Neuropsychologia 48 (2010) 989–996

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Neural long-term effects of emotion regulation on episodic memory processes

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ARTICLE INFO

Article history:
Received 5 June 2009
Received in revised form
20 November 2009
Accepted 23 November 2009
Available online 27 November 2009

Keywords:
Amygdala
fMRI
Hippocampus
Mesolimbic brain regions

ABSTRACT

Emotions can enhance memory which is on the one hand advantageous, but on the other hand may be detrimental in the long term, for example in the case of traumatic events. Although cognitive emotion regulation may reduce emotion experience and corresponding neural activation, at present little is known about its influence on long-term memory. We investigated memory for emotional pictures in healthy female subjects 1 year after voluntary emotion regulation using fMRI. Whereas memory performance was not affected by regulation, our data revealed a dissociation of brain regions involved in memory encoding and recognition depending on whether emotional engagement during encoding had been downregulated. Emotional engagement during encoding resulted in a long-term subsequent memory effect in mesolimbic brain regions and hippocampus, and in recognition-related activation in the amygdala. In contrast, when negative emotions had been downregulated during encoding memory performance was predicted by prefrontal activation. Our data suggest that memory for emotionally encoded stimuli is supported by emotional re-activation, whereas memory for successfully encoded items during emotion regulation is rather supported by recognition of features and cognitive contents. These results contribute to research on long-term effects of emotion regulation in everyday life and open new avenues to understand and possibly influence traumatic memory traces.

1. Introduction

It is well known that long-term memory is improved for emotional events due to specific neural and hormonal mechanisms that are not engaged during memory for neutral material (Cahill, Prins, Weber, & McGaugh, 1994; LaBar & Cabeza, 2006; Phelps, 2004). Although the temporal development of the emotional modulation of memory processes is still unclear (Wolf, 2008), it is assumed that memory enhancement by emotion reflects the neuromodulatory influence of the amygdala on consolidation processes in the medial temporal lobe (MTL) through engagement of adrenergic stress hormones (McGaugh, 2004; Strange & Dolan, 2004; van Stegeren et al., 2005).

But what are the effects of emotion regulation on these well known processes? Although emotion regulation is an essential ability in everyday life, its effects on long-term memory processes have not been sufficiently researched.

Brain imaging studies have shown that amygdala activation during *encoding* of emotional items is related to improved long-term memory (for a review see LaBar & Cabeza, 2006) due to a modulating effect on the MTL memory system (Dolcos, LaBar, & Cabeza, 2004; Richardson, Strange, & Dolan, 2004). In addition, enhanced memory for emotional material seems to be primarily influenced by arousal rather than valence characteristics of the stimuli (Anderson, Wais, & Gabrieli, 2006; Kensinger & Corkin, 2004) (but see also Mickley & Kensinger, 2008). In post-traumatic stress disorder (PTSD) where patients suffer from hyperarousal and re-experiencing phenomena such as flashbacks of traumatic experiences (Etkin & Wager, 2007), it has been suggested that prolonged states of adrenergic activation lead to overconsolidation of traumatic memories (Pitman et al., 2002; Vaiva et al., 2003). In healthy subjects, administration of the beta-adrenergic antagonist propranolol during encoding has been shown to reduce amygdala-dependent memory for emotional events after minutes (Strange, Hurlemann, & Dolan, 2003), hours (Strange & Dolan, 2004) or weeks (Cahill et al., 1994), presumably through a central adrenergic blockade.

However, it is not known whether non-pharmacological, i.e., cognitive, emotion regulation can likewise influence long-term memory.

Only a few studies have shown amygdala involvement during short-term (hours to days) *recognition* of emotional memories (Kensinger & Schacter, 2005; Sharot, Delgado, & Phelps, 2004). Recently it was reported that even 1 year after incidental encoding memory for emotionally arousing items, compared to neutral non-arousing items, was enhanced and was accompanied by greater

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doi:10.1016/j.neuropsychologia.2009.11.022

amygdala and hippocampal activation (Dolcos, LaBar, & Cabeza, 2005). By using this long retention interval the authors are able to distinguish retrieval from early consolidation processes, which cannot be disentangled when testing memory after shorter delays of days or weeks.

