

Neural correlates of 'distracting' from emotion during autobiographical recollection

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Remembering emotional autobiographical memories (AMs) is important for emotional well-being, and investigation of the role of emotion regulation (ER) during AM recollection has relevance for understanding mental health issues. Although significant progress has been made in understanding the brain mechanisms underlying ER and AM, less is known about the role of ER during AM recollection. The present study investigated how focusing away (or 'distracting') from the emotional content during AM recollection influences the subjective re-experiencing of emotions and the associated neural correlates, by manipulating the retrieval focus of participants who remembered emotional AMs while fMRI data were recorded. First, focusing away from emotion led to decreased self-reported emotional responses, along with increased engagement of ER-related regions (ventro-medial prefrontal cortex, vmPFC), and reduced activity in emotion-related regions (amygdala, AMY). Second, increased vmPFC activity was linked to reduced emotional ratings, during the non-emotional focus. Third, mediation analysis identified vmPFC as a functional hub integrating affective signals from AMY and mediating their impact on the subjective re-experiencing of emotion, according to the current retrieval focus. Collectively, these findings shed light on the neural mechanisms underlying the ability to effectively switch attentional focus away from emotions during AM recollections and have direct relevance for understanding, preventing and treating affective disorders, characterised by reduced ability to regulate emotions.

Keywords: personal memories; emotion control; ventro-medial PFC; emotional disorders

INTRODUCTION

Emotional autobiographical memories (AMs), such as the birth of a child, winning an award or failing an exam, play an important role in the construction of personal identity, in future planning and in decision-making. Hence, they are key factors in the personal emotional well-being. In some circumstances, excessive focus on the emotional aspects of negative personal experiences can have debilitating consequences and lead to psychiatric disorders. To avoid such consequences, it is important to be able to control our emotional responses by switching our attentional focus away from the emotional aspects of our memories, and maintain healthy cognitive and affective functioning. Although there has been recent progress in understanding the brain mechanisms underlying emotional control and emotional AM recollection, much less is known about how focusing on or away ('distracting') from the emotional content during the recollection of memories for life experiences might influence the subjective re-experience of emotion and the associated neural correlates. The present study addressed this issue by using functional magnetic resonance imaging (fMRI) in conjunction with an AM task that involved manipulation of the attentional focus during retrieval of emotional personal experiences and recording of participants' subjective ratings of their emotional responses.

Understanding how people deal with emotional AMs has relevance for understanding both normal healthy functioning and the dysfunction and negativity bias observed in patients with affective disorders. Indeed, excessive focus on emotional aspects of unpleasant memories

has been associated with increased susceptibility to affective disorders, such as depression and post-traumatic stress disorder (PTSD) (Brewin *et al.*, 1999; Rubin *et al.*, 2008b, 2011), which are characterised by impaired emotion regulation (ER) (Mayberg, 1997; Gotlib and Joormann, 2010). Recently the topic of ER has gained considerable interest, as the ability to cope adaptively with emotionally challenging situations is vital for physical and mental health, and understanding its mechanisms has important implications for understanding and treating affective disorders (Ochsner and Gross, 2005; Gross, 2008).

In general terms, attentional deployment involves shifts in attention to or away from the emotional aspects of emotion eliciting stimuli or events, which can be achieved by focusing either outwards (e.g. by engaging in a competing task) or inwards (e.g. by changing the focus of memories or thoughts), in order to alter the emotional responses (Gross, 2008). The effectiveness of ER strategies involving attentional deployment, such as distraction, has been confirmed by a recent meta-analysis (Webb *et al.*, 2012). Regarding the neural correlates, available evidence points to down-regulation of emotion-sensitive brain regions (amygdala, AMY) by the engagement of cognitive (prefrontal cortex, PFC) and attentional (parietal cortex, PC) control regions during attentional deployment, similar to other ER strategies, such as reappraisal (Ochsner *et al.*, 2004; Wager *et al.*, 2008; McRae *et al.*, 2010; Kanske *et al.*, 2011).

Moreover, studies directly comparing neural correlates underlying cognitive distraction and reappraisal reported greater decreases in AMY activation and greater increases in activation in PFC and PC regions during distraction relative to reappraisal (McRae *et al.*, 2010; Kanske *et al.*, 2011). Interestingly, AMY down-regulation was impaired when using reappraisal but not when using distraction in remitted depressed participants (Kanske *et al.*, 2012), thus suggesting that cognitive distraction, as a type of attentional deployment, could be particularly useful to immediately deal with emotional situations in depression. It should be noted, however, that in some cases if clear instructions are given, reappraisal could be relatively effective in unmedicated patients with depression (Dillon and Pizzagalli, 2013) and remitted bipolar disorder (Gruber *et al.*, 2013).

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The available brain imaging research tended to investigate ER strategies mainly during viewing emotional images, rather than during retrieval of real-life emotional memories, which are at the basis of maintaining depression and PTSD (Brewin *et al.*, 1999; Rubin *et al.*, 2008a, 2008b). Thus, the neural correlates of focusing away or ‘distracting’ from emotion during autobiographical recollection are not clear. The very few studies investigating ER in the context of emotional AM retrieval focused particularly on reappraisal (Kross *et al.*, 2009; Fabiansson *et al.*, 2012; Holland and Kensinger, 2012) and reported that reappraisal can lead to decrease in self-reported emotion. However, the accompanying changes in the neural response are not conclusive, particularly in emotion-related brain regions. For instance, Holland and Kensinger (2012) reported increased activity in cognitive control regions in the lateral and medial PFC when participants down-regulated their emotional reactions using reappraisal during the (re)construction of AMs, but this was also associated with increased, rather than decreased activity in emotion-related regions. The other two studies did not report specific activations related to reappraisal, which could be due to the use of a few memories repeatedly presented across different conditions and/or due to delayed instructions to regulate (i.e. after the engagement of memory retrieval) (Kross *et al.*, 2009; Fabiansson *et al.*, 2012).

These findings suggest that in the case of AM retrieval, down-regulation instructions should be given early, before the engagement in the retrieval process, especially because AM research revealed early involvement of emotion processing regions during recollection of personal events (Daselaar *et al.*, 2008). However, to our knowledge, the use of other ER strategies than reappraisal during retrieval of emotional AMs has not been explored. Relevant for the applicability to clinical conditions, one might expect that using reappraisal to regulate emotional personal memories in affective disorders might be a costly strategy and more difficult to apply, due to overall decreased cognitive/executive abilities in these patient populations (Kanske *et al.*, 2012). Therefore, it would be important to explore whether manipulation of attentional deployment, which has been shown to have immediate beneficial effects in reducing the emotional impact of viewing emotional images and to have clinical utility (Kanske *et al.*, 2012), is also effective in down-regulating the subjective emotional re-experiencing of AMs and the associated activity in emotion-related regions.

The main goal of the present study was to investigate the neural correlates of focusing away from emotion during autobiographical recollection, by manipulating the attentional focus during AM retrieval. Manipulation of the attentional focus was performed by cueing participants, before engaging in the retrieval process, to focus either on emotional (*Emotion* condition) or on non-emotional contextual (*Context* condition) aspects of their memories, with the latter expected to decrease emotional responses during AM recollection (Philippot *et al.*, 2003; Neumann *et al.*, 2007). fMRI data were recorded while participants performed this AM task manipulating the retrieval focus. Based on previous evidence from ER studies, we made the following three predictions. First, we expected that diverting attention from emotion during AM recollection would be associated with reduced experiencing of emotional content of personal memories, reflected in a reduction of self-reported emotional responses. At the neural level we expected that this behavioural effect would be accompanied by increased involvement of ER-related brain regions (PFC) and reduced activity in emotion-related brain regions (AMY). Second, we expected a link between activity in ER-related brain regions, during the *Context* focus condition, and changes in self-reported emotional responses of the associated AM recollections. Third, we also expected that these effects would involve interactions between the PFC and AMY.

