How mood challenges emotional memory formation: An fMRI investigation

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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.

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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, 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), and 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 emotion, we 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/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 (Unner 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
count down in steps of 3 pressing the left button for each step. After speaking aloud the final number reached, the cycle finished with the verbal responses in the free-recall phase. Participants were cued to say aloud each word they could remember, with a 30-second response limit, which was sufficient time in all cases to complete the word recall. These responses were digitally recorded and transcribed for off-line analysis. Head motion was restricted via the use of foam padding.

Image acquisition and data analysis

Functional MR imaging was performed on a 1.5 T Siemens Avanto scanner (Erlangen, Germany) using axial echo-planar imaging (32 slices, 212 mm FOV, 64×64 matrix, 2340 ms TR, 35 ms TE) with final voxel dimensions of 3.3×3.3×3.7 mm. For each imaging session, data was collected continuously throughout the mood induction and memory cycles. All fMRI data was processed using SPM5 software (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK). Participants were instructed to remain still with foam pads secured against the head to limit movement. Images were realigned, slice-time corrected and co-registered to each participant’s high-resolution T1 scan, which was used in normalizing to the standard Montreal Neurological Institute (MNI) template. Finally, images were smoothed using an 8×8×8 FWHM Gaussian kernel and entered into a first-level general linear model analysis. To account for error variance across the large time-series in this experiment, the parametric analysis contained six main regressors of interest and two regressors of no interest. The regressors of interest were derived from each participant’s recall performance for each word valence: positive remembered/forgotten, neutral remembered/forgotten and negative remembered/forgotten modeled using the standard SPM delta function convolved with a canonical hemodynamic response function (HRF). The mood induction and distraction periods were modeled using a square-wave function convolved with a standard HRF as regressors of no interest. A high-pass filter (128 s cut off) was used to remove low-frequency signal drift. Parameter estimates for each contrast of interest were calculated and entered into a second-level group analysis with an ANOVA design to evaluate the main effects of Subsequent Memory, Valence and Mood. These main effects were examined initially at the whole-brain level corrected for false-discovery rate (FDR) with a threshold of p<.05. An additional region of interest (ROI) analysis was conducted on these main contrasts for a-priori regions of interest in the amygdala, hippocampus, orbito- and lateral pre-frontal cortices using anatomical regions derived from the AAL database (Tzourio-Mazoyer et al., 2002). Lastly, the three-way interaction between these variables was examined for activity that corresponded with mood-congruent memory formation. An exploratory analysis examining these interactions was run across the entire brain contrasting activity for remembered versus forgotten words in each category to examine differences between congruent and incongruent successful versus unsuccessful encoding. Effects in this 3-way analysis surviving an exploratory threshold of p<.001 uncorrected across the entire brain are reported and discussed with respect to prior findings in similar regions of the brain.

Results

Baseline mood scores

No participants reported elevated depression scores prior to the beginning of the study (mean BDI-II score: 2.4±1.9, range: 0–7). Baseline measures of affect did not differ prior to the happy and sad mood induction sessions: mean PANAS-positive scores: 26.5±6.0 vs. 27.7±5.2 respectively, p=.28; mean PANAS-negative score: 12.5±
between Mood and Valence on recall rates \(F(18)=7.6, p=.04\), but a strengthened interaction between mood and valence \(F(18)=3.86, p=.04\]. A subsequent 2×2 ANOVA excluding neutral words revealed no main effects of Mood \(F(19)=2.26, p=.15\] and an interaction between mood and valence \(F(18)=6.45, all p<.001\] throughout the entire experiment.

**Mood induction**

Mood induction successfully induced mood changes (see Fig. 2b). One-sample t-tests comparing baseline mood ratings with subsequent mood ratings revealed that participants had higher mood ratings following happy mood induction \(min t(19)=2.1, all p<.05\) and lower mood ratings following sad mood induction \(min t(19)=−6.45, all p<.001\] throughout the entire experiment.

