Emotion regulation modulates anticipatory brain activity that predicts emotional memory encoding in women

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It has been shown that the effectiveness with which unpleasant events are encoded into memory is related to brain activity set in train before the events. Here, we assessed whether encoding-related activity before an aversive event can be modulated by emotion regulation. Electrical brain activity was recorded from the scalps of healthy women while they performed an incidental encoding task on randomly intermixed unpleasant and neutral visual scenes. A cue presented 1.5 s before each picture indicated the upcoming valence. In half of the blocks of trials, the instructions emphasized to let emotions arise in a natural way. In the other half, participants were asked to decrease their emotional response by adopting the perspective of a detached observer. Memory for the scenes was probed 1 day later with a recognition memory test. Brain activity before unpleasant scenes predicted later memory of the scenes, but only when participants felt their emotions and did not detach from them. The findings indicate that emotion regulation can eliminate the influence of anticipatory brain activity on memory encoding. This may be relevant for the understanding and treatment of psychiatric diseases with a memory component.

Keywords: emotion regulation; anticipation; emotional memory; event-related potentials

INTRODUCTION

When anticipating an aversive event, individuals generally experience an increase in emotional responding. This includes changes in subjective experiences, autonomic reactions and neural responses (Drabant et al., 2011). Neuroimaging studies have shown that activity in brain regions such as the amygdala, prefrontal cortex, insula and anterior cingulate cortex increases during the anticipation of negative events (Nitschke et al., 2006; Paulus and Stein, 2006; Herwig et al., 2007). While emotional reactivity can be adaptive to some extent, excessive negative anticipation may affect the development and maintenance of psychiatric symptoms (Beck, 1967; Eysenck, 1992). Enhanced anticipatory activity in the brain regions reported earlier has been found in clinical psychiatric populations (Abler et al., 2007; Strigo et al., 2008) and in individuals with high levels of neuroticism (Drabant et al., 2011) and trait anxiety (Simmons et al., 2006, 2011).

Anticipatory brain activity not only relates to the perceptual intake of an emotional event but also to the likelihood that the event will be encoded into long-term memory. Neural activity before an emotional event has been found to predict whether the event will later be remembered (Mackiewicz et al., 2006; Galli et al., 2011; Padovani et al., 2011). Anticipatory activity is particularly relevant for the encoding of unpleasant events (Mackiewicz et al., 2006; Galli et al., 2011), especially in women (Galli et al., 2011). Anticipatory activity may play a role in the preparation to process an impending aversive event in an emotional manner, which in turn affects encoding into long-term memory. This mechanism may be particularly evident in women due to enhanced emotional responsiveness (Bradley et al., 2007; Gard and Kring, 2007).

Given the relevance of anticipatory brain activity for the encoding of emotional events, it is of interest to determine whether this activity can be modulated by emotion regulation. Emotion regulation is a widely used method in clinical and research settings to exert control over emotions (Ochsner and Gross, 2005). Several regulation strategies have been reported. Cognitive reappraisal involves the reconstruction of the emotion-generating experience to change its emotional impact (Lazarus and Alfert, 1964). One reappraisal strategy, known as detachment or self-focused reappraisal, requires individuals to distance themselves from the aversive event by adopting the perspective of a detached observer. By doing so, individuals decrease their emotional responding and thus the experiential and behavioral components of negative emotion.

In the present study, we assessed how emotion regulation affects anticipatory brain activity predicting emotional memory formation. Because the relationship between brain activity before an aversive event and encoding is primarily found in women (Galli et al., 2011), only female participants were included in the experiment. In the study phase, electrical brain activity was recorded from the scalps of healthy volunteers while they performed an incidental encoding task on neutral and unpleasant pictures. A cue presented just before each picture indicated the upcoming valence. In half of the trials, participants were instructed to let their emotions arise in a natural way. In the other half, they were asked to decrease their emotional response by adopting the perspective of a detached observer. One day later, a surprise recognition memory test had to be performed. All the pictures from the study phase were presented again alongside new ones, and participants were asked to judge whether they remembered a picture from the study phase. Event-related potentials (ERPs) elicited by cues preceding neutral and unpleasant pictures in the two regulation conditions were contrasted according to whether the pictures were remembered or forgotten in the memory test. The question of interest was whether anticipatory activity would predict later memory of unpleasant pictures when emotions were felt but not, or less so, during emotion regulation.

MATERIALS AND METHODS

Participants

Thirty female volunteers (M age = 23.3 years, s.d. = 2.9) took part in the experiment. All had normal or corrected-to-normal vision and reported to be native English-speaking, right-handed and not to have, or have had, any psychiatric or neurological conditions. The experimental procedures were approved by the University College London Research Ethics Committee. Each participant provided written...
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Informed consent before participating and was remunerated at a rate of £7.50/h.

Stimulus materials

In all, 504 pictures were selected from the International Affective Picture System (IAPS, Lang et al., 1997). Pictures subtended a visual angle of ~6.8° horizontally and 3.1° vertically. Among them, 252 depicted neutral scenes and 252 unpleasant scenes. The two picture sets differed significantly in valence [unpleasant pictures M = 2.55, s.d. = 1.52; neutral pictures M = 5.20, s.d. = 1.36; t(251) = 56.65, P < 0.001] and arousal [unpleasant pictures M = 5.72, s.d. = 2.21; neutral pictures M = 3.61, s.d. = 2.00; t(251) = 30.70, P < 0.001] according to the normative rating data of the IAPS. Twelve pictures from each valence set were used to create practice lists. The remaining 240 pictures in each set were randomly split into three groups of 80. Two of the groups were designated as old items and one as new item. The particular groups that were used as old and new items were counterbalanced across participants. Old pictures (160 unpleasant and 160 neutral) were randomly allocated to a study list of 320 items to be used during the encoding phase. The test list consisted of 480 randomly allocated pictures, 320 of which were old and 160 new (80 unpleasant and 80 neutral). A new random sequence was generated for each participant. Study lists were split into six blocks and test lists into eight blocks to provide brief rest periods.

Procedure

The experiment involved an incidental encoding task, followed by a recognition memory test approximately 1 day later. In the study phase, participants viewed a series of randomly intermixed neutral and unpleasant pictures. Pictures were shown centrally on a computer screen on a gray background for 1 s. Participants were asked to decide whether a picture depicted an indoor or outdoor scene and press one of two buttons with their right or left index finger to indicate their decision (responding hand counterbalanced across participants). Each picture was preceded by a cue that indicated the valence of the upcoming picture. Cues were cartoon faces with downward or neutral mouths to indicate unpleasant and neutral scenes, respectively. Cues were presented 1.5 s before picture onset and remained on the screen until 100 ms before the picture was shown. The time in between successive picture onsets varied randomly between 3 and 4.5 s. At both study and test, a fixation point (a black plus sign) was continuously present in the center of the screen except when experimental stimuli were presented. Upon completion of the test phase, participants filled in the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970) and Emotion Regulation Questionnaire (ERQ) (Gross and John, 2003). They were then debriefed and reimbursed for their time.

Electroencephalography acquisition and analysis

Electroencephalography (EEG) was recorded from 32 scalp sites with sintered silver/silver-chloride electrodes embedded in an elastic cap according to an equidistant montage (www.easycap.de/easycap/e/electrodes/13_M10.htm). Vertical and horizontal eye movements were recorded bipolarly from, respectively, electrodes attached to the supra- and infraorbital ridges of the right eye and to the outer canthus of each eye. The data were recorded continuously using a midfrontal reference site and amplified, band-pass filtered (0.01–35 Hz, 3 dB roll-off) and digitized at a rate of 500 Hz (12 bit resolution). Impedances were kept below 5 kΩ. Offline, the EEG was digitally filtered between 0.05 and 20 Hz (96 dB roll-off), downsampled to 125 Hz and algebraically re-referenced to the average of the left and the right mastoids. The online midfrontal reference site was re-instated and used as a scalp site of interest.

The primary interest was in activity elicited by cues, but activity in response to pictures was also considered for completeness. Cue-elicited and picture-elicited activity was analyzed separately to allow each to be aligned to the time period immediately before each event (Otten et al., 2006, 2010; Gruber and Otten, 2010; Galli et al., 2011, 2012). This approach assesses whether pictures elicit activity above and beyond any activity elicited by cues. Epochs of 2048 ms duration surrounding cues and pictures, starting 100 ms before their onset, were extracted from the continuous record. ERPs were computed for each subject, electrode site and emotion regulation condition by averaging trials containing unpleasant and neutral pictures that were given ‘confident old’, ‘unconfident old’, ‘confident new’ and ‘unconfident new’ judgments in the recognition memory task. The ERP waveforms were aligned to the 100 ms prestimulus period. Blinks were minimized with a linear regression procedure that uses activity on the vertical eye movement channel to estimate and remove blink-related activity from each scalp site (Rugg et al., 1997). Trials with horizontal and non-blink vertical movements were excluded from the averaging process, as were trials containing drifts (± 50 μV), amplifier saturation or muscle artifacts.

The comparisons focused on ERP activity that differed between trials containing pictures that were later remembered vs forgotten (i.e. subsequent memory effects; Sanquist et al., 1980). Encoding-related activity was collapsed across confident and unconfident responses to obtain a sufficient number of trials (only eight participants had at least 15 relevant artefact-free trials to restrict the analyses to confident judgments). On average, 38 and 35 remembered and forgotten trials contributed to the ERPs for neutral items in the regulation...
condition and 38 and 34 remembered and forgotten trials to the ERPs for neutral items in the no-regulation condition. For unpleasant items, these numbers were 45 and 28 in the regulation condition and 46 and 27 in the no-regulation condition, respectively.

The quantification of the ERP waveforms and statistical analyses were guided by the findings in Galli et al. (2011). In that study, encoding-related activity was found to precede unpleasant pictures in women. This activity took the form of a positive-going deflection that was largest over right centroparietal scalp sites and present from 300 ms after cue onset until the appearance of the unpleasant picture. The initial analyses evaluated whether the same deflection was evoked in the no-regulation condition in the present experiment. The waveforms were therefore quantified by measuring mean amplitude values at right centroparietal scalp sites in the 300–1500 ms interval where encoding-related anticipatory activity was expected to emerge. As in Galli et al. (2011), the interval was separated into three to assess possible differences over time. The final latency intervals of interest were therefore 300–700, 700–1100 and 1100–1500 ms following cue onset. Figure 1 depicts the scalp sites used for the statistical analyses. The values were submitted to repeated measures analyses of variance (ANOVAs) incorporating factors of subsequent memory (remembered/forgotten), valence (unpleasant/neutral), regulation (regulation/no-regulation) and electrode site (eight positions). The Greenhouse–Geisser correction for violations of sphericity was applied to factors with more than two levels (Keselman and Rogan, 1980) and only effects involving subsequent memory were considered.

Picture-related activity was expected to emerge over anterior scalp sites in the form of a positive-going deflection following pictures that were later remembered from 200 ms onwards (Galli et al., 2011). Values in the 200–600, 600–1100 and 1100–1900 ms intervals were extracted from anterior scalp sites and submitted to repeated measures ANOVAs incorporating the same factors as employed for cue-related activity. As for cue-related activity, encoding-related activity was expected to be present throughout this period but partitioning the period allowed an assessment of differences over time (cf. Galli et al., 2011). The electrode site factor comprised 14 rather than 8 positions to accommodate right as well as left electrode sites.

Correlational analyses were performed to assess whether individual differences in anxiety level affected encoding-related anticipatory activity. These correlations were restricted to activity preceding unpleasant pictures in the two regulation conditions. The correlations assessed the relationship between STAI scores and differences in ERP activity preceding remembered and forgotten unpleasant pictures at centroparietal scalp sites in the 700–1500 ms interval after cue onset (the time period in which significant encoding-related activity was found). An additional correlation was conducted to assess whether individual differences in emotion regulation affected encoding-related activity preceding unpleasant items in the regulation condition. This analysis used the ERQ scores.

RESULTS

STAI and ERQ

Mean scores for the STAI were 38.7 for state and 42.0 for trait anxiety (s.d. = 10.7 and 7.9, respectively; ranges 20–66 and 28–59). Mean scores for the ERQ were 30.3 for reappraisal and 13.7 for suppression (s.d. = 4.5 and 5.6, respectively; ranges 20–37 and 5–22).

Task performance

Mean response times for indoor/outdoor judgments on neutral and unpleasant pictures were, respectively, 902 ms (s.d. = 297 ms) and 1005 ms (s.d. = 432 ms) in the no-regulation condition and 857 ms (s.d. = 206 ms) and 892 ms (s.d. = 255 ms) in the regulation condition. These times were compared in a repeated measures ANOVA with factors of valence and emotion regulation. Main effects of valence [F(1.0, 29.0) = 12.32, P = 0.001] and emotion regulation [F(1.0, 29.0) = 4.21, P = 0.049] indicated that judgments were on the whole slower for unpleasant than neutral pictures and during the no-regulation than regulation conditions. Although responses to unpleasant pictures were especially slow in the no-regulation condition, the interaction between valence and emotion regulation was not statistically significant (P = 0.086). Given the subjective nature of many indoor/outdoor judgments, study accuracy was not considered.

Recognition performance is summarized in Table 1. Accuracy of recognition judgments was assessed with the discrimination index Pr (the proportion of hits minus the proportion of false alarms; Snodgrass and Corwin, 1988). Mimicking the ERP analyses below, Pr was first collapsed across confidence judgments. An ANOVA with factors of valence and regulation did not reveal significant differences between conditions (Ps > 0.416). When the analyses were restricted to confident judgments, again no significant differences emerged (Ps > 0.631). Although hit rate was slightly higher for unpleasant pictures, so was false alarm rate.

Anticipatory activity related to encoding

Figure 2 displays the group-averaged ERPs elicited by cues preceding neutral and unpleasant pictures in the two emotion regulation conditions. In the no-regulation condition, activity before the onset of unpleasant pictures differed depending on whether pictures were recognized or forgotten 1 day later. This encoding-related activity took the form of a more positive-going waveform preceding unpleasant pictures that were later remembered, an effect that was largest over central and right posterior scalp sites and present from ~500 ms after cue onset. This effect strongly resembles the positive-going anticipatory effect observed in Galli et al. (2011). In stark contrast, when participants were instructed to reduce their emotional responses, activity before unpleasant pictures exhibited only small encoding-related differences. Activity preceding neutral pictures did
not differ according to later memory performance in either regulation condition.

The statistical analyses were guided by the effect observed by Galli et al. (2011). Mean amplitude values were measured at right centro-parietal scalp sites in the same intervals as employed earlier (300–700, 700–1100 and 1100–1500 ms after cue onset). Mean amplitude values averaged across electrode sites for cues preceding later remembered and forgotten pictures in the different conditions are reported in Table 2. These values were submitted to repeated measures ANOVAs. No significant effects emerged in the first latency interval. In the second and third intervals, the ANOVAs gave rise to a significant interaction between subsequent memory, valence and regulation \([F(1.0, 29.0) = 5.98, P = 0.021, \text{for the second and } F(1.0, 29.0) = 5.09, P = 0.032, \text{for the third time interval}]\). This interaction was unpacked by performing separate analyses in each regulation condition. These analyses revealed that the interaction between subsequent memory and valence was significant in the no-regulation condition \([F(1.0, 29.0) = 6.53 \text{ and } 5.70 \text{ in the two intervals, respectively, } P = \text{0.016 and } 0.024])\), but not in the regulation condition \((Ps > 0.544)\). In the no-regulation condition, a significant subsequent memory effect only emerged for unpleasant pictures \([F(1.0, 29.0) = 4.64 \text{ and } 4.40 \text{ in the two intervals, respectively, } P = 0.040 \text{ and } 0.045; Ps > 0.927 \text{ for neutral pictures}]\). These analyses support the visual impression that anticipatory activity predicted subsequent memory of unpleasant pictures in the no-regulation condition only. The correlational analyses to assess whether this activity was associated with an individual’s anxiety level or ability to regulate emotions did not reveal significant correlations \((Ps > 0.118)\).

### Encoding-related activity after picture onset

Activity following picture onset also differed as a function of later memory performance (Figure 3). As typically observed
Table 2. Mean amplitude values (μV) averaged across right centroparietal scalp sites for cues preceding later remembered and forgotten pictures

<table>
<thead>
<tr>
<th></th>
<th>Neutral</th>
<th>Unpleasant</th>
<th>Neutral</th>
<th>Unpleasant</th>
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</thead>
<tbody>
<tr>
<td>700–1100 ms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remembered</td>
<td>0.49 (1.88)</td>
<td>1.19 (1.69)</td>
<td>1.15 (1.83)</td>
<td>1.27 (1.77)</td>
</tr>
<tr>
<td>Forgotten</td>
<td>0.93 (1.71)</td>
<td>0.35 (2.73)</td>
<td>0.69 (1.99)</td>
<td>0.76 (1.80)</td>
</tr>
<tr>
<td>1100–1500 ms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remembered</td>
<td>−0.75 (2.32)</td>
<td>−0.56 (1.91)</td>
<td>0.17 (2.05)</td>
<td>−0.07 (1.92)</td>
</tr>
<tr>
<td>Forgotten</td>
<td>−0.23 (1.83)</td>
<td>−1.52 (2.64)</td>
<td>−0.40 (2.15)</td>
<td>−0.38 (1.85)</td>
</tr>
</tbody>
</table>

Standard deviations are displayed in parentheses. Values are reported for the two latency intervals that showed a significant interaction between subsequent memory, valence and regulation conditions.

P<0.001], but not in the third (P=0.091). Crucially, encoding-related activity elicited by pictures did not differ as a function of emotion regulation.

**DISCUSSION**

Consistent with previous research, brain activity before an emotional event was related to the efficacy with which the event is encoded into long-term memory (Mackiewicz et al., 2006; Galli et al., 2011; Padovani et al., 2011). Electrical brain activity elicited by a cue that indicated an upcoming unpleasant visual scene was more positive-going over right posterior scalp sites when the scene was recognized 1 day later (Galli et al., 2011). This only occurred, however, when participants were instructed to feel their emotions and not during emotional detachment. When participants attempted to experience their emotions in a natural way, brain activity before unpleasant events affected later memory performance. The influence of anticipatory activity on memory encoding was abolished when an emotion regulatory strategy was used.

The data indicate that emotion regulation modulates anticipatory brain activity predicting emotional memory encoding. Such activity may play an active role in the preparation to process an upcoming negative event in an emotional manner, which in turn affects the likelihood that the event will be encoded into memory. The particular type of anticipatory activity that was observed here, a widespread positive-going deflection, has been linked to motivational processes (Gruber and Otten, 2010; Galli et al., 2011; Padovani et al., 2011). The activity cannot merely reflect the increased levels of arousal associated with emotional relative to neutral events. Whereas activity preceding unpleasant pictures predicts encoding success, activity preceding pleasant pictures equated for arousal does not (Galli et al., 2011). The current data do not add further insights into the functional role of encoding-related anticipatory activity, but they do indicate that the processes associated with the activity are no longer engaged when the emotional content of upcoming information needs to be toned down.

Cognitive reappraisal is a strategy in which the emotional response to a negative stimulus is reduced by reinterpreting its meaning (Ochsner and Gross, 2005). This type of emotion regulation not only changes the subjective emotional experience (Gross, 1998) but also alters peripheral (Jackson et al., 2000) and neural (Ochsner et al., 2002, 2004; Hajcak and Nieuwenhuis, 2006; Foti and Hajcak, 2008) responses. Importantly, emotion regulation strategies, including reappraisal, can be applied during the presentation of a stimulus as well as during its anticipation (Erk et al., 2006; Herwig et al., 2006; Moser et al., 2009). Although cognitive reinterpretation is only possible after meaning has been discerned, coping strategies to counteract the impact of a negative event can be engaged prior to the event itself.

In the present study, participants may have started placing themselves in a distant mode of observation when the cue signalled an impending unpleasant picture. In this respect, it is worth noting that less time was taken for indoor/outdoor judgments in the regulation condition. This suggests that participants tried to engage as little as possible with the study material during emotion regulation. Importantly, however, memory performance did not differ across regulation conditions. This indicates that the lack of encoding-related anticipatory activity during emotional detachment cannot simply be explained by a shallower depth of processing (cf. Otten et al., 2006). Previous studies have also shown that emotion regulation does not affect memory performance (Richards and Gross, 2000; Erk et al., 2010), even when encoding-related neural activity does (Erk et al., 2010). One possibility is that effects found at the neural level are important for memory performance, but that there is no necessary...
relationship between the two. For example, items that lead to weak representations during encoding may still be remembered because of compensatory processes that happen during later consolidation and retrieval. Conversely, strongly encoded items may ultimately not be remembered because of what happens during later memory stages. It is also possible that an effect of emotion regulation on memory performance will emerge if memory is probed in another way or at a different time. An alternative scenario is that effects seen at the neural level do not have a behavioral consequence. On this account, emotion regulation may involve the engagement of neurally distinct but equally effective encoding strategies. Further studies are needed to assess if, and at which stage of processing, different emotional encoding strategies exert an influence on memory performance.

It will be of interest to determine how pathological individuals use anticipatory brain activity during memory encoding. None of the participants in our sample reported psychiatric disorders, and all anxiety scores fell within normal range. This may explain the lack of a correlation between anticipatory brain activity and anxiety levels. As mentioned earlier, negative anticipation plays an important role in some clinical psychiatric populations, and psychiatric diseases are often characterized by altered memory for emotional information (McNally, 1997a,b). Our finding that an emotion regulatory strategy can abolish the influence of anticipatory activity on memory encoding may therefore be relevant for the understanding and treatment of psychiatric disorders. The fact that individuals are able to voluntarily adopt regulatory strategies, and control the engagement of anticipatory activity, is especially encouraging in this respect.

Brain activity after picture onset was also predictive of subsequent memory performance. Later remembered pictures elicited more positive-going waveforms than later forgotten ones (Friedman and Johnson, 2000). However, picture-related encoding activity did not differ between regulation instructions. This is consistent with our previous study, which showed encoding-related effects of emotional material during anticipation but not following the presentation of the pictures themselves (Galli et al., 2007). In contrast, recent functional magnetic resonance imaging studies have shown that upon presentation of an emotional stimulus different brain regions predict memory performance depending on the regulation instructions (Erk et al., 2010; Hayes et al., 2010). It is possible that the time course of the hemodynamic response is too slow to dissociate encoding processes surrounding event onset.

In conclusion, our findings demonstrate a relationship between anticipatory brain activity and encoding of negative events in women when emotional processes are engaged but not during emotional detachment. These findings suggest a close link between emotional engagement, negative anticipation, and long-term memory in at least women. This could be of relevance for psychiatric diseases with a strong memory component, such as anxiety or post-traumatic stress disorder. Regulating emotions before a negative event in everyday life or in a clinical setting may help reduce the impact of a negative event on memory. Although only women were considered in the present study, there is no reason to assume that regulatory strategies cannot extend to other groups of individuals.

**REFERENCES**


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**Conflict of Interest**

None declared.


