Persistent affective biases in human amygdala response following implicit priming with negative emotion concepts

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ABSTRACT
To what extent do past experiences shape our behaviors, perceptions, and thoughts even without explicit knowledge of these influences? Behavioral research has demonstrated that various cognitive processes can be influenced by conceptual representations implicitly primed during a preceding and unrelated task. Here we investigated whether emotion processing might also be influenced by prior incidental exposure to negative semantic material and which neural substrates would mediate these effects. During a first (priming) task, participants performed a variant of the hangman game with either negative or neutral emotion-laden words. Subsequently, they performed a second, unrelated visual task with fearful and neutral faces presented at attended or unattended locations. Participants were generally not aware of any relationships between the two tasks. We found that priming with emotional words enhanced amygdala sensitivity to faces in the subsequent visual task, while decreasing discriminative responses to threat. Furthermore, the magnitude of the induced bias in behavior and amygdala activation was predicted by the effectiveness of semantic access in the priming task. This demonstrates that emotional processing can be modulated by implicit influence of environmental information processed at an earlier time, independently of volitional control.

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Introduction

The extent to which past experiences can shape our behaviors, perceptions, and thoughts unconsciously has long been discussed in psychology, psychiatry, and philosophy. Abundant research has shown that many cognitive processes can be implicitly influenced by information incidentally encountered at a prior time, for example, using priming paradigms (Bargh, 2005; Schacter, 1987). However, much of this research has used experimental procedures where priming information is presented immediately before another task-relevant stimulus (Kihlstrom and Heindel, 1984; Moors et al., 2005; Spruyt et al., 2007), and these priming effects are often considered to be short lasting when they operate without conscious awareness (Kouider and Dehaene, 2007). Yet, there is also considerable evidence that cognitive performance, memory, or goal-directed behavior can be modulated outside the realm of volition in a more sustained manner by activating conceptual representations incidentally, prior to a task of interest (Bargh, 2005; Custers and Aarts, 2010; Zemack-Rugar et al., 2007).

For instance, incidental priming by incentive cues or words referring to specific values, concepts, or goals (e.g., cooperation, achievement, elderliness, etc.) will bias information processing and influence behavior in a subsequent, unrelated task (Aarts et al., 2008; Bargh et al., 2001). Thus, activating representations related to the notion of exertion will increase the participants’ effort in a subsequent handgrip task (Aarts et al., 2008), whereas activating representations of ageing cause college students to walk more slowly when leaving the experimental session (Dijksterhuis and Bargh, 2001). In these experiments, conceptual priming is typically achieved using word search puzzle games, anagrams, or verbal completion procedures prior to the main experiment (Bargh et al., 2001). Crucially, these effects occur even without any awareness of the relation between tasks or of the bias itself (Bargh et al., 2001) and without adopting a conscious strategy. These long-lasting implicit biases have been attributed to unconscious activation or facilitation of attention to the primed conceptual representations, but the exact neural substrates of these effects remain unknown (Custers and Aarts, 2010).

Besides such effects on cognitive performance and behavior, incidental conceptual priming can also influence some forms of emotional regulation (Schweiger Gallo and Gollwitzer, 2007; Williams et al., 2009). Thus, participants previously exposed to emotional expression concepts show increased anger in a subsequent anger provocation paradigm, relative to participants previously exposed to control-related concepts (Mauss et al., 2007). These implicit effects contrast with the traditional view that emotion regulation is associated with conscious volition and effortful top-down processes (Ochsner and Gross, 2005; Ochsner et al., 2009).
Furthermore, in human neuroscience, the degree of automaticity and control in the processing of emotional information remains vigorously debated (Pessoa et al., 2002, 2003; Vuilleumier, 2005). Several fMRI studies have shown that the amygdala, a brain region critically involved in fear and vigilance (Davis and Whalen, 2001; Phelps and LeDoux, 2005), responds to various types of threat-related stimuli such as fear or anger expressed in faces, actions or voices (Pichon et al., 2009; Sander et al., 2005; Whalen et al., 2001), regardless of conscious awareness (Crichley et al., 2002; Jiang and He, 2006; Morris et al., 2001; Pasley et al., 2004; Whalen et al., 1998; Williams et al., 2004), spatial attention (Anderson et al., 2003; Dolan and Vuilleumier, 2003; Grandjean et al., 2005; Vuilleumier et al., 2001), or explicit task demands (Bach et al., 2008; Critchley et al., 2000; Winston et al., 2003). In contrast, other experiments have shown that the amygdala response to threat can be altered by direct attention elsewhere or by increasing the perceptual demands of another concurrent task (Bishop et al., 2007; Lim et al., 2008; Mitchell et al., 2007; Pessoa et al., 2002; Pichon et al., 2012). In addition, amygdala responses can be up- or down-regulated by re-interpreting the emotional stimulus as a function of the immediate contextual information available (de Gelder et al., 2006; Kim et al., 2004; Sinke et al., 2010; Vrticka et al., 2008) or by modifying one's own interpretation of a negative situation (Ray et al., 2005). Amygdala activation is also enhanced when ambiguous stimuli such as faces with surprise expressions are immediately preceded by situational context cues with negative (vs. positive) information (i.e., a sentence stating “she just found/lost $500”; see Kim et al., 2004) Together, these data indicate that emotional responses can be biased by cognitive evaluation processes and volitional control (Ochsner et al., 2009), even though the precise mechanisms remain poorly understood.