**Behavioral results**

A mood-congruent memory bias was found in the free-recall data (see Fig. 2a). We performed a 2 (Mood)×3 (Valence) ANOVA on recall rates, which showed both a main effect of Mood \(F(19)=4.63, p<.04\] and an interaction between mood and valence \(F(18)=3.86, p<.04\]. A subsequent 2×2 ANOVA excluding neutral words revealed no main effect of Mood \(F(19)=2.26, p=.15\], but a strengthened interaction between Mood and Valence on recall rates \(F(18)=7.6, p<.01\]. Post-hoc paired-sample T-tests comparing recall rates between mood conditions and word valence indicated that this interaction was driven by better recall of positive compared to negative words during happy mood \((54.8±12.7\% vs 48.3±11.5\%, p<.01\) Recall of negative compared to happy words during sad mood also went in the same direction \((50.8±10.8\% vs 47.6±10.8\%, p<.01\] but this effect did not reach significance \(p=.18\). The interaction between mood and recall rates was driven primarily by better recall of neutral words in the happy mood compared to sad condition \((50.1±15.2\% vs 45±13.2\%, p<.03\).

**fMRI results**

**Main effect of subsequent recall**

The whole-brain analysis (FDR corrected at \(p<.05\) for subsequent memory effects (all recalled versus forgotten words) gave rise to a main effect of subsequent memory in the left IFG \((-38, 42, −14; p_{FDR}<.001\] angular gyrus \((-34, −62, 42; p_{FDR}<.001\], inferior-temporal gyrus \((-60, −42, −8; p_{FDR}<.001\], superior-frontal gyrus \((-6, 24, 50; p_{FDR}<.003\) as well as the left hippocampus \((-28, −12, −14; p_{FDR}<.01\] (see Fig. 3a). This replicates earlier findings on verbal memory formation (Cabeza et al., 2002).

**Distinct effects of mood and valence**

Examining the influence of stimulus valence on encoding, regardless of mood or subsequent recall, we found that processing of affective words (both negative and positive) was marked by increased activity compared to neutral words in the left superior medial gyrus \((-6, 54, 36; p_{FDR}<.001\] rectal gyrus \((-2, 50, −18; p_{FDR}<.001\] and posterior cingulate cortex \((-6, −48, 26; p_{FDR}<.003\) (see Fig. 3b).

**Three-way interaction between mood, valence and recall**

The exploratory whole-brain examination of the three-way interactions between mood, valence and subsequent recall revealed activity in three regions: the left IFG \((-48, 22, 10\] left OFC \((-16, 28, −14\] and left middle-frontal gyrus (MFG), which survived an uncorrected threshold of \(p<.001\) (see Fig. 4). Paired t-tests conducted on extracted beta values from peak voxels in these areas comparing activity separately for each stimulus valence indicated that this interaction is driven primarily by differential processing of negative and neutral words. Following sad mood induction, subsequent memory effects for negative words were significantly greater in the left OFC compared to activity for negative words following happy mood induction. Conversely, subsequent memory effects were larger for negative words during happy compared to sad mood in the left IFG and MFG while no such effect was found for subsequent memory with happy words. To summarize these findings, differential activity in the left IFG and MFG was associated with mood-incongruent memory formation while activity in the left OFC showed a pattern of activity associated with mood-congruent memory formation.

**Discussion**

To our knowledge, this study provides the first full-factorial, comprehensive neuroimaging investigation on the effects of happy...
and sad moods for emotional memory formation using positive, negative and neutral stimuli. The paradigm employed was designed to produce the maximum impact of mood on subsequent memory via an effective mood-induction paradigm using relatively lengthy and effective emotional movie clips followed by an open-ended free recall memory task. Subsequent recall of both positive and negative words

Fig. 3. Main effects of a) recall b) valence and c) mood on the encoding of affective words. Activation patterns in images a and b are FDR corrected using a threshold of $p < .05$, while image c shows activity for a cluster that was found using our region of interest approach ($p < 0.05$ small volume corrected).

Fig. 4. Interactions between mood, valence and recall show differential activity in the orbito-frontal cortex as well as inferior- and middle-frontal gyri ($p < .001$ uncorrected). Bars graphs indicate extracted beta-estimates for differences in activity between remembered and forgotten words for each mood and valence condition, with error bars indicating one standard error.
was influenced by mood in the expected direction, indicating that the underlying brain activity could be probed for patterns reflecting mood-congruent memory processing. This was accomplished by exploring the three-way interactions between mood, stimulus valence and subsequent recall. More general neural processes were probed by looking at the main effects of mood, stimulus valence and subsequent recall in separate analyses.