MATERIALS AND METHODS

Participants

Eighteen right-handed young healthy adults participated in this study (six men; age range 18–46 years, mean = 26 years, s.d. = 7.02). One subject dropped out the study after the first run of the fMRI session, hence data from 17 subjects (six men, mean age = 26.06 years; s.d. = 7.20) were analysed. All participants had English as first language and had no history of neurological, psychological or psychiatric illness. The experimental protocol was approved by the institutional Research Ethics Board, and all participants provided written informed consent and received payment for their participation.

Collection and selection of emotional AMs

Personal memories were elicited from each participant during an interview performed about 5 weeks prior to the fMRI session, similar to the procedure employed by other neuroimaging studies of AM (Markowitsch *et al.*, 2000; Addis *et al.*, 2004). This procedure allows increased control over the properties of the memories to be used in different trial types, compared with studies involving AM retrieval directly in the scanning session (Cabeza and St Jacques, 2007; St Jacques, 2012). It should also be noted that the disadvantage of reactivation is attenuated by interposing sufficient time between the pre-scan interview and the subsequent scanning session (Maguire and Mummery, 1999). We used an autobiographical memory questionnaire (AMQ) specifically constructed to target the assessment of emotional personal episodes and their recollective qualities (Denkova *et al.*, 2012), which comprised a list of 115 written cues for distinct life events (e.g. ‘the birth of a family member’ and ‘being hospitalised’), resulting from a combination and extension of lists employed by other authors (Levine *et al.*, 2002; Sharot *et al.*, 2007). For each cue, participants were asked to remember a unique episode from their life, that occurred in a specific place and time (e.g. one instance when s/he played in a specific basketball game), rather than remembering general or repeated events (e.g. playing high school basketball). Upon recollection, participants were asked to provide a brief description of the memory, which was then used as a personalised memory cue during fMRI scanning; notably, at the time of collecting the AMs, participants were naïve to the specific purpose of the pre-scanning interview. To assess phenomenological characteristics of each event, participants dated their memories and rated them on several Likert scales, similar to other AM studies (Addis *et al.*, 2004; Greenberg *et al.*, 2005), as follows: emotional valence (on a 7-point scale: -3 = very negative, 0 = neutral and $+3$ = very positive), emotional intensity, personal significance, the amount of contextual details, vividness (i.e. the amount of visuo-perceptual details) and frequency of retrieval (all of latter used a 7-point scale: 1 = not at all, 7 = extremely).

Then, for each participant, the 40 most emotional memories (20 positive and 20 negative) were selected, based on the ratings provided in the AMQ (i.e. rated 2 or 3 and -2 or -3 , respectively). Half of the memories were assigned to the *Emotion* AM condition and the other half of the memories were assigned to the *Context* AM condition. The memories in the two conditions were matched as closely as possible in order to avoid differences in terms of age and phenomenological properties, and to ensure that any differences between the two retrieval foci during the fMRI session would not be due to initial differences in the properties of the memories assigned to the two conditions (Table 1).

fMRI tasks

The fMRI session comprised two AM tasks, differing according to the focus of retrieval (*Context* and *Emotion*), and a semantic memory (SM) control task. Immediately before performing the fMRI tasks,

participants were given detailed instructions and performed practice trials in order to familiarise themselves with the tasks and ensure that they understood the instructions.

The AM task: Context vs Emotion focus

Participants were asked to retrieve the memories associated with each personalised memory cue by either focusing on non-emotional contextual (*Context* condition) or on emotional (*Emotion* condition) aspects of their memories (Figure 1). For the Context condition, participants were instructed to focus on the 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 in the event). 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 in the stomach). Each memory cue was preceded by an instruction cue ('Remember Context' or 'Remember Emotion', for the Context and Emotion conditions, respectively). After each memory cue appeared on the screen, participants had to indicate by a button press once they recognised the cue as belonging to them, and then continued

remembering details of the event until cued again to rate the recollected memory. Each recollection was rated on three 5-point Likert scales including emotional intensity, vividness and reliving (1 = very low and 5 = very high). Participants were instructed to make quick and accurate responses and to use the whole scale.

Noteworthy, given that focusing away from or on emotional aspects of AMs was the main goal of ER manipulation in the present study, collecting ratings of emotional intensity was essential for assessing the effectiveness of this manipulation during AM retrieval on the subjective re-experiencing of the associated emotions. In addition, ratings of vividness and reliving were also collected, similar to other studies (Addis et al., 2004; Rubin and Siegler, 2004; Talarico et al., 2004; Daselaar et al., 2008).

The SM control task

In line with other AM functional neuroimaging studies (Greenberg et al., 2005; Young et al., 2013), we used a control condition involving SM retrieval, which involved generation of exemplars from 20 different semantic categories (e.g. musical instruments and sports) (Battig and Montague, 1969); also, similar to the AM retrieval task, the SM task involves searches in memory and extended retrieval time. The participants were presented with a semantic category name cue (e.g. fruits and vegetables) and instructed to recall as many exemplars as possible for each category. Each semantic category cue was preceded by an instruction cue ('Generate Examples'). Once the category cue appeared on the screen, participants had to indicate by a button press that they started recalling exemplars from the category, and then they continued recalling until cued again for memory ratings. To be consistent with the AM conditions, each exemplar generation was rated on three 5-points Likert scales appropriate for SM generation, as follows: vividness, difficulty of the task (1 = very low; 5 = very high) and approximate number of recalled items (1 = 1-3 items; 2 = 4-7 items; 3 = 8-10 items; 4 = 11-14 items and 5 = 15 or more items).

Table 1 Average characteristics of the memories assigned to *Context* and *Emotion* conditions

	Context	Emotion	P-values
Age (months)	74.28 (37.88)	70.76 (36.07)	0.18
Emotional intensity	5.50 (0.61)	5.47 (0.59)	0.22
Contextual details	5.11 (1.13)	5.16 (1.06)	0.44
Vividness	5.32 (0.65)	5.37 (0.65)	0.29
Personal significance	4.53 (0.93)	4.56 (0.93)	0.54
Frequency of rehearsal	3.43 (0.86)	3.49 (0.90)	0.24

Standard deviations are given in parentheses; P-values are from paired t-tests.