Hence, most studies on the modulation of emotion processing have focused on tasks requiring deliberate control and effortful attentional processes (Ochsner and Gross, 2005; Pessoa et al., 2002) or used explicit tasks with a direct and immediate relationship between the priming cues and emotional stimuli (e.g., Kim et al., 2004). This is in sharp contrast with the implicit effects induced by conceptual priming via independent tasks that are not directly related to the information to process and given several minutes before the experimental condition of interest (Aarts et al., 2008; Bargh et al., 2001). Indeed, implicit biases on emotional and motivational states induced by prior exposure to unrelated material can arise without any subjective feeling of effort or intentionality (Bargh et al., 2001) take place without awareness of the links between the prime and target information and last up to several minutes after exposure, contrary to other forms of implicit priming which effects are considered to be evanescent and cease to be detectable after 500 ms (Dehaene and Changeux, 2011; Kouider and Dehaene, 2007).

In the present study, we therefore examined whether persistent biases can be induced by prior implicit exposure to emotion-related concepts during an incidental task and thus affect emotion processing in the amygdala and related brain areas. Participants were told that they would participate in two different studies performed in alternating sessions to make the experiment less repetitive. Conceptual priming was induced by using a word completion task, which was a variant of the hangman game. This priming task was administered just prior another visual attention task and manipulated the nature of semantic representations to which participants were exposed, using either affectively negative or neutral words. Specifically, we asked whether implicit priming with emotional concepts could modify the subsequent processing of emotional faces in the amygdala (Vuilleumier et al., 2001; Whalen et al., 2001) and/or the fusiform face area (FFA) in extrastriate visual cortex (Kanwisher et al., 1997). We predicted that priming by emotional concepts may induce persistent biases in the response profile of the amygdala and interconnected brain regions during the subsequent visual task. Such effects would demonstrate that human amygdala activity is not solely under the control of bottom-up or effortful regulatory processes, but can also be implicitly influenced by prior exposure to emotion-laden material. In addition, because previous behavioral research suggests that processing biases induced by incidental conceptual priming may operate via an implicit modulation of attentive processes (Dijksterhuis and Aarts, 2010), we also manipulated whether emotional stimuli were presented in task-relevant (attended) or irrelevant (unattended) conditions.

Methods

Participants

Twenty right-handed volunteers (11 females, mean age ± SD: 26.8 ± 5.9 years; and 10 males: 24.8 ± 4.4 years) without neurological or psychiatric history participated in the imaging study. All provided written informed consent according to guidelines of the local research ethics committee and were paid for their participation.

Experimental procedure

Subjects performed two separate tasks (Fig. 1a) while undergoing functional MRI; a word completion priming task (inspired from Mauss et al., 2007) and a subsequent attention task that used pictures of faces and places and manipulated spatial attention (similar to Vuilleumier et al., 2001). Participants were told that they would participate in two different studies performed in alternating sessions to make the experiment less repetitive. Subjects were exposed to only one semantic field during a given session of the priming task. Each subject performed both tasks twice in alternation (AB–AB) so that we could examine brain responses in the attention task as a function of the semantic field (emotional or neutral) primed in the preceding word completion task. The order of semantic fields was counterbalanced across subjects. Thus, the protocol formed a $2 \times 2$ balanced factorial design crossing priming context (emotional, neutral), emotion expression of the face (fear, neutral), and attention condition (face attended, face unattended) as within-subject factors. Critically, we predicted that emotion-laden semantic representations primed during the word completion task would bias information processing in the subsequent attention task.