While the mood ratings obtained in this study are in line with previous findings that negative mood inductions have a greater effect than positive mood induction (Westermann et al., 1996), elevated initial baseline ratings and negative effects on mood of the scanner environment and task difficulty should be taken into account in judging the efficacy of the manipulation. The behavioral finding in this study that the memory bias was statistically more robust for positive words than for negative could be due to an overall performance increase for cognitive processing associated with happy mood, rather than a lack of memory bias for negative words. This phenomenon has been reported previously, particularly for memory for positive and neutral stimuli (Ashby et al., 1999). However, the number of recalled negative words also matched the expected direction, leading to the overall significant findings of mood-congruent memory bias. The heterogeneous effects of mood induction noted above may also help account for the finding of unbalanced mood-congruent processing in that positive and negative words were selected for very high or low valence, respectively, while the negative mood induction resulted in more intense changes in ratings.

In line with the growing body of research on episodic memory formation (for example Davachi et al., 2003; Tendolkar et al., 2007), we found significant hippocampal involvement in the successful encoding of words with additional contributions from the left inferior-frontal, angular, inferior-temporal and superior-frontal gyrus. These later regions are part of a fronto-parietal-cingulate-thalamic circuit involved in episodic memory as well as attention and visual perception (see Cabeza et al., 2002, 2003; Naghavi and Nyberg, 2005). In the present study, only the inferior-frontal gyrus was additionally associated with mood-incongruent memory during encoding (see below), indicating that the general memory system may remain largely unaffected by mood-congruency. The involvement of the IFG generally in encoding subsequently recalled stimuli (independent of mood or stimulus valence) as well as more specific involvement in successful encoding of mood-incongruent stimuli implies that this region deserves greater attention for both future studies on, as well as theories on the origins and nature of MCM.

A broad network of frontal structures including the left superior medial as well as rectal gyrus together with the posterior cingulate was differentially engaged as a function of biological salience during memory formation independent of subsequent recall. Both frontal regions involved in the effects of valence showed greater activity for emotional (both positive and negative) compared to neutral words suggesting a role in valence-detection and emotional memory (Lewis et al., 2005, 2007). The posterior cingulated cortex (PCC) is thought to represent a key junction between pre-frontal regions and hippocampal-based mnemonic processing, implicated in episodic memory formation (Maddock, 1999) and mediation of interacting emotional and mnemonic processes (Maddock et al., 2003). While we found a direct relationship with PCC to stimulus valence, this area was not involved in any subsequent general or mood-congruent recall phenomenon. This finding is in line with the notion that the PCC is involved in more general processing of emotional material that may reflect less specific processes such as determination of self-relevancy and serving as a central hub in the default-mode network (Andrews-Hanna et al., 2010). An activity increase in the default-mode network has been found in depressed patients, potentially accounting for disordered self-referential thoughts that are particularly relevant during an acute phase of depression (Sheline et al., 2009). Our findings of an activity increase in the PCC under mood induction may indicate that the down-regulation of the default network is altered during processing of emotional stimuli in an acute mood state. It was somewhat surprising that we did not find amygdala involvement in processing emotional compared to neutral words (Hamann and Mao, 2002) or for amygdala specificity in processing negative words (see Herbert et al., 2009 for a review). However, it is important to take into account that processing of emotional stimuli may have a reduced impact on subsequent memory during an induced or chronic negative mood state, as the amygdala may be maintained at a persistently higher state of activity, resulting in a lower range of possible responses to valenced stimuli.

In analyzing the main effect of mood on stimulus encoding, we indeed found overall stronger amygdala activity throughout the sad, compared to the happy mood. This finding supports a generic role for amygdala in the experience of negative affect (see Phan et al., 2005). This general increase in amygdala activity across both valenced and neutral words during a sad mood indicates that a general priming of the amygdala may occur under a sustained sad mood, which may overwhelm the ability to detect mood-congruent activity in subsequent tasks. Findings of sustained amygdala activity in depressed populations (Sible et al., 2007; van Wingen et al., 2010) indicate that similar effects could counteract or overshadow any amygdala involvement in mood-congruent stimulus detection. Moreover, our data are in line with studies using stress-induction in healthy controls (van Marle et al., 2009), where there is a shift of amygdala function towards heightened sensitivity with lower levels of emotional specificity following an experimental stress-induction procedure, a pattern of results suggestive for a state of indiscriminate hyper-vigilance. The idea of amygdala hyperactivity during an acute mood-state that will put more brain systems on alert is very well in line with recent theories of depression (Whalen et al., 2002). Our findings together with those of van Marle et al. (2009) add to that by showing that a mood-induced indiscriminate hyper-vigilance of amygdala seems to have a general adaptive value that also applies to the general population.

Most important for our original hypotheses, we analyzed the imaging data for evidence of modulating effects of a sad versus a happy mood on subsequent recall rates for congruent and incongruent stimuli. Three-way interactions between mood, valence and memory revealed clusters of activity in the IFG, MFG and OFC that discriminate between remembered and forgotten negative and neutral words in different mood conditions. The significance of mood-dependent processing of negative words indicates a potentially important implication for research of MCM in depression and other mood disorders. In particular, OFC activity increased during encoding of subsequently recalled negative words during a sad compared to a happy mood, while inferior- and middle-frontal gyri showed greater activity for subsequently recalled negative words during a happy, compared to a sad mood. Both of these later two regions also demonstrated increased activity associated with subsequent recall for neutral words that was greater in the sad, compared to happy mood condition. These findings suggest that, in healthy controls, a sad mood may affect the processing of neutral words. On a related line, we have shown in depressed patients that subsequent memory effects for neutral stimuli is also altered as a function of a sad mood (van Wingen et al., 2010). Though this prior effect was mainly found in the amygdala, our findings may suggest that during a sad mood neutral stimuli are processed in a mood-congruent way, forming an additional basis for negative memory biases.

Prior research implicates the OFC in memory enhancement for emotionally salient events, possibly due to increased arousal (Cahill et al., 1995; Hamann et al., 1999). Our data are also in line with those of Lewis et al. (2005, 2007) who found that sub-regions of the OFC were involved in memory formation and displayed valence-specific activity for emotional words. Moreover, the OFC is known to be involved in an emotional network that relies on mood perception as mediated by the amygdala (Bechara et al., 2000; Phillips et al., 2003). Given that we
observed global increases in amygdala activity during a sad mood, this may have triggered enhanced memory formation observed in OFC specific to negative words during a sad mood. Links between amygdala activity and OFC function, especially for aversive material are well-established in the neuroscience literature (Zald and Pardo, 1997) and can even predict the attenuation of negative affect following an emotional reappraisal task (Banks et al., 2007).

Activity of the left IFG has an equally long history of being linked to conceptual semantic processes during successful memory formation (Gabrieli et al., 1996), in particular for verbal information (Buckner et al., 1999; Fletcher and Henson, 2001). Labeling of emotionally valenced stimuli requires the recruitment of semantic networks in addition to the affective neural network. Our findings of IFG involvement in successful memory formation for mood-incongruent stimuli suggest that more conceptual, semantic processes are needed when the mood state does not match the stimulus valence, violating an obvious semantic association. The semantic incongruity may be also interpreted as a novelty effect (Dobbins and Wagner, 2005; Kirchhoff et al., 2000) resulting in a pre-frontal top-down memory modulation.

Our results suggest that increased activity in the inferior- and middle-frontal gyri facilitate monitoring and attention for mood-incongruent negative words, acting to override the default mood-congruent (semantic) processing and directs attention towards semantically-incongruent stimuli. This idea is supported by prior research showing IFG involvement in semantic violations (Newman et al., 2001) as well as for processing incongruent semantic verifications (Hoenig and Scheef, 2008). Similar findings in the MFG, an area associated with information monitoring in episodic memory (Fletcher and Henson, 2001), is also consistent with previous findings on mood-congruent memory (Lewis et al., 2005). Both of these later two regions also demonstrated increased activity associated with subsequent recall for neutral words that was greater in the sad, compared to happy mood condition. These findings suggest that, in healthy controls, sad mood may affect the processing of neutral words. On a related research line, we have previously shown in depressed patients that subsequent memory effects for neutral stimuli are also altered as a function of a sad mood (van Wingen et al., 2010). Though this prior effect was mainly found in the amygdala, our findings may suggest that during a sad mood neutral stimuli are processed in a mood-congruent way forming the additional basis for negative memory biases. We would thus like to adopt the view that in-congruency between mood and valence at the time of learning requires extra cognitive effort, which is provided by the additional engagement of the left IFG and MFG.

In sum, this study investigated mood-congruent and mood-incongruent memory formation and showed that while the amygdala and hippocampus were engaged in overall mood and recall interactions during successful memory formation, the left IFG and MFG had a differential neural response to positive and negative feedback in planning and guessing tasks. Neuropsychologia 35, 1395–1404.

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