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How mood challenges emotional memory formation: An fMRI investigation

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ABSTRACT

Experimental mood manipulations and functional magnetic resonance imaging (fMRI) provide a unique opportunity for examining the neural correlates of mood-congruent memory formation. While prior studies in mood-disorder patients point to the medial temporal lobe in the genesis of mood-congruent memory (MCM) bias, the interaction between mood and emotional memory formation has not been investigated in healthy participants. In particular it remains unclear how regulatory structures in the pre-frontal cortex may be involved in mediating this phenomenon. In this study, event-related fMRI was performed on 20 healthy participants using a full-factorial, within-subjects repeated-measures design to examine how happy and sad moods impact memory for valenced stimuli (positive, negative and neutral words). Main effects of mood, stimulus valence and memory were examined as was activity related to successful memory formation during congruent and in-congruent moods. Behavioral results confirm an MCM bias while imaging results show amygdala and hippocampal engagement in a global mood and successful recall, respectively. MCM formation was characterized by increased activity during mood-congruent encoding of negative words in the orbito-frontal cortex (OFC) and for mood-incongruent processing of negative words in medial- and inferior-frontal gyri (MFG/IFG). These findings indicate that different pre-frontal regions facilitate mood-congruent and incongruent encoding of successfully recalled negative words at the time of learning, with OFC enhancing congruency and the left IFG and MFG helping overcome semantic incongruities between mood and stimulus valence.

Introduction

Memory facilitation for emotional events is a well-recognized phenomenon with clear advantages to adaptive behavior (McGaugh, 2004). Memory can be enhanced when mood state at time of learning or retrieval matches the valence of emotional stimuli (Blaney, 1986; Leppänen, 2006). Surprisingly, studies that explore the neural underpinnings of mood-congruent memory biases remain sparse. Neuroimaging findings come mainly from acutely depressed patients (Hamilton and Gotlib, 2008; van Wingen et al., 2010) and recovered patients undergoing mood-induction (Ramel et al., 2007) which point to the amygdala as one mediator of mood congruent memory (MCM). While these studies impart important information and targets for further investigation, they are limited in relevance for normal memory function or for discriminating state versus trait mood effects.

Lewis et al. (2005) found neuroimaging evidence in healthy controls for the classical idea of associative networks (Bower, 1981) being reactivated when mood at retrieval matches stimulus-valence at encoding. Activity for mood-congruent stimuli increased in the subgenual cingulate for positive words and in the orbito-frontal cortex (OFC) for negative words, independent of recall success. However, the analysis employed was limited to conjunctions (overlapping activity) between encoding and retrieval activity, excluding regions involved specifically in MCM formation. Formation of biased emotional memory in depression has been shown to involve discrete neuronal regions for encoding and retrieval (van Wingen et al., 2010), indicating that investigations into MCM should discriminate between the two processes.

We hypothesized that the amygdala was involved in MCM based on its overall role in emotional memory (Cahill et al., 1995; Canli et al., 1999), its modulation of hippocampal activity during emotional memory formation (Dolcos et al., 2005) and from memory studies examining brain function in depressed patients (i.e. Hamilton and Gotlib, 2008). Other previously implicated regions include parts of the pre-frontal cortex (PFC) associated with sensations of mood and emotion regulation (Depue et al., 2007; Phan et al., 2005). Specifically, lateral pre-frontal areas may preferentially process mood-congruent stimuli, having an established role in cognitive control (Ridderinkhof

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et al., 2004) and for emotional memory for non-arousing information (Kensinger and Corkin, 2004). Additionally, the OFC has been associated with MCM formation for emotional words (Lewis et al., 2005), with sensitivity for stimulus valence (Lewis et al., 2007). OFC activity has also been associated with coupled affective odor and faces (Gottfried et al., 2002), pleasant and unpleasant tastes (Small et al., 2003) as well as responses to positive and negative feedback and reward (Elliott et al., 2000, 2007). Thus, with the expectation that regions involved in emotional learning, valence-appraisal and emotional regulation would be involved in mediating mood-congruent learning, the above regions (amygdala, lateral PFC, OFC), subserving various aspects of mood and emotional memory were investigated for involvement in successful encoding of valenced stimuli under different mood conditions. The present study investigated MCM formation from the standpoint that both control and valence-detection regions likely interact during memory formation and are influenced by mood-congruency and -incongruity.

To test this hypothesis, we employed a full-factorial cross-over design, examining interactions between Mood (happy/sad), Valence (positive/neutral/negative) and Subsequent Memory (remembered/forgotten) to dissociate neural correlates of mood-congruent and -incongruent memory formation. First, we expected to find a behavioral MCM bias reflected by increased recall of mood-congruent words. Activity associated with subsequently remembered words, word valence and general mood (regardless of mood-congruency) was examined using whole-brain analyses as well as a region-of-interest approach for the areas mentioned above. Due to the limited body of neuroimaging literature on mood-congruent memory bias, the investigation of three-way interactions between Mood, Valence and Subsequent Memory performance on brain activity was directionless and more exploratory, examining activity across the entire brain using an uncorrected threshold.

Methods and materials

Participants

Twenty-four Dutch speaking volunteers (7 males, mean age 22.8 ± 3.7 years) gave written informed consent in accordance with the local research ethics committee to participate in this study. Participants reported themselves as physically and mentally healthy and were free of current DSM-IV disorders as determined by a structured interview using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998). To avoid possible confounds due to sub-threshold depressive symptoms, subjects were screened for depression using the Dutch version of the Beck Depression Inventory-II (BDI-II; Beck et al., 1996) with a cut-off score of less than 10. Three participants (1 male) dropped out of the study, unable to tolerate scanning due to the length of the study sessions, with an additional participant excluded from the final analysis due to technical failure.

Experimental procedures

The memory task was performed on two separate days approximately one week apart for sad and happy mood induction in a cross-over design with counterbalanced order. For each experimental session, participants completed the BDI-II and rated their level of current affect using the 20-item Positive and Negative Affect Schedule (PANAS; Watson et al., 1988). They were subsequently given detailed written information regarding the memory, distraction and mood rating tasks. Participants were told that they would watch both happy and sad film clips, and were instructed to use the situations and emotions depicted to put themselves in as strong a mood as possible. This was to be maintained throughout the session, with repeated probes to rate their subjective mood using a 20-point visual-analogue scale. Participants underwent a total of four mood inductions per scanning session, intermixed with 20 study–test cycles, all the while lying in the scanner. Each memory cycle consisted of a study phase for emotional and neutral words, followed by a serial-subtraction task serving as a distraction period and finished by a 30 s free recall period as described below. The overview of this procedure is illustrated in Fig. 1.

Mood induction

In keeping with a previous study that had shown to provide robust mood-induction effects (Urner et al., in press) four film clips (12, 6, 5 and 7 minutes), chosen for their unipolar and unambiguously sad content were extracted sequentially from 'Sophie's Choice', a movie often employed for the induction of a sad mood (e.g. Sanna, 1999). A matched set of sequential clips of the same duration showing unambiguously happy scenes were selected from the animated video 'Happy Feet'. Prior to presentation, subjects were explicitly instructed to use the situation and emotions depicted in each video clip to enter the target mood, a procedure shown to elicit strong changes in mood (Westermann et al., 1996). Each session began with a long initial mood induction period followed by the first of five memory cycles, this design was replicated for the three shorter booster clips. Participants rated their mood before and after each mood induction and memory cycle using a visual-analogue scale from −10 (saddest mood ever) to +10 (happiest mood ever) using the left/right button presses. Mood ratings were averaged per block in the behavioral analysis to reflect sustained, rather than initially large changes in mood following each mood induction.

Stimuli

Neutral, positive and negative Dutch words of five to 13 letters (mean: 8.6 ± 2.2) were used in the memory task. These were based primarily on the well-validated English ANEW list (Affective Norms for English Words; Bradley and Lang, 1999). In a pilot experiment conducted prior to the current study, these words were rated by 15 healthy participants for their perceived valence ranging from 1 (very negative) to 15 (very positive) with neutral centered at a score of 8. Positive words had a mean rating on a scale of 1–15 of 12.34 ± .49, negative words had a mean rating of 3.24 ± .68, and neutral words had an average rating of 8.42 ± .40. For the current study, words with more than one response deviating from these ranges were excluded. Thus, the 160 most negative, 160 neutral and 160 most positive words were selected for this study from an initial list of 977 words. These words were subsequently divided into matched sets of 12 stimuli each, with four words per emotional category, counterbalanced for frequency of use (CELEX database; Baayen et al., 1995), length and number of verbs, nouns and adjectives. Forty different sets of words were used across the two experimental fMRI sessions, with set order counterbalanced between the first and second session as well as between mood inductions.

Memory task

Participants performed a free-recall memory task using the emotional and neutral words described above. While undergoing functional imaging, each mood induction of 5–12 min duration was followed by five memory cycles, each including a study, distraction, and free recall phase. In the study phase, participants were instructed to silently read and remember each of the 12 sequentially presented words in random order displayed centrally on the screen for 500 ms, with a white font on black background. The inter-stimulus interval was randomly varied between 4 and 8 s, with 2 'null events' per cycle — i.e. two lengthier ISIs averaging 12 s per cycle. Following each learning phase, a distraction task was employed wherein a random number between 80 and 100 was displayed for 25 s, with the instructions to