Priming task

During the priming task, participants played a variant of the hangman game. This word completion task was used to prime implicitly
(a) Protocol

Neutral priming

Emotion priming

(c) Attention task

(d) Semantic priming predicts increased sensitivity to faces during the attention task

Semantic priming predicts increased sensitivity to faces during the attention task
semantic representations. Similar tasks requiring active retrieval of lexical information from a circumscribed semantic field have been previously used to induce unconscious biases in cognitive or behavioral performance according to the primed concepts (Aarts et al., 2008; Bargh et al., 2001). Each session comprised 80 trials, half consisting of real words from one given semantic field (either emotional or neutral), the other half consisting of readable pseudo-words (e.g., centranor, conomer, egalition, etc.). In each participant, two distinct semantic fields were induced in two successive sessions of this task. One session used emotionally arousing words with a broadly negative content (nightmare, terror, irritation, ferocity, depression, melancholy, etc.), as these have previously been shown to be effective in activating the amygdala (Lewis et al., 2007). The other session used neutral words related to the concept of calmness (concentration, confidence, patience, quietude, etc.). During the experiment, participants saw word or pseudo-word fragments, with two randomly chosen letters omitted, and had 4 s to indicate whether the incomplete stimulus was a real word or not, using a response pad placed in their right hand. Words and pseudo-words were selected from a wider set of stimuli, based on recognition performance measured in a pilot study. Their length was 7–11 letters and was matched between semantic fields. Selected words had less than 3 orthographic neighbors (www.lexique.org). Lexical frequencies did not differ between the two sets of words ($t_{xy} = -0.4, \ p > 0.05$). Intertrial intervals (ITI) were pseudo-randomly generated using a Poisson distribution with a mean of 3000 ms, lower and upper bounds of 2000 and 7000 ms, respectively. Faces or houses appeared equally often in the vertically or horizontally paired position. Half of the pairs were composed of identical pictures and the other half consisted of different pictures. Within a pair of faces, we always used the same emotional expression (neutral or fearful). We controlled for face identities, so that for a given subject, the actors used to express fear always differed from the actors used for neutral expressions. New pairs were created for each subject. All possible combinations of stimulus position, same/different identity for faces or houses, and facial expressions were counterbalanced across conditions and presented in random order. Each picture subtended 4.4° of visual angle vertically and 3.8° horizontally. We used black-and-white pictures of houses ($n = 32$) and faces ($n = 32$ actors with two expressions, NimStim MacBrain set, www.macbrain.org). We collected a total of four sessions comprising 64 trials each, for a total of 256 trials over the whole study. Total duration per session was 6 min 22 s.

Localizer task

At the end of the protocol, subjects also performed a standard localizer task to identify amygdala, FFA (Kanwisher et al., 1997) and PPA (Epstein et al., 1999) independently of the attention task. We used a 1-back task during blocked presentation of neutral faces, houses, and scrambled images. We scanned 24 blocks, each containing 11 pictures presented for 600 ms followed by a 500 ± 100 ms fixation. Subjects were required to push a button whenever a stimulus was presented twice in a row. The interblock interval was 3 s and blocks were presented in random order.

fMRI data acquisition

Gradient-echo $T_2^*$-weighted transverse echo-planar images (EPI) with BOLD contrast were acquired with a 3 T Magnetom TIM Trio scanner (Siemens, Erlangen, Germany). Participants used earplugs to attenuate scanner noise, and head movement was restricted by a vacuum pillow. Each volume contained 35 axial slices acquired in a sequential manner (TR/TE/flip angle = 2000 ms/30 ms/80°, FOV = 192 mm, resolution = 64 × 64, isotropic voxels size of (3 mm)$^3$, distance factor 20%). An automatic shimming procedure was performed to minimize inhomogeneities of the static magnetic field. At the beginning of each session, image acquisition started after the recording of three dummy volumes to avoid $T_1$ saturation effects. We collected a total of 1572 functional volumes for each subject (for the localizer, priming, and attention tasks), as well as a high-resolution $T_1$-weighted anatomical image (TR/TE/flip angle = 1900 ms/900 ms/2.32 ms/9°, FOV = 230 mm, resolution = 256 × 256, slice thickness = 0.9 mm, 192 sagittal slices). We administered the behavioral protocol using the Matlab toolbox Cogent (mathworks.com and vislab.ucl.ac.uk).

fMRI image processing

Image processing and statistical analyses were carried out using SPM2 (Wellcome Dept. of Cognitive Neurology, London, UK;.fil.ion.ucl.ac.uk/spm). Functional images were reoriented to the AC–PC line, spatially realigned to the first volume by rigid body transformation, corrected for time differences in slice acquisition using the middle slice in time as reference, spatially normalized to the standard Montreal Neurological Institute (MINI) EPI template to allow group analysis, resampled to an isotropic voxel size of 2 mm, and spatially smoothed with an isotropic 8 mm full-width at half-maximum (FWHM) Gaussian kernel (Friston et al., 1995).