Here we were interested in the effects of *emotion regulation* on long-term episodic memory. Emotion regulation has been subject to a number of studies reporting significant reduction of amygdala activation during active regulation of negative events (for a review see Ochsner & Gross, 2005; Phillips, Ladouceur, & Drevets, 2008). However, effects of emotion regulation on long-term memory have so far only been investigated in a few behavioral studies showing diverging effects, depending on the regulation strategy used. Thought suppression (Rassin, Merckelbach, & Muris, 1997) as well as cognitive reappraisal (Dillon, Ritchey, Johnson, & LaBar, 2007; Richards & Gross, 2000, 2006) had no effect on memory for emotional items, whereas expressive suppression did have an effect (Dillon et al., 2007; Richards & Gross, 2000, 2006).

In order to investigate the *neural* effects of emotion regulation on long-term memory, we studied memory in subjects 1 year after they participated in an emotion regulation experiment. We tested whether recognition was modulated by emotion regulation during encoding. Moreover, we also analyzed encoding data and investigated, whether brain activation during incidental encoding could predict memory for the respective item 1 year later, and whether this potential subsequent memory effect was modulated by emotion regulation—thus potentially resembling the pharmacological effects of beta-adrenergic blockade. Emotion regulation effectuates reduction of arousal, mostly reflected in reduction of amygdala activation (Ochsner & Gross, 2005; Phillips et al., 2008) and arousal seems to be a crucial factor of emotional memory by facilitating encoding and consolidation processes (Hamann, 2001; Kensinger & Corkin, 2004; McGaugh, 2004). Therefore, we expected to find effects of successful recognition as well as a subsequent memory effect during encoding in regions of the MTL, including the amygdala, *only* in cases where emotions were experienced in a natural way, but *not* when subjects regulated their emotions during encoding.

2. Materials and methods

2.1. Subjects

Sixteen female volunteers (mean age 23.8 ± 2.8, all right-handed), with no history of neurological or psychiatric illness participated in an emotion regulation study and in the subsequent recognition study between 10 and 12 months after the initial encoding experiment. The protocol of the study was approved by the local ethics committee. All subjects gave written informed consent.

2.2. Experimental design

In the initial emotion regulation study subjects were presented with 30 negative and 30 neutral pictures from the International Affective Picture System (IAPS). Half of the stimuli were assigned to the regulation condition. Stimuli in the respective cells were matched for content of faces, scenery, food and nature (mean valence (V) and arousal (A) values: negative no regulation: $V = 2.7$, $A = 5.4$, negative regulation: $V = 2.8$, $A = 5.4$, neutral no regulation: $V = 5.7$, $A = 3.4$, neutral regulation: $V = 5.7$, $A = 3.2$). Subjects were instructed to either regulate their emotions by taking the position of a distant observer (regulation condition) or to experience their emotion in a natural way (no-regulation condition). Assignment of pictures to conditions was similar for all subjects. The task instruction for the regulation condition was: "Look at the following picture directly but try to take the position of a noninvolved observer, thinking about the present picture in a neutral way", and for the no-regulation condition was: "Look at the following picture directly and permit feeling your emotions". After the instruction (2 s) subjects were presented with a negative or neutral picture for 8 s followed by a baseline of 20 s, where subjects were instructed to relax. Subjects were unaware of a subsequent memory test to be taken approximately 1 year later. For detailed results of the initial emotion regulation study, see Walter et al. (2009). In sum, fMRI results revealed a significant downregulation of bilateral amygdala activation during regulation of negative affect and a significantly stronger activation of a prefrontal–parietal network during regulation, which was positively correlated with the amount of amygdala downregulation. All subjects confirmed that they succeeded in regulating their emotions in a semistructured interview conducted after the scanning session. Success was rated on average as 3.39 (1 = very successful, 9 = not successful). Furthermore, a control experiment using fMRI and on-line ratings demonstrated that physiological downregulation was accompanied by downregulation of subjective negative affect. Finally, subjective ratings of general picture valence and arousal outside the scanner revealed that negative pictures were rated significantly more negative and arousing than neutral pictures, and that picture sets assigned to regulation and non-regulation cells did not differ with respect to valence or arousal.

In the recognition study participants were scanned while being presented with the 60 pictures from the initial study together with 30 new, unknown pictures 1 year after incidental encoding. The picture set thus consisted of 30 old (15 formerly regulated, 15 formerly non-regulated) and 15 new negative and 30 old (15 formerly regulated, 15 formerly non-regulated) and 15 new neutral pictures. New pictures were matched with old pictures with respect to content (faces, scenery, food, and nature), valence (negative = 2.7, $p = 0.7$, neutral = 5.7, $p = 0.9$) and arousal (negative = 5.6, $p = 0.6$, neutral = 3.4, $p = 0.7$). Subjects had to make a remember/know/new-decision (Tulving, 1985) by pressing one of three buttons. They were instructed to respond "remember", if they were convinced that the picture was presented during the encoding task and retrieved details and contextual information (reflecting retrieval of specific, detailed attributes) and to respond "know", if the picture seemed familiar, i.e., they knew that they had seen the picture before but could not retrieve associated informations. Subjects had to respond "new" in case they were convinced that the picture had not been shown in the encoding task. Pictures were presented for 3 s with an intertrial interval of 12 s and a variable jitter between ±0.9 TR, i.e., ±1.8 s).

2.3. FMRI acquisition

Data acquisition parameters were the same for both the emotion regulation (incidental encoding) and recognition experiments. Imaging was performed on a 3 T Siemens Allegra scanner equipped with a head coil. T2* weighted functional MR images were obtained event-related using echoplanar imaging in a axial orientation. Image size was 64 × 64 pixels, with a field of view of 192 mm, flip angle was 90°. One volume covering the whole brain consisted of 31 slices. Slice thickness was 3 mm with a 25% gap resulting in a voxel size of 3 mm × 3 mm × 3.75 mm. Volumes were obtained every 2000 ms (TE 35 ms). Stimuli were presented with LCD video goggles (Resonance Technologies, Northridge, CA). Three-dimensional T1 weighted anatomical volumes were acquired for each subject.

2.4. FMRI data analysis

Data preprocessing and statistical analysis were carried out with SPM2 (Statistical Parametric Mapping, Wellcome Institute of Cognitive Neurology, London, UK) and Matlab 6.5.1 (MathWorks, Natick, MA) for both experiments. The first four images were discarded to account for equilibration effects. Individual functional images were corrected for motion by realignment to the first volume of each session. All images were spatially normalized (2 mm × 2 mm × 2 mm) to an echo planar image in MNI space and spatially smoothed with an 8 mm full width at half maximum isotropic Gaussian kernel. For each trial the variance of each voxel was estimated according to the General Linear Model. Intrinsic autocorrelations were accounted for by an autoregressive model of 1st order (AR(1)) and low frequency drifts were removed via a high pass filter of 128 s.

The first-level model for the recognition analysis consisted of a set of 9 regressors of interest. Cells were assigned according to emotion (negative, neutral), regulation mode during encoding (formerly regulated, formerly non-regulated), and memory (hits, misses), resulting in the following individual regressors (regulated = formerly regulated): 'negative-regulated-hits', 'negative-regulated-misses', 'negative-non-regulated-hits', 'negative-non-regulated-misses', 'neutral-regulated-hits', 'neutral-regulated-misses', 'neutral-non-regulated-hits', and 'neutral-non-regulated-misses'. Additionally, we modelled the button press as a regressor of no interest. All regressors were convolved with a delta function that modelled a prototypical hemodynamic response before inclusion into the regression model. Thus, each subjects design matrix consisted of an individual set of stimuli per cell. Additionally, six regressors describing residual motion were included into the model. (Due to the limited number of items we restrict the fMRI analysis to hits and misses, thereby collapsing remember and know answers into one regressor.)

The first-level model for the incidental encoding analysis also consisted of a set of 9 regressors of interest. Cells were assigned according to emotion (negative, neutral), regulation mode (regulated, non-regulated), and subsequent memory (hits, misses), resulting in the following individual regressors: 'negative-regulated-hits', 'negative-regulated-misses', 'negative-non-regulated-hits', 'negative-non-regulated-misses', 'neutral-regulated-hits', 'neutral-regulated-misses', 'neutral-non-regulated-hits', and 'neutral-non-regulated-misses'. We additionally modelled the regulation instruction. All regressors were convolved with a delta function that modelled a prototypical hemodynamic response before inclusion into the regression model. Thus, again each subjects design matrix consisted of an individual set of stimuli per cell. Additionally, six regressors describing residual motion were included into the model. (Due to the limited number of items we also restricted the encoding anal-