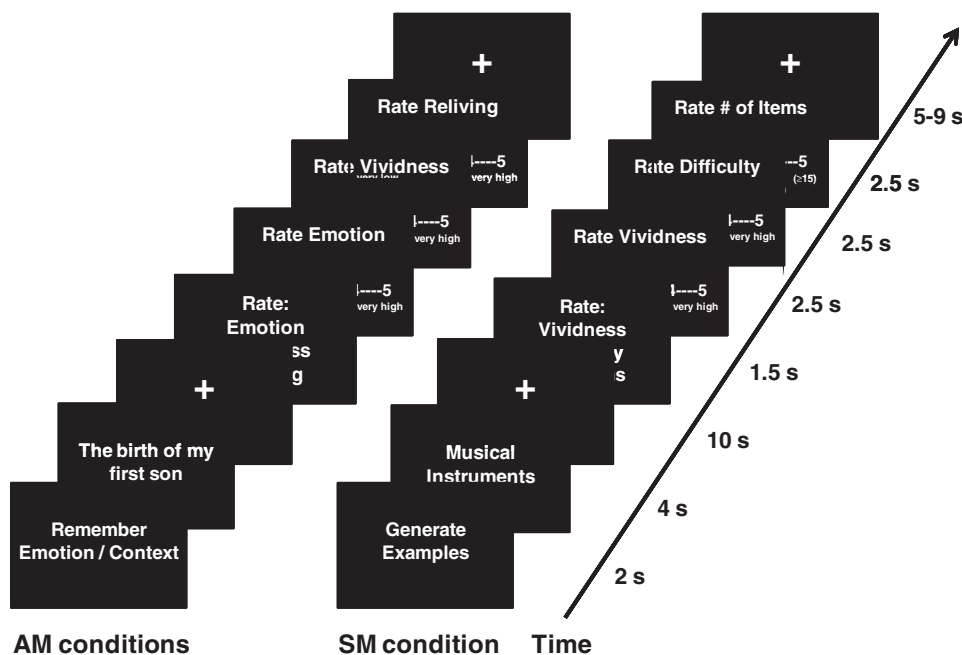


Fig. 1 Diagram of the scanned tasks. During the AM conditions, the participants remembered highly emotional personal memories, by focusing either on emotional (*Emotion* focus) or on non-emotional contextual (*Context* focus) details of their recollections. Then, participants rated each recollected memory for *emotional intensity*, *vividness* and *reliving*, on 5-point Likert scales (1 = very low, 5 = very high). During the SM control condition, participants generated as many exemplars from a given semantic category as possible, and then rated each of them for *vividness*, *difficulty* and *number of items* on 5-point Likert scales.

fMRI design and procedure

The two AM conditions (Context and Emotion) and the SM control condition had the same general structure (Figure 1). Each trial began with an instruction screen for 2 s, immediately followed by a memory cue for 4 s. After the cue offset, a fixation screen was presented for 10 s, during which participants elaborated their personal memories or generated exemplars. The end of the retrieval period was marked by the presentation of an instruction screen for upcoming ratings, for 1.5 s. Then, each of the three ratings was presented for 2.5 s in a counter-balanced order across trials. The ratings were followed by an inter-trial interval of variable duration (2–9 s, average = 6 s), before the beginning of the next trial.

The scanning session was divided into two blocks of four runs. Each run started with 6 s of a fixation to allow stabilisation of the fMRI signal and comprised five trials from each condition (Emotion, Context and SM). To avoid induction of longer-lasting effects, the trials within each run were pseudo-randomised, so that no more than two consecutive trials of the same type were presented. To prevent possible biases from using the same run order, participants were assigned different run orders. Similar to other AM neuroimaging studies (Greenberg et al., 2005), in order to increase statistical power, the four runs from the first block were immediately repeated in the second block of the scanning session, and the order of runs was counter-balanced across participants. Stimuli were projected on a screen directly behind the subjects' head within the scanner, which subjects viewed through a mirror.

All stimuli appeared in white letters against a black background created in Adobe Photoshop, and the CIGAL software (<http://www.nitrc.org/projects/cigal/>) was used for stimulus presentation and collection of behavioural responses during the fMRI session. All responses were made on a four-button MRI-compatible response box placed under the subject's right hand; the fifth rating was indicated by the participants with a double click on button #1.

MRI data collection

MRI data were recorded using a 1.5-T Siemens Sonata scanner. The anatomical images were 3-D MP-RAGE anatomical series (repetition time [TR] = 1600 ms, echo time [TE] = 3.82 ms, field of view = 256 × 256 mm, number of slices = 112, voxel size = 1 × 1 × 1 mm). The functional images consisted of a series of images acquired axially using an echoplanar sequence (TR = 2000 ms, TE = 40 ms, field of view = 256 × 256 mm, number of slices = 28, voxel size = 4 × 4 × 4 mm), thus allowing for full-brain coverage.

Behavioural and fMRI data analyses

To investigate the effect of the retrieval focus on the qualities of the remembered memories, differences in ratings for emotional intensity, vividness and reliving between Emotion and Context conditions were assessed using repeated measures ANOVA and planned *t*-tests. All neuroimaging data were pre-processed and analyses were performed with SPM2 (Statistical Parametric Mapping). Standard pre-processing steps included quality assurance, TR alignment, motion correction, coregistration, normalisation and smoothing (8 mm full-width half maximum isotropic Kernel). At the individual level, each event was modelled by the canonical haemodynamic response function (*hrf*) and its temporal derivative. Movement parameters calculated during the realignment were included as parameters of no interest to control for movement artefacts. In both AM and SM conditions, the *hrf* was time-locked to the closest TR linked to the subjects' responses signalling the recognition of the memory cues (for AMs) and the semantic categories (for SMs), and the beginning of elaborating AMs/generating SM exemplars. Specifically, the *hrf* was time-locked to 2 s (1TR) following the

onset of the memory cues, in the Emotion and Context AM conditions, and 1 s (0.5TR) after the onset of the category cue, in the SM condition. This procedure was guided by the present RT data, which showed that the beginning of AM elaboration following the cues occurred at an average RT of 1.67 s (±0.44), and the beginning of SM exemplar generation at an average RT of 1.03 s (±0.40). Hence, this procedure allows comparisons of the fMRI signal associated with the AM and SM retrieval, by accounting for differences in the timing of memory identification and reducing the impact of initial processing of the cues *per se*. This is consistent with procedures used in previous neuroimaging AM studies, which typically do not include in the analyses the time spent on viewing/reading the memory cue, and hence account for differences in the temporal profiles of AM and SM responses (Addis et al., 2007; Spreng and Grady, 2009; Ford et al., 2011).

Individual analyses produced whole-brain activation maps for the contrasts of interest, identifying main effects of each AM condition relative to the SM control condition (i.e. Context vs SM and Emotion vs SM). These individual contrasts were then entered into group-level random-effects *t*-tests analyses, which allowed investigation of the common and dissociating effects for the Context and Emotion retrieval foci. The common effects were investigated through conjunction analyses (i.e. [Context vs SM] ∩ [Emotion vs SM]), in which the statistical activations maps of the two contributing contrasts (Context vs SM) and (Emotion vs SM) were inclusively masked with each other. This procedure allowed identification of the brain regions that showed increased activation in both conditions. The dissociating effects of the retrieval focus were investigated through interaction analyses using paired *t*-tests (i.e. [Context vs SM] > [Emotion vs SM] and [Emotion vs SM] > [Context vs SM]), whose outputs were also inclusively masked with the corresponding main effects (i.e. Context vs SM and Emotion vs SM, respectively). This procedure ensured that the interaction differences are due to existing differences in the contrasts of interest compared with the SM baseline (e.g. Context vs SM), and not because of differences going in opposite direction in the contrast being compared with (i.e. Emotion vs SM). For the medial temporal lobe (MTL) regions targeted as a priori regions of interest (amygdala-AMY and hippocampus-HC), we used anatomical ROI masks derived from Wake Forest University Pick Atlas toolbox. Overall, unless otherwise noted, for the analyses directly comparing each AM condition with the SM control condition (main effects), an intensity threshold of $P < 0.001$ uncorrected was used in each of the contributing maps to the conjunction, and for the interaction analyses an intensity threshold of $P < 0.05$ was used. The latter were further inclusively masked with the activation map of the corresponding main contrasts, set up at $P < 0.001$.