fMRI whole-brain analysis

All results reported here focus on the attention task analyzed as a function of the preceding priming task. We performed standard
analyses using the general linear model (GLM) as implemented in SPM2, where event-related signal changes were modeled separately for each subject. For each block of the attention task, we specified a linear model including four event types according to whether a fearful face was attended (FA) or unattended (FU) and whether a neutral face was attended (NA) or unattended (NU). The vertical or horizontal orientations of the attended pair was not considered (Bentley et al., 2003; cf. Vuilleumier et al., 2001). Because accuracy was generally high (87%) and the number of errors did not differ between the two priming contexts ($t_{19} = 0.68, p = 0.502$), both correct and incorrect responses were included in the same regressors. For each condition, a covariate was calculated by convolving delta functions with a canonical hemodynamic response function (HRF). The length of each event encompassed the stimulation and the response period. Temporal derivatives of the realignment parameters were included to capture residual movement-related artifacts. A constant covariate represented the session-specific mean over scans. The model included a high-pass filter of 128 s to account for low-frequency noise of the scanner. Effects at each brain voxel were estimated using a least squares algorithm to produce condition-specific images of parameter estimates for each experimental condition. As the factor priming context was manipulated across sessions, this yielded a total of eight contrasts per subject, one for each cell of the factorial design. Similarly, for the localizer task, contrasts were estimated for each category of picture.

At the group level, we used a whole-brain analysis approach to determine the influence of the priming context on the attention task. Images of parameter estimates were entered in a random-effect ANOVA crossing the factors context (emotional, neutral), emotion expression of the face (threat, neutral), and attention condition (face attended, face unattended). In this way, the variance estimates at the group level incorporated appropriately weighted within-subject and between-subject variance effects. A non-sphericity correction was applied for variance differences across conditions.

Whole-brain statistical maps were corrected for multiple comparisons using standard Bonferroni whole-brain correction or small volume correction (Worsley et al., 1996) for a priori regions of interest such as the amygdala (FWE, $p < 0.05$). Parameter estimates extracted from ROI in the attention task were submitted to $2 \times 2 \times 2$ repeated measures ANOVAs in SPSS crossing the factors priming context (emotional, neutral), emotion expression of the face (threat, neutral), and attention condition (face attended, face unattended). In this way, the variance estimates at the group level incorporated appropriately weighted within-subject and between-subject variance effects. A non-sphericity correction was applied for variance differences across conditions.

**MRI ROI analysis**

To investigate interactions between context and attention or stimulus expression, the whole-brain approach was completed by an ROI analysis for a priori defined regions, namely the FFA, PPA, and amygdala (see Vuilleumier et al., 2001) that were determined by the independent localizer task. This additional ROI approach allowed us to confirm the robustness of priming effects using unbiased selection of activated clusters. We identified relevant clusters activated in the group-level analysis of the localizer (amygdala and FFA by contrasting faces > houses, PPA using the reverse contrast, $p < 0.05$, FWE corrected), and then examined the degree of activation (extracted beta values averaged across all voxels) evoked by each trial type in the attention task for each subject and each semantic context. The FFA and PPA ROI were bilateral (i.e., each ROI included the cluster from both hemispheres as all effects were generally symmetrical, e.g., see Vuilleumier et al., 2001). Because only the right amygdala responded to threatening faces in the whole-brain analysis of the attention task, we restricted our analysis to the right amygdala cluster defined by the localizer. For the PPA, as the resulting clusters encompassed other regions than the parahippocampal cortex proper, we confined this ROI to a 4-mm sphere centered on the clusters’ maximum peak of the parahippocampal gyrus.

**Psycho-physiological interactions (PPI) analysis**

To investigate the source of the context-dependent modulation of amygdala responses, we conducted a psycho-physiological interaction (PPI) analysis (Friston et al., 1997). This method estimates effective connectivity via changes in inter-regional covariance as a function of different experimental manipulations or tasks. First eigenvariate values were extracted for each participant from the filtered BOLD signal in the right amygdala ROI showing the main effect of threat versus neutral, independently of attention and priming context. These time series were adjusted to exclude effects of no interest (movement parameters) and mean corrected. PPI requires a psychological variable distributed within each session to estimate the critical interaction term. Because the factor context was distributed across-sessions in our study, we selected the factor emotion (threat > neutral) as a psychological factor, which interacted with the factor context (as shown in Fig. 2b). The time series were deconvolved to obtain an estimate of the neural response, multiplied by the psychological context of interest (i.e., threat versus neutral stimuli), and reconvolved using the canonical HRF to obