proper functioning and are affected in emotional disturbances. These results are consistent with the current conceptualization of FA as an ER strategy with minimal processing requirements (Mauss et al. 2007), which is deployed faster compared with other strategies (Thiruchselvam et al. 2011; Hajcak Proudfit et al. 2014; Schönfelder et al. 2014), and whose effectiveness resides in limiting the processing of incoming emotional information in the subsequent stages of the emotional response (Denkova et al. 2015; Gross 1998; 2014, 2005; Ochsner and Gross 2005). Thus, deployment of a minimally taxing ER strategy, such as FA, is an effective way of dealing with negative emotions associated with the recollection of distressing memories, while also being able to perform the cognitive task at hand.

These results are also consistent with the idea that focusing on context during AM recollection allows better deployment of attention to representations active within WM (Joormann and Gotlib 2008; Gotlib and Joormann 2010). In other words, downregulating the emotional experience while minimally taxing the cognitive system may allow for more WM resources available to maintain the memoranda. This could be an advantage of FA over more demanding ER strategies (such as cognitive reappraisal) or even manipulations of other attentional deployment strategies (e.g., “cognitive distraction” by engaging in demanding tasks: complex calculations), which may lead to reduced emotional experience via resource depletion (Sheppes and Meiran 2008; Van Dillen et al. 2009), but would very likely also impact performance in the concurrent cognitive task. While the clarification of such an issue was beyond the scope of the present investigation, future studies could compare the effects of engaging different ER strategies on ongoing cognitive performance.

Opposing Patterns of Response to Internal Emotional Distraction in VAS and DMN Versus DES Regions

The findings showing increased activity in VAS (AMY, vlPFC) and greater deactivation relative to Control in DES (LPC) regions suggest that the neural responses to internal emotional distraction are, in part, similar to the ones previously reported for external emotional distraction (Jordan, Dolcos, and Dolcos 2013), and are consistent with the idea of a more general

involvement of VAS and DES, independent of the originating source of distraction (i.e., external or internal). In addition, the findings showing increased activation in midline cortical regions (mPFC, PCC) points to specific engagement of the AM retrieval/DMN regions by internal emotional distraction (Addis et al. 2004; Svoboda et al. 2006; Buckner and Carroll 2007; Cabeza and St Jacques 2007; Daselaar et al. 2008; Spreng et al. 2009; Andrews-Hanna et al. 2014; Denkova et al. 2015). The present DES results are consistent with previous findings linking deactivation in frontoparietal areas to the effects of emotional distraction on WM processing regions (Dolcos and McCarthy 2006; Dolcos et al. 2006, 2008, 2013; Anticevic et al. 2010; Denkova et al. 2010; Diaz et al. 2011; Oei et al. 2012; Jordan, Dolcos, Denkova et al. 2013; Jordan and Dolcos 2017). The LPC is the posterior “hub” in the frontoparietal executive network, which also includes the dlPFC (Dosenbach et al. 2006, 2007, 2008; Seeley et al. 2007; Power et al. 2011; Yeo et al. 2011; Power and Petersen 2013), and increased activity in DES regions has been implicated in active maintenance of task-relevant information (Fuster 1997; Smith and Jonides 1999; Hopfinger et al. 2000; Corbetta and Shulman 2002; D’Esposito et al. 2006; Koenigs et al. 2009; Nee et al. 2012; Niendam et al. 2012).

Interestingly, a deactivation in the dlPFC was not observed in response to internal emotional distraction, unlike the case of external emotional distraction (Dolcos and McCarthy 2006; as reviewed in Dolcos et al. 2011; Jordan, Dolcos, Dolcos et al. 2013). Also, the level of activity in LPC did not dissociate between Emotion and Context focus, despite the differences in WM performance between the 2 conditions. Instead, such dissociations were reflected in increased activation and coactivation of specific dlPFC and LPC areas to Context focus. This suggests that the advantage of focusing away from emotion during task-irrelevant AM recollection allowing maintenance of concurrent WM performance is linked to more complex neural dynamics than just differential impact on LPC activity. As discussed below, this interpretation is also supported by the findings showing differences in activity in VAS regions, aside from the differences in functional connectivity within DES regions, for Context compared with Emotion focus.

Reduced VAS Activity and Greater Engagement of DES and Context Retrieval Regions Under ER

The findings showing both reduced activity in VAS regions associated with SN (AMY, dACC, aINS) and increased activity in executive (dlPFC) and context retrieval regions (PHC, AG) for Context focus provide strong support for the effectiveness of manipulating attentional focus to cope with internal emotional distraction. These findings show that the beneficial effects of FA on both emotional experience and cognitive performance were linked to a shift from emotion processing to recollecting other nonemotional contextual details of personal memories. First, compared with Emotion focus, Context focus was associated with downregulation of activity in SN regions. The salience network is a large system anchored in the dACC and frontoinsula cortex, which has been implicated in detection, integration, and filtering of salient external and internal events (Seeley et al. 2007; Corbetta et al. 2008; Bressler and Menon 2010). This network also includes subcortical structures, such as the AMY, and has been implicated in emotion processing (Seeley et al. 2007; Barrett and Satpute 2013) and stimulus driven (“bottom-up”) reorienting of attention (Corbetta et al. 2008). Hence, decreased activity in SN regions under Context focus likely reflects reduced processing of distracting emotions,

which in turn leads to less cognitive interference. Of note, decreased activity under Context focus in the left AMY successfully replicates previous results using FA as an ER strategy during AM recollection (Denkova et al. 2013b, 2015).

Another possibility is that greater SN engagement under Emotion versus Context focus may instead reflect difficulty in suppressing contextual details, consistent with evidence suggesting that recollection of spatial contexts occurs quickly and spontaneously (Robin et al. 2015) and that regions of the contextual association network operate automatically during AM recollection (Bar and Aminoff 2003; Gilmore et al. 2016). In the present study, however, results of brain-behavior correlation analyses performed on all trials showed a positive correlation between activity in a SN hub (dACC) and emotional ratings under Emotion versus Context focus, further supporting our interpretation that increased SN activity reflects greater emotional response and potentially increased conflict (Luo et al. 2014; Ridderinkhof et al. 2004; Seeley et al. 2007). These results complement our initial findings showing reduced SN activity under Context focus for correct WM trials, by identifying a more generic relation between SN activity and overall emotional experience independent of WM performance.

Second, the present results also showed that Context focus was associated with upregulation of activity in executive (dlPFC) and memory-related regions associated with the retrieval of contextual information (parahippocampal/fusiform gyri and angular gyrus, AG). The left PFC has been implicated in executive operations associated with WM and attention, as well as in episodic memory (Kahn et al. 2004), and in particular in subsequent elaboration and maintenance of AMs (Daselaar et al. 2008). Furthermore, results of supplementary analyses showing that greater dlPFC engagement was characteristic of successful WM performance and that the Context > Emotion dlPFC cluster overlapped with a Neurosynth meta-analytical map for “cognitive control” further support our interpretation that greater dlPFC activity under Context focus likely reflects engagement of cognitive control. In addition, both the Context > Emotion dlPFC cluster and the Neurosynth “cognitive control” meta-analytical map overlapped with a Neurosynth “semantic” meta-analytical map. Although most of the “semantic” map is located ventral and lateral to the “cognitive control” map, the overlap suggests potential involvement of language/semantic processing mechanisms. This is consistent with their putative engagement in self-regulation in general and emotion regulation in particular (see Ochsner et al., 2012 for a discussion), and with evidence regarding the recruitment of cognitive control in certain aspects of language/semantic processing (Davey et al. 2016; see also Fedorenko 2014).

Thus, whereas activity in Salience (dACC, aINS) and context retrieval (PHC) regions was elicited independently of the correctness criterion, consistent with a role in experiencing AM recollection under Emotion or Context focus, respectively, greater left dlPFC engagement under Context focus was specific for correct WM performance, consistent with a role in controlling the impact of distraction. Together, these findings suggest potential dissociations among the roles of these regions, with dACC activity linked with increased emotional experience and possibly signaling increased conflict, dlPFC potentially engaged to solve the conflict, and PHC involved in context processing regardless of performance.

The medial and lateral aspects of the temporal lobe, including the parahippocampal and fusiform gyri, have also been implicated in episodic spatial recollection. The PHC is a key node in the posterior medial memory system (Ranganath and

Ritchey 2012), and has been implicated in episodic reconstructions that involve familiar visuospatial/situational contexts (Hassabis and Maguire 2007), which are similar to AMs recollection (Buckner and Carroll 2007). Similarly, the fusiform gyrus has also been implicated in both autobiographical recollection and mental navigation (Greenberg et al. 2005; Hoescheidt et al. 2010). Some neuropsychological evidence also points to the role of AG in integrating or attending to contextual information (Cabeza et al. 2008; Vilberg and Rugg 2008). In particular, lesions in the ventral parietal cortex (which includes AG) have been associated with less vivid and overall impoverished spontaneous recollections (Davidson et al. 2008), in the absence of clear deficits when patients are probed about specific episodic details (Berryhill et al. 2007), which suggests a potential role of AG in spontaneous availability of contextual details.

Interestingly, the ventromedial (vmPFC) and ventrolateral PFC, two brain regions previously associated with emotion regulation and coping with external emotional distraction, did not show increased response under Context compared with Emotion focus. This might seem surprising, given previous evidence linking vmPFC and vlPFC activity with affect regulation (Kober et al. 2008; Vytal and Hamann 2010; Diekhof et al. 2011; Ochsner et al. 2012; but see Buhle et al. 2014 and evidence linking vlPFC with spontaneous, nonspecific coping with emotional distraction (Dolcos and McCarthy 2006; Dolcos et al. 2006), as reviewed in Dolcos et al. 2011; Iordan, Dolcos, Dolcos et al. 2013). It should be noted, however, that unlike our previous investigation that linked vmPFC engagement with switching the retrieval focus during AM recollection, the present study employed the FA manipulation as a secondary task embedded in a demanding WM task. Thus, it is possible that the dual-task setting might have promoted a switch from vmPFC-dependent ER, relying more on internal representations (Olsson and Ochsner 2008; Ochsner et al. 2012), to a more strategic form of “top-down” control, implemented by the dlPFC (Buhle et al. 2014; Ochsner et al. 2012). To clarify this issue, future studies should directly compare ER tasks in single- and dual-task settings.

Turning to the null result regarding the vlPFC, it is worth noting that, by contrast with the present study, previous ER investigations have typically used pictorial stimuli to elicit emotional responses. Also, our previous study investigating FA as an ER strategy during AMs recollection did not identify dissociations in vlPFC activity for Context compared with Emotion focus (Denkova et al. 2015; but see Denkova et al. 2013a for valence-related dissociations). Hence, this null result might reflect differences in the mechanisms involved in regulating emotion elicited by “external” (percepts) versus “internal” (memories) distraction. It is also possible that vlPFC is involved in general/nonspecific coping, rather than when FA is specifically engaged in isolation (Denkova et al. 2015) or in the context of a dual-task, as employed here. To clarify this issue, future studies should directly compare the effect of engaging FA to cope with external versus internal emotional distraction.

Temporal Dissociation in DMN Activity, in Response to Emotion Versus Context Focus

The difference in timing between the responses in salience versus executive and context retrieval regions, with the former occurring slightly earlier (TR 8/9) than the latter (TR 10/11) (Fig. 4), is consistent with previous AM evidence showing earlier involvement of emotion processing regions during recollection of personal events (Daselaar et al. 2008). In addition,

examination of the time-course of activity in the left dlPFC revealed a pattern of more sustained increased activity for Context relative to Emotion focus, hence suggesting a role in “top-down” control operations necessary to bias processing towards further elaboration of the contextual aspects. These results support the interpretation that the change in processing bias from emotion to context during AM recollection is linked to both diminished earlier engagement of emotion/salience processing regions and more sustained engagement of executive and context retrieval regions. These findings also emphasize the importance of “priming” downregulation of emotional responses through FA instructions given before the engagement in the retrieval process (Denkova et al. 2015).

The idea of an ER-driven change in processing bias from emotion to context is also supported by the results showing a temporal dissociation within DMN, with the “dorsal” subcomponent showing earlier engagement under Emotion focus and the “ventral” subcomponent showing later engagement under Context focus (Fig. 5). The present results are consistent with previous evidence regarding both fractionation of DMN (Uddin et al. 2009; Andrews-Hanna et al. 2010; Leech et al. 2011; Kim 2012; Qin et al. 2012; Zabelina and Andrews-Hanna 2016; Tailby et al. 2017) and temporal dissociations in brain activity linked to AM recollection (Daselaar et al. 2008; Tailby et al. 2017; Inman et al. 2018). Although DMN generally responds to a broad range of self-related tasks, it can also be fractionated in subcomponents (e.g., dorsal vs. ventral, anterior vs. posterior), which have been associated with distinct functions, such as episodic retrieval and prospective construction, and inferring the mental states of others (reviewed in Zabelina and Andrews-Hanna 2016). On the other hand, earlier/transient activity during AM recollection has been linked to initial accessing and state setting in response to AM cues, whereas delayed/protracted activity has been linked to AM elaboration and context reconstruction (Daselaar et al. 2008). Convergent with both lines of evidence, the “earlier” response in the “dorsal” DMN subcomponent under Emotion focus suggests faster engagement of regions associated with initial accessing and processing of self-relevant content (mPFC, PCC, hippocampus), possibly related to the high personal relevance of the negative memories. On the other hand, the later response in the “ventral” DMN subcomponent under Context focus suggests prolonged recruitment of regions associated with memory-based construction of mental scenes (retrosplenial cortex, precuneus, PHC), likely driven by the regulation instruction to attend to contextual details of recollected AMs. However, given that the time resolution of fMRI is typically too coarse for subtle timing-related dissociations, these results should be treated with caution and further clarified in future research.

Greater Functional Connectivity Between Executive and Context Retrieval Regions for Context Focus

The findings showing greater dlPFC coupling with other frontoparietal control regions and with regions involved in context retrieval, for Context compared with Emotion focus, suggest better integration both within FPCN and between FPCN and the “ventral” DMN subcomponent, linked to the ER manipulation. These results are consistent with previous evidence showing increased prefrontal–parietal coupling during WM tasks (Honey et al. 2002; Ma et al. 2012; Cohen et al. 2014), and suggest a potential mechanism by which goal-relevant representations of the memoranda were better maintained in WM under Context focus, which was also the condition associated with better WM

performance in the presence of internal emotional distraction. Interestingly, the right parietal region showing increased functional connectivity with the dlPFC was also more impacted by internal distraction, as reflected in the pattern of deactivation to negative AMs relative to Control in the LPC (BA 40), irrespective of the ER manipulation (see Supplementary Table S2). Thus, although the parietal cortex did not dissociate between Emotion and Context focus in terms of the mean amplitude of activity, it showed increased trial-by-trial functional coupling with the dlPFC under Context focus, consistent with the idea that better integration among FPCN regions results in downregulation of emotion when attention is focused away from emotion.

Furthermore, increased coupling between dlPFC and AM network/DMN regions involved in context retrieval under ER suggests top-down engagement of executive control under the Context focus. This is consistent with previous evidence showing that flexible coupling between FPCN and other brain networks (e.g., dorsal attention network, DMN), as a function of task domain, supports goal-oriented processing (Spreng et al. 2010; Zabelina and Andrews-Hanna 2016). For instance, investigations contrasting autobiographical and visual planning (Spreng et al. 2010) have shown differential coupling between FPCN and DMN versus dorsal attention network regions, suggesting that FPCN and DMN subcomponents may cooperate to support goal-oriented processing. Although the correlation-based FC does not allow for determining directionality, overall, our results are consistent with the idea that dlPFC modulates both LPC and context retrieval regions, supporting a critical role of the dlPFC in controlling activity in other task-related brain regions (D’Esposito 2007).

Potential Relevance for Clinical Research

The current approach implemented an explicit strategy for regulating negative emotional responses associated with recollection of unpleasant events, and enabled dissociations between neural systems putatively engaged in the experience versus cognitive regulation of unpleasant affective responses. Therefore, the present findings are relevant for further elucidating mechanisms involved in affective disorders, which are characterized by dysfunctional alterations in the engagement of cognitive control. For instance, evidence from investigations in war-veterans with PTSD suggests the possibility of a link between recollection of negative AMs with enhanced personal significance and increased cognitive distraction observed in these patients (Morey et al. 2009). That is, retrieval of traumatic memories, triggered by cues related to traumatic events (e.g., combat-related pictures) or by other cues, may produce impairing effects on ongoing goal-oriented processing (Dolcos 2013). Similarly, studies of inhibition impairment in depression have focused more on alterations in the encoding of new experiences and relatively less on mechanisms that may help individuals to cope with existing long-term memories, which are likely linked to rumination (Gotlib and Joormann 2010; Sacchet et al. 2017). Hence, approaches that could potentially inform about both cognitive control impairments and rumination, such as in the present study, might be useful in clarifying core features of depression and other disorders characterized by difficulties in controlling negative thoughts (Sacchet et al. 2017). Also, evidence for greater and more sustained activity in emotion processing regions, coupled with reduced activity in cognitive control regions in depression, has previously been identified (Siegle et al. 2007). Such studies point to a link between alterations in

emotional and cognitive aspects of processing in depression, but they tend to be based on responses associated with successively administered separate emotional and cognitive tasks. However, approaches that capture affective-cognitive interactions based on combining both a primary, goal-oriented cognitive task and a secondary, emotional task, such as the present study, might be better able to capture the putatively altered interplay between cognitive and affective neural systems in depression (see also Wang et al. 2008; Young et al. 2015). Future studies using clinical samples are necessary to further clarify this aspect.

Conclusions

In summary, the present findings identified neural mechanisms associated with the role of attentional/retrieval focus in the impact of internal emotional distraction on the emotional response and performance in a concurrent cognitive task, following autobiographical recollection. Consistent with the idea of beneficial effects of FA as an ER strategy, the present results show that focusing away from emotion and on the nonemotional contextual aspects while recollecting task-irrelevant negative AMs is associated with both diminished emotional experience and diminished cognitive interference. The present fMRI findings identified specific responses to internal emotional distraction in midline regions (mPFC, PCC), in the context of overall similar responses in dorsal (LPC) and ventral (AMY, vPFC) brain regions to those previously observed for external distraction (Jordan, Dolcos, and Dolcos 2013). Linked to the engagement of FA as an ER strategy to cope with internal distraction, our results identified both downregulated responses in regions associated with emotion detection, integration, and filtering (aINS, dACC), part of the salience-related network, and upregulated engagement of executive (dlPFC) and contextual memory-related (PHC, AG) regions, under Context compared with Emotion focus. Moreover, there were different patterns of connectivity between the frontoparietal and context-retrieval regions, for Context versus Emotion focus. Overall, these findings show that FA is an effective ER strategy that can be promptly deployed to cope with internal emotional distraction, and that its engagement is linked to a shift in processing bias from emotion/salience regions to executive and context retrieval regions. Collectively, the present study provides initial brain imaging evidence regarding the neural mechanisms of FA as an ER strategy deployed to resist the detrimental impact of internal distraction on both emotional (re)experience and cognitive performance. These findings have implications for understanding affective disorders, such as depression and PTSD, which are characterized by increased emotional distractibility due to intrusive distressing memories (McNally 2006; Gotlib and Joormann 2010), and point to possible interventions to alleviate their detrimental impact on well-being.

Supplementary Material

Supplementary material is available at *Cerebral Cortex* online.

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Authors' Note

F.D., S.D., and A.D.I. designed the study; A.D.I. collected the data and performed the analyses, with input from F.D. and S.D.; A.D.I., F.D., and S.D. wrote the article. All authors provided feedback to, and approved the content of, the article.

Notes

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