To further explore the link between brain activity and self-reported re-experience of emotion in each AM condition, linear regression analyses were performed between activity in the Context vs SM contrast and emotional ratings of the context-focused AMs and between activity in the Emotion vs SM contrast and the emotional ratings of the emotion-focused AMs. Again, to make sure that these correlations with ratings occurred in brain areas showing significant effects in the contrasts of interest, the resulting co-variation maps were further inclusively masked with the corresponding activation maps (Context vs SM and Emotion vs SM, respectively). The results of those analyses provided the basis for additional data-driven correlation and mediation analyses (see the 'Results' section for more details). A threshold of $P < 0.05$, uncorrected, was used for all correlations, and a threshold of $P < 0.001$ uncorrected was used for the masks (except for the AMY, targeted as a priori region of interest, for which a threshold of $P < 0.05$ was used). An extent threshold of 10 contiguous voxels was used in all analyses, except for the MTL regions, where due to their a priori

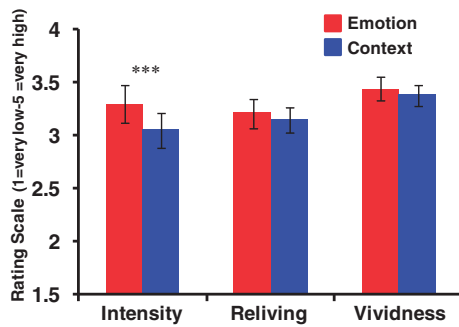


Fig. 2 Decreased subjective re-experiencing of emotion during the *Context* focus. Self-reported ratings for emotional intensity were lower in the *Context* than in the *Emotion* AM condition ($***P < 0.001$), while the ratings for reliving and vividness were similar in the two conditions ($P > 0.20$ and $P > 0.25$, respectively).

selection as regions of interest, an extent threshold of five contiguous voxels was used.

Finally, the SPM analyses were complemented by analyses performed with in-house MATLAB tools (Dolcos and McCarthy, 2006), which allowed extraction of the fMRI signal and examination of the time course of activity related to different conditions, across the whole length of the trials.

RESULTS

Behavioural results

Decreased subjective re-experiencing of emotion when focusing away from emotional aspects of recollected AMs

As expected, the ANOVA examining the effect of the two retrieval foci (*Emotion vs Context*) on the three ratings (emotional intensity, vividness and reliving) identified a significant focus \times ratings interaction ($F_{(1,16)} = 4.14, P = 0.025$). *Post hoc* paired *t*-tests revealed a decrease in ratings for emotional intensity in the *Context* condition compared with the *Emotion* condition ($P < 0.001$), while there were no significant differences in the ratings for vividness ($P > 0.25$) and reliving ($P > 0.20$) between the two conditions (Figure 2). Thus, the ratings assessed immediately after recollection of AMs in the scanning sessions showed that our manipulation of the retrieval focus worked to reduce the subjective emotional experience, when the focus was on non-emotional aspects of the retrieved AMs, without affecting other ratings.

fMRI results

Dissociable effects in ventro-medial PFC and AMY when focusing away from emotional content of AMs

In the context of the overall common pattern of neural correlates corresponding to the typical AM retrieval network (Table 2 and Figure 3) (Svoboda *et al.*, 2006), subtle manipulation of the retrieval focus also yielded differential involvement of emotion control (ventro-medial PFC, vmPFC) and basic emotion processing (AMY) brain regions, linked to whether participants were instructed to focus away from or on emotional aspects of their personal memories.

Specifically, focusing away (*Context* condition) compared with focusing on emotional details (*Emotion* condition) led to increased activity in ventral areas of the medial PFC (BA10/11) and decreased activity in the left AMY (Figure 4). Other brain regions showing either increased ($[Context vs SM] > [Emotion vs SM]$) or decreased ($[Emotion vs SM] > [Context vs SM]$) activity for the *Context* focus are reported in Table 3.

Increased vmPFC activity linked to reduced self-reported emotional ratings

Investigation of brain-behaviour relations using correlation analyses between brain regions sensitive to *Context* (*Context vs SM*) or *Emotion* (*Emotion vs SM*) focus and the ratings of emotional intensity during recollection in *Context* and *Emotion* AM conditions, respectively, revealed a negative correlation ($R = -0.66, P = 0.004$) in the vmPFC (BA 10) for the *Context* condition only (Figure 5). Specifically, participants who had greater activity in this region also had lower emotional ratings while focusing on non-emotional aspects (*Context*) of recollected AMs, and this effect was not significant for the *Emotion* condition ($R = -0.23, P = 0.37$). The difference between the two *R* coefficients was also tested using the *R* to *Z* Fisher's transformation, which is considered a very strict method. This comparison revealed a marginally significant difference between the two correlation coefficients ($z = 1.48, P = 0.069$). Interestingly, this medial PFC area showing the negative correlation is in close proximity to the vmPFC region showing specific increased engagement in the ($[Context vs SM] > [Emotion vs SM]$) contrast illustrated in Figure 4. Other brain regions associated with *Context* and *Emotion* conditions that showed significant correlations with the corresponding self-reported emotion ratings are reported in Table 4.

vmPFC mediates the link between AMY activity and emotional ratings

Given the evidence of bidirectional influences between medial PFC and AMY (Ongur *et al.*, 2003; Price, 2007) and of co-variation between activity in these regions (Urry *et al.*, 2006; Johnstone *et al.*, 2007), we also sought for evidence supporting the idea of functional interactions between vmPFC and AMY, in the present study. Specifically, to further investigate whether activity in the vmPFC is linked to activity in the AMY, data-driven correlation and mediation analyses were performed to elucidate possible relations between these brain regions, linked to the subjective experience of emotion. Again, the resulting correlation maps were inclusively masked with the activation maps of the corresponding main effects (see also the 'Methods' section). Finally, to ensure the specificity of these co-variations to the *Context* or *Emotion* focus conditions, the correlation maps were exclusively and reciprocally masked with each other. That is, the map for the *Context* condition was exclusively masked with the correlation map of the *Emotion* condition and vice versa.

The focus was on the vmPFC area associated with reduced emotional ratings during *Context* and the AMY region showing common engagement during the *Context* and *Emotion* conditions (Table 2). Specifically, we extracted the fMRI signal from the peak voxels in the two regions for each condition and correlated these values with each other. These analyses revealed a significant positive correlation between vmPFC and AMY for the *Context* condition ($x = -28, y = -1, z = -20; R = 0.64, P = 0.006$) and a similar effect for the *Emotion* condition ($x = -28, y = 7, z = -24; R = 0.71, P = 0.001$). In other words, participants showing increased AMY activity also had increased vmPFC activity, and this effect was observed for both *Context* and *Emotion* conditions.

Consistent with previous evidence regarding AMY-PFC interactions in ER (e.g. Dolcos *et al.*, 2006), these findings suggest that the AMY (as a basic emotion processing region) signals the vmPFC (an emotion integration and ER brain region) about the emotional charge of retrieved AMs. In turn, the vmPFC takes action by exerting control over the experienced emotions according to the focus of the task (away from or on the emotional aspects). To test this idea, we further explored the possibility that the relation between AMY activity and emotional ratings is mediated by changes in vmPFC activity. This

Table 2 Brain regions common to *Context* and *Emotion* conditions

Brain regions	Side	BA	Talairach coordinates			T-values			Cluster size
			x	y	z	Emotion vs SM ($P < 0.001$)	Context vs SM ($P < 0.001$)	AM vs SM ($P < 0.05$ FWE)	
Lateral frontal cortex									
Middle frontal gyrus	L	6	-44	14	47	7.20	7.29	8.17	38
Inferior frontal gyrus	R	45	55	27	6	8.53	4.91	7.53	23
Fronto-temporal junction									
Inferior frontal gyrus	L	47	-48	34	-15	6.64	6.32	7.32	158
Superior temporal gyrus	L	38	-44	18	-21	5.42	4.04	5.22	
Middle frontal gyrus	R	11	44	30	-15	6.59	5.72	6.88	62
Inferior frontal gyrus	R	47	40	27	-11	5.50	4.14	7.10	
Superior temporal gyrus	R	38	36	10	-24	5.22	4.77	5.82	
Medial frontal cortex									
Superior frontal gyrus	L	6	-8	19	62	8.60	6.74	8.59	197
Superior frontal gyrus	L	9	-8	56	30	7.07	5.63	6.91	
Medial frontal gyrus	L	10	0	54	-3	5.80	9.99	7.86	
Superior frontal gyrus	R	8	4	37	46	6.84	4.04	6.44	
Lateral temporal cortex									
Middle temporal gyrus	L	22	-59	-35	2	7.72	6.03	7.45	334
Inferior temporal gyrus	L	20	-55	-9	-23	7.30	5.84	6.99	
Middle temporal gyrus	L	21	-51	-1	-23	6.72	6.97	7.22	
Middle temporal gyrus	R	21	59	-5	-20	5.12	6.30	6.12	12
Medial temporal lobe									
Parahippocampal Gyrus	R	35	20	-39	-5	4.53	4.03	4.48	7
Hippocampus**	L		-20	-27	-5	4.38	3.58	4.29	20
Hippocampus**	R		20	-24	-9	3.68	3.98	4.08	9
Amygdala*	L		-28	7	-24	3.58	2.78	4.06	8
Temporo-parietal junction									
Angular gyrus	L	39	-48	-57	32	7.78	9.55	9.13	185
Angular gyrus	R	39	40	-57	32	7.17	5.82	7.58	60
Posterior/occipito-parietal cortices									
Cuneus	R	18	8	-81	15	9.39	9.14	9.59	1494
Lingual gyrus	R	18	8	-70	7	6.75	5.47	7.26	
Precuneus	R	31	8	-45	35	6.36	7.66	7.55	
Cuneus	L	17	-8	-77	11	8.37	8.01	8.06	
Precuneus	L	7	-8	-53	36	6.69	7.34	7.35	
Posterior cingulate	L	29	0	-42	9	6.48	6.14	7.06	

The regions common to Emotion and Context focus are identified by conjunction analysis ($[\text{Emotion vs SM}] \cap [\text{Context vs SM}]$). For this, the Emotion vs SM map was inclusively masked with the Context vs SM map. The intensity threshold was set up at $P < 0.001$ ($t \geq 3.69$) in each of the contributing maps. The areas identified by the conjunction analysis are part of the autobiographical memory (AM) retrieval network, and most of them also survived a FWE-corrected threshold of $P < 0.05$ ($t \geq 6.78$) for the general AM vs SM contrast (as indicated by the text in bold font in the AM vs SM column); for this analysis, the two AM conditions were merged together and compared with the SM condition. Activations in the MTL regions were identified using anatomical ROI masks (significance noted with asterisks), and also survived structural ROI corrections for the AM vs SM contrast (except for the right hippocampus). *Significant at $P < 0.01$ in each of the contributing maps, **Significant at $P < 0.005$ in each of the contributing maps; BA, Brodmann's area; R, right; L, left.

mediation analysis (Preacher and Hayes, 2004) explicitly tested whether the relation between AMY activity (the predictor variable, denoted as X in Figure 6) and emotional ratings (the outcome variable, denoted as Y) can be explained by activations in the vmPFC (denoted as M , the mediator). Following standard conventions for mediation analysis, path a refers to the X to M relation (AMY to vmPFC), path b refers to the M to Y relation controlling for X (vmPFC to emotional ratings, controlling for AMY), and the interaction between path a and path b ($a \times b$) reflects the mediation effect (indirect effect).

This analysis identified a significant ($P = 0.009$) negative mediation effect of vmPFC on the relation between the AMY and emotional ratings during context-focused retrieval, and a significant ($P = 0.03$) positive direct effect (path c' , X to Y controlling for M) between AMY and emotional ratings when controlling for vmPFC influence. The opposite signs in the indirect and direct effects (Wager et al., 2008; Kober et al., 2012) explain why the total effect of the AMY on emotional ratings (path c , X to Y , without considering M) is not significant ($P = 0.66$). Importantly, this mediation effect was specific to the *Context* condition, as it was not significant for the *Emotion* condition ($P = 0.22$).

DISCUSSION

The present study yielded three main novel findings regarding the neural correlates of ER during emotional autobiographical recollection. First, focusing away from emotion (*Context* focus) led to decreased self-reported emotional responses, along with increased engagement of ER brain regions (vmPFC) and reduced activity in basic emotion brain regions (AMY). Second, activity in the vmPFC was negatively correlated with subjective ratings of emotion during *context*-focused AM recollection. Third, mediation analysis identified a role of the vmPFC as a functional hub integrating affective signals from the AMY and mediating their impact on the subjective re-experiencing of emotion, according to the current retrieval focus. These findings will be discussed in turn below.

Dissociable effects in vmPFC and AMY when focusing away from emotional content of AMs

Decreased self-reported emotion and AMY activity in the *Context* condition extend previous ER studies (McRae et al., 2010; Kanske et al., 2011), by showing that focusing away from emotional aspects of memories is an efficient ER strategy during AM recollection. To our

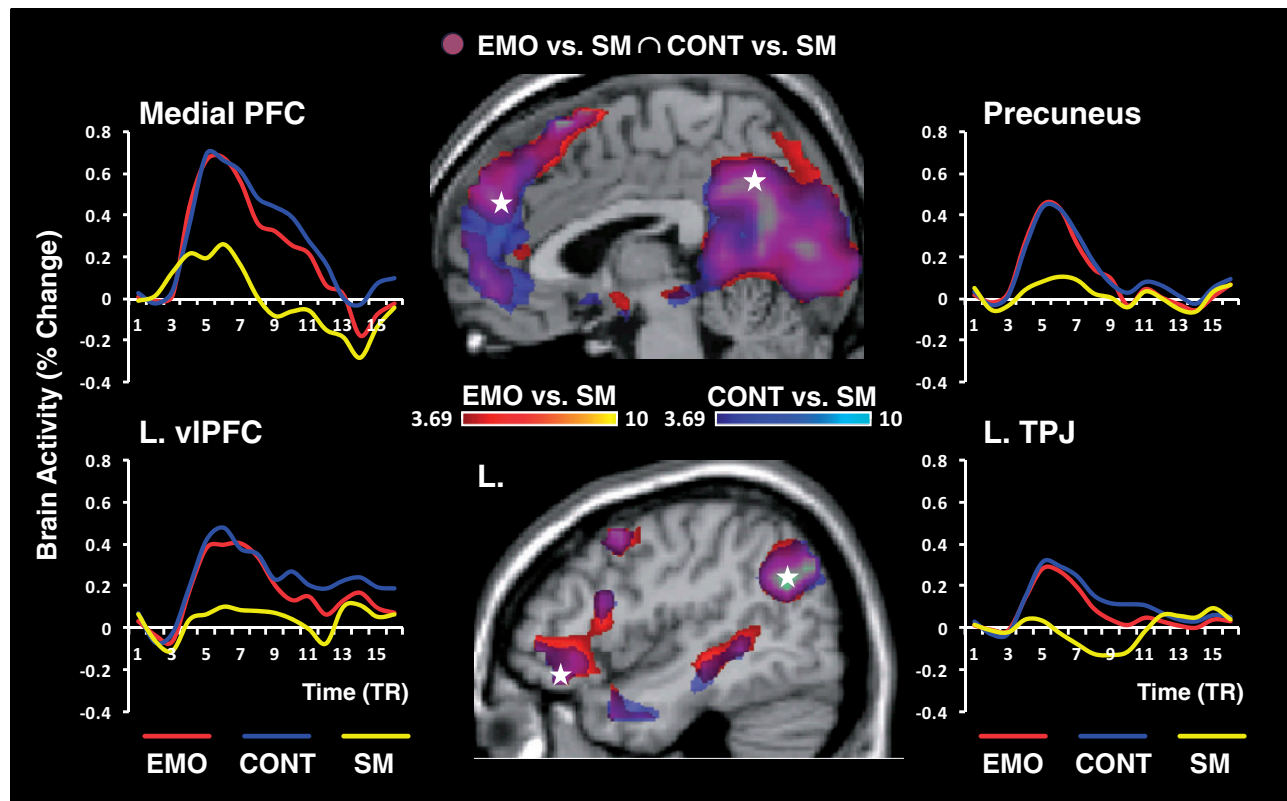


Fig. 3 The AM retrieval network. Compared with SM, retrieval of AMs, with either Emotion (EMO) or Context (CONT) focus, yielded overlapping increased activity in typical regions of the AM retrieval network. As also illustrated in Table 2, this network included midline cortical structures (medial PFC and precuneus), lateral frontal, temporal and parietal areas, as well as MTL structures (amygdala and hippocampus, data not shown). The activations maps for Emotion vs SM and Context vs SM were set up at a threshold of $P < 0.001/t \geq 3.69$ ($k \geq 10$ voxels), and superimposed on high-resolution brain images displayed in sagittal views. The coloured horizontal bars show the gradient of the t -values. The line graphs show the time course of responses from typical AM retrieval areas, as extracted from peak voxels (indicated by the white stars) reaching a FWE-corrected threshold of $P < 0.05$ ($t \geq 6.78$) for the AM vs SM contrast (see Table 2, for all peak locations). PFC, prefrontal cortex; vIPFC, ventro-lateral PFC; TPJ, temporo-parietal junction; L, left; TR, repetition time (1 TR = 2 s).

knowledge, the present study is the first to provide insights into the behavioural and neural effects of manipulation of attentional focus during the retrieval of emotional AMs (see also Denkova et al., 2013a, 2013b). The finding that simply focusing away from emotional aspects of AMs can reduce the subjective re-experiencing of emotion demonstrates that this is an efficient and easy to use ER strategy when remembering unwanted personal memories.

Overall, the present finding has direct relevance for potential training avenues for affective disorders, which are characterised by excessive focus on emotional personal memories (Brewin et al., 1999; Rubin et al., 2008a, 2008b) and impaired use of ER strategies such as reappraisal (Aldao et al., 2010; Gotlib and Joormann, 2010; Joormann and Gotlib, 2010), along with a lack of flexibility in deploying attention to different aspects of representations active within working memory (Joormann and Gotlib, 2008; Gotlib and Joormann, 2010). Related to this idea, a recent fMRI study showed that ER strategies involving attentional deployment might, in fact, be more efficient in down-regulating emotion than reappraisal in remitted depressed patients (Kanske et al., 2012). It should be noted that focusing on non-emotional contextual details does not completely eliminate reactivation of emotional aspects, but rather it attenuates the effect of emotion as a result of subtly manipulating the attentional focus during retrieval away from the emotional aspects. This is reflected in the fact that overall both AM conditions produced greater AMY activity compared with the SM condition. Thus, the present difference between the two conditions is a matter of degree, rather than of 'all or none responses'. This finding is also consistent with suggestions from the AM literature that effortful reconstruction of the contextual elements during AM

retrieval might spontaneously attenuate the reliving of the associated emotion (Conway and Pleydell-Pearce, 2000; Philippot et al., 2003; Neumann et al., 2007) and may provide a possible explanation for inconsistent AMY activation reported across typical AM studies (Svoboda et al., 2006; Dolcos et al., 2012).

It is important to note that while in other ER studies manipulation of attentional deployment involves engagement in cognitively demanding tasks, to divert attention from the main emotional task and distract participants from the emotional aspects, the manipulation used here involves simply switching the retrieval focus while the main task remains the same (i.e. recollection of personal memories). This remarkably subtle manipulation has therefore the advantage of still changing the focus of AM recollections without distorting the actual memories. With this idea in mind, our findings could be linked to and extend recent preliminary studies showing that training to be more concrete and specific in recollecting memories might have beneficial effects in depression (Raes et al., 2009; Watkins et al., 2009). Therefore, our findings provide support for cognitive behavioural therapies involving ER training to 'distract' from emotional aspects of personal memories, by focusing on and elaborating non-emotional contextual aspects of retrieved AMs, which in turn leads to reduced self-experienced emotion.

Increased vmPFC activity linked to reduced self-reported emotional ratings

Regarding the neural correlates of the observed behavioural effect, the opposing patterns of response in vmPFC compared with that observed in the AMY suggest that changing the focus of recollections involves

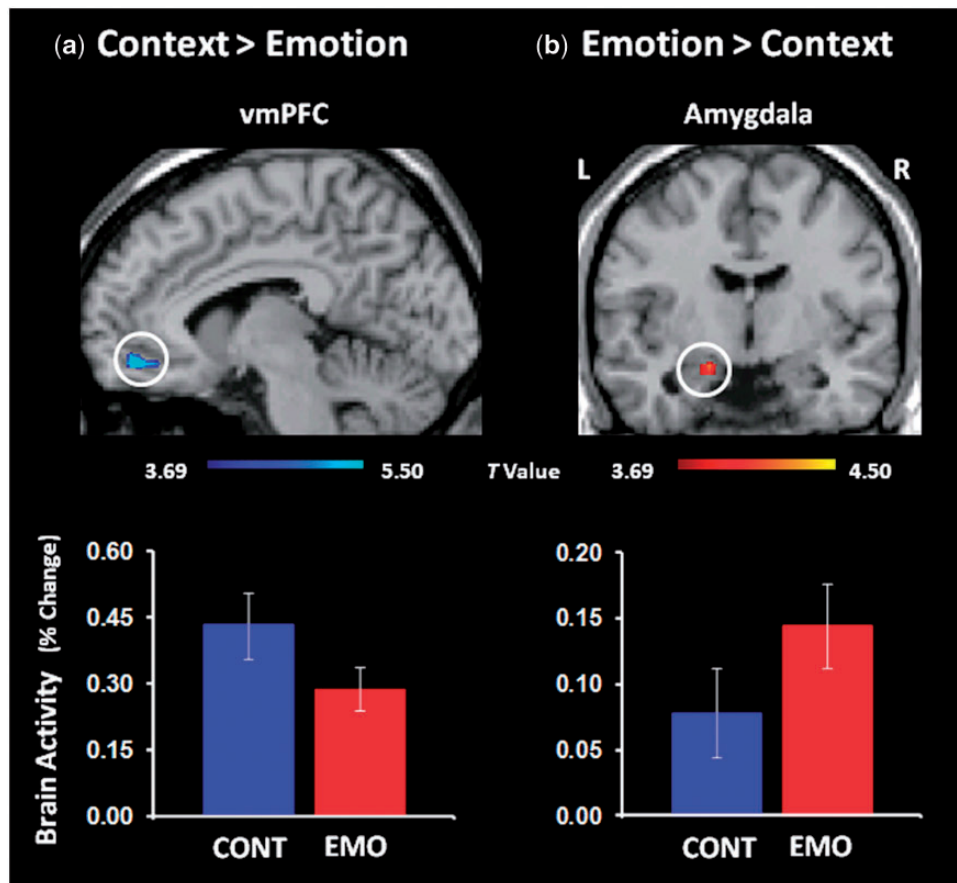


Fig. 4 Dissociable patterns of brain activity in emotion control vs basic emotion processing regions during the *Context* focus. Focusing away from emotion during AM recollection was associated with increased engagement of the ventro-medial PFC (vmPFC) (a) and decreased engagement of the left amygdala (AMY) (b). To ensure that the interaction differences are due to existing differences in the contrasts of interest compared with the SM baseline (e.g. Context vs SM), the interaction maps were inclusively masked with the activation map for Context vs SM and Emotion vs SM, respectively; the resulting maps are superimposed on high-resolution brain images displayed in sagittal (vmPFC) and coronal (AMY) views. The interaction maps were set up at $P < 0.05$, uncorrected, and were also inclusively masked with the activation map of the corresponding main contrasts, set up at $P < 0.001$ ($t = 3.69$). The gradient colour bars start at $P < 0.001$ ($t = 3.69$). The bar graphs represent the percent signal changes extracted from the displayed regions. The error bars correspond to the standard errors of the means. CONT, Context; EMO, Emotion; L, Left; R, Right.

active engagement of ER-related brain regions, possibly reflecting the switch from emotional aspects of the memories to other contextual details (time, location, etc.). In the neuroimaging research, the medial PFC has been linked to a variety of functions (Amodio and Frith, 2006), including self-referential (Northoff *et al.*, 2006; Wagner *et al.*, 2012) and emotional (Kober *et al.*, 2008) processing, mentalising (Frith and Frith, 2003; Denny *et al.*, 2012) and felt rightness (Moscovitch and Winocur, 2002). Also relevant to the present study, medial PFC has been implicated in ER (Etkin *et al.*, 2011; Ochsner *et al.*, 2012) and particularly in distancing from emotions (Koenigsberg *et al.*, 2010). In the present study, the activity in vmPFC was linked to switching between goal/context appropriate behaviours (focusing on emotional or non-emotional aspects of personal memories), which is in line with recent evidence highlighting its role as a functional hub in coordinating adaptive emotional behaviour (Roy *et al.*, 2012).

Although the negative co-variation between vmPFC and emotional ratings in the Context condition is consistent with a role of this region in attenuating the emotional response when the focus is not on emotional aspects, the exact mechanisms are not clear. One possibility is that the vmPFC exerts top-down control on emotion generation regions, but it is also possible that the vmPFC itself is contributing to emotion generation. At any rate, the present results suggest a role of the vmPFC in switching the retrieval focus during AM recollection, which leads to reduced emotional ratings when the focus is on

non-emotional aspects of the recollected memories. This idea is further supported by the results of the mediation analyses discussed below.

vmPFC mediates the link between AMY activity and emotional ratings

The present study also points towards a link between AMY response and emotional ratings, through a mediating effect of the vmPFC. Previous research also attributed a mediator role to the vmPFC, but linked to a top-down effect between this region and AMY (Urry *et al.*, 2006; Johnstone *et al.*, 2007). Namely, these studies showed that during ER, the vmPFC mediated the relationship between other PFC control regions and the AMY, such that activity in those PFC regions was found to be positively linked to vmPFC, which in turn was negatively linked to activity in the AMY. Here, we expand this finding by revealing a mediating role of the vmPFC, linked to a bottom-up effect from the AMY. Overall, the present data suggest that AMY is signalling the emotional relevance of the memories to the vmPFC, which is integrating and interpreting them according to the current goals, and as a result of switching the focus away from emotion in the Context condition it leads to decreased re-experienced emotions. The positive co-variation between the overall AMY activity (for both Context vs SM and Emotion vs SM) and the vmPFC activity is consistent with the idea that, given their emotional content, all AMs trigger AMY activity, which in turn signals vmPFC through bottom-up processing.

Table 3 Brain regions dissociating *Context* and *Emotion* conditions

Brain regions	Side	BA	Talairach coordinates			T-values		Cluster size
			X	y	z	Interaction	Mask	
(A) [Context vs SM] > [Emotion vs SM] inclusively masked with [Context vs SM]								
Ventro-medial frontal cortex								
Medial frontal gyrus	R	10/11	8	46	-16	2.83	6.58	12
Parietal cortex								
Inferior parietal lobule	R	39	48	-68	40	3.14	3.86	14
Medial temporal cortex								
Parahippocampal Gyrus*	L	37	-32	-39	-5	2.17	2.88	5
(B) [Emotion vs SM] > [Context vs SM] inclusively masked with [Emotion vs SM]								
Lateral frontal cortex								
Middle frontal gyrus	L	6	-48	6	48	2.79	3.81	15
Fronto-temporal junction								
Inferior frontal gyrus	L	47	-32	19	-8	4.24	4.61	130
Inferior frontal gyrus	R	47	40	31	-5	4.09	4.30	101
Dorso-medial frontal cortex								
Superior frontal gyrus	L	8	0	30	50	3.97	5.48	173
Superior frontal gyrus	R	6	12	30	50	3.61	3.92	
Superior/medial frontal gyrus	L	10	-16	59	8	3.58	5.20	21
Lateral temporal cortex								
Superior temporal gyrus	L	22	-51	-27	1	3.88	4.58	67
Superior temporal gyrus	L	41	-40	-39	6	3.17	4.23	
Middle temporal gyrus	R	21, 22	55	-39	2	2.88	4.08	10
Medial temporal lobe								
Parahippocampal gyrus	L	28	-20	-20	-6	4.17	4.14	11
Amygdala	L		-20	-5	-13	5.11	4.50	5
Posterior/parieto-occipital cortices								
Precuneus	L	7	0	-63	58	4.19	4.78	37
Lingual gyrus	L	17	-4	-89	-2	4.10	4.65	642
Middle occipital gyrus	L	18	-20	-81	19	3.04	4.51	
Posterior cingulate	R	31	24	-65	18	3.61	5.59	
Midbrain								
Hypothalamus	L		-4	0	-7	3.86	4.51	17
Cerebellum								
Culmen	R		16	-47	-4	2.87	4.17	13

The regions dissociating *Context* and *Emotion* focus are identified by interaction analyses ([Context vs SM] > [Emotion vs SM] and [Emotion vs SM] > [Context vs SM]). The resulting interaction maps set up at $P < 0.05$ were inclusively masking with the corresponding main contrasts of interest (*Context vs SM* and *Emotion vs SM*, respectively) set up at $P < 0.001$; exceptions in the MTL are noted with asterisks. *Significant at $P < 0.05$ in the interaction and $P < 0.01$ in the mask; BA, Brodmann's area; R, right; L, left.

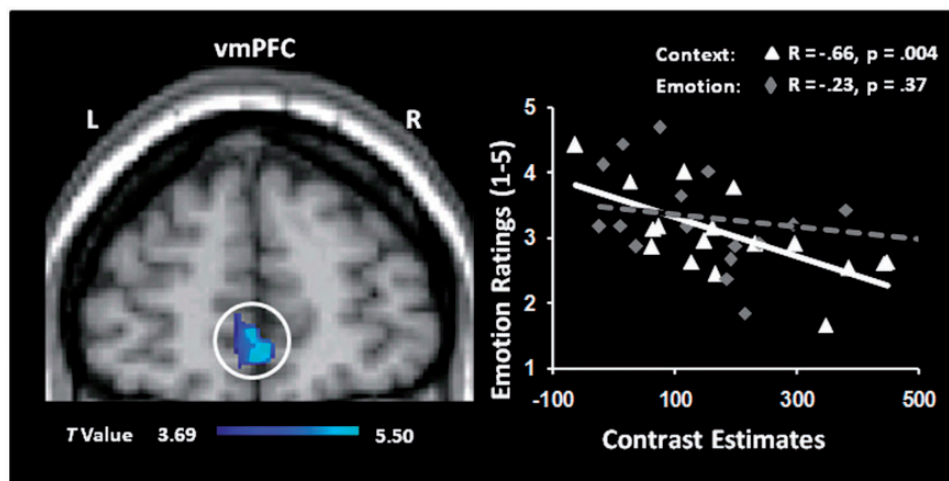


Fig. 5 Activity in the vmPFC was linked to reduced emotional ratings during the *Context* focus. Increased activity in the vmPFC for *Context vs SM* correlated negatively with emotional ratings for the AMs retrieved with a *Context* focus. To ensure that these correlations with ratings occurred in brain areas showing significant effects in the contrasts of interest, the resulting co-variation maps were inclusively masked with the activation map for *Context vs SM* contrast; the resulting map is superimposed on a high-resolution brain image displayed in a coronal view. The scatterplots are based on the contrast estimates extracted from the peak voxel of the area showing the overlap between the co-variation and activation maps. To illustrate the specificity of this correlation to the *Context* focus condition, the correlation for the *Emotion* focus condition is also plotted. L, left; R, right.

Table 4 Brain-behavioural co-variations for *Context* and *Emotion* conditions

Brain regions	Side	BA	Talairach coordinates			<i>R</i> -Values (<i>P</i>)	<i>T</i> -Values		Cluster size
			<i>x</i>	<i>Y</i>	<i>z</i>		Correlation	Mask	
(A) Context									
Negative correlations									
Medial frontal gyrus	L	10	-4	54	-9	-0.66 (0.004)	3.43	5.21	18
Positive correlations									
Medial frontal gyrus	R	9	8	44	20	0.70 (0.002)	3.75	4.08	22
Inferior parietal lobule	L	40	-51	-52	43	0.60 (0.01)	2.90	4.21	12
Lingual gyrus	L	18	-12	-73	7	0.53 (0.02)	2.41	5.72	12
(B) Emotion									
Positive correlations									
Inferior frontal gyrus	L	47	-32	19	-11	0.78 (0.0002)	4.79	5.30	16
Superior frontal gyrus	L	6	0	15	62	0.65 (0.005)	3.29	6.02	11
Cuneus	L	18	-12	-81	15	0.62 (0.008)	3.04	6.06	60
Middle occipital gyrus	R	18	28	-78	1	0.57 (0.02)	2.72	3.94	23
Precuneus	R	7	4	-61	29	0.52 (0.03)	2.35	5.50	34

The covariation maps, set up at $P < 0.05$, were inclusively masked with the statistical maps of the corresponding main contrasts (Context vs SM and Emotion vs SM, respectively), set up at $P < 0.001$. No negative correlations were observed for the Emotion condition. BA, Brodmann's area; R, right; L, left.

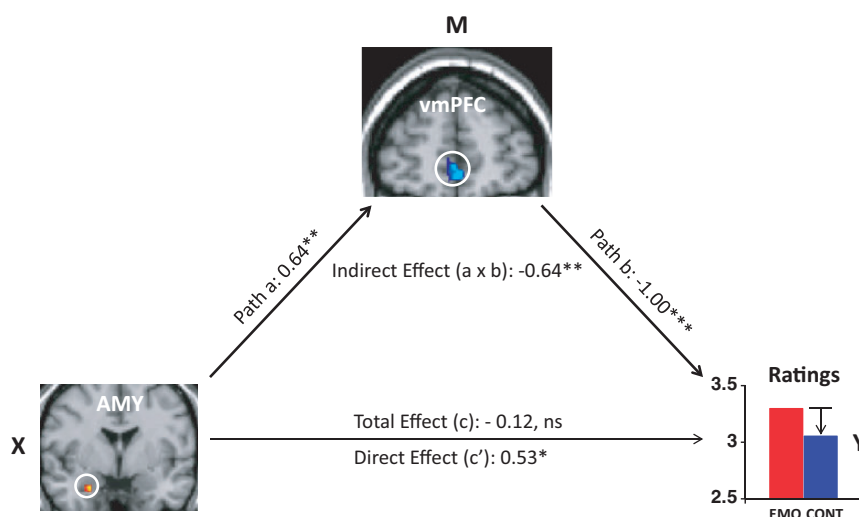


Fig. 6 Vento-medial PFC mediates the link between amygdala and emotional ratings, during the *Context* but not the *Emotion* focus. Path *a* refers to the *X* to *M* relation (i.e. Amygdala, AMY, to vmPFC), path *b* refers to the *M* to *Y* relation controlling for *X* (i.e. vmPFC to emotional ratings controlling for AMY), and the interaction between path *a* and path *b* ($a \times b$) reflects the mediation effect (indirect effect). This analysis identified a significant ($P = 0.009$) negative mediation effect of vmPFC on the relation between the AMY and emotional ratings during context-focused retrieval, and a significant ($P = 0.03$) positive direct effect (path *c'*, *X* to *Y* controlling for *M*) between AMY and emotional ratings when controlling for vmPFC influence. The mediation effect was specific to the *Context* condition, as it was not significant for the *Emotion* condition ($P = 0.22$). Standardised coefficients and significance noted with asterisks are reported for each path. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ (two-tailed); ns, not significant.

This idea is supported by findings of positive co-variations between AMY and PFC (Dolcos et al., 2006) in AM (Greenberg et al., 2005) and ER (Wager et al., 2008) studies and could be related to the timing of presenting the instruction cues and the type of ER strategies (Wager et al., 2008).

The result of the mediation analysis is consistent with our overall interpretation of the present results, suggesting bottom-up effects from AMY to vmPFC, which in turn mediates the effect on emotional ratings in the Context focus. This is consistent with neuroimaging research suggesting a role of the vmPFC in integrating information from different systems, in assigning emotional significance and in coordinating adaptive behaviours (Dolan, 2007; Roy et al., 2012). Also, consistent with this idea, lesion research shows that vmPFC damage can lead to context-inappropriate emotional responses in both human and

animals (Beer et al., 2003; Murray and Izquierdo, 2007). The fact that, when accounted for the vmPFC involvement in our mediation model, there is a significant positive relationship between the AMY and emotional ratings is consistent with the well-established role of this region in processing emotional arousal (Zald, 2003; McGaugh, 2005; Phelps, 2006). Finally, it is also possible that different AMY and vmPFC sub-regions are involved in slightly different aspects of processing engaged at different moments of the retrieval process. Although fMRI measures lack the most proper specificity in finely clarifying timing-related aspects, it is possible that the AMY–vmPFC relationship (path *a*) in our mediation model reflects earlier processing that informs the vmPFC about the emotional content of the AMs, whereas the vmPFC–Ratings relationship (path *b*) reflects later processing associated with the level of re-experienced emotion linked to the focus of AM recollection.

Future studies targeting elucidation of sub-regional specificity in AMY and vmPFC, and investigating the timing of their interaction in the context of ER manipulation are needed to address this issue.

Caveats

One limitation of the present study is linked to the absence of objective measures to verify what exactly the subjects are doing, as it is often the case in ER and AM studies. Specifically, it is not clear whether participants are consistently diverting their attention to contextual details in the Context condition, which then resulted in reduced emotional ratings. Instead, it is possible that reduced emotional ratings in the Context compared with the Emotion condition were caused by potentially different task demands in the two conditions. However, this does not seem to be the case, given that no differences were observed between the Emotion and Context conditions in other ratings (vividness and reliving). Hence, it is more likely that the differences in emotional ratings were caused by differential experiencing of emotion when focusing on or away from the emotional content of the recollected AMs. Future investigations using additional psychophysiological recordings (e.g. skin conductance) could help further clarify this issue.

CONCLUSIONS

In summary, the present study sheds light on the neural underpinnings of focused attention as an effective ER strategy during emotional autobiographical recollection. Three main findings emerged from the present investigation. First, focusing away from emotion led to decreased self-reported emotional responses, along with increased engagement of vmPFC and reduced AMY activity. Second, increased activity in the vmPFC was linked to reduced self-reported ratings of emotion during the context-focused AM retrieval. Third, mediation analyses identified a role of the vmPFC as a functional hub integrating affective signals from the AMY and mediating their impact on the subjective re-experiencing of emotion, according to the current retrieval focus. Overall, by demonstrating the usefulness of focusing attention on non-emotional aspects of recollected AMs, these findings have direct relevance for understanding, preventing and treating affective disorders, and provide fruitful avenues for application of this ER strategy in both healthy and clinical groups.

Conflict of Interest

None declared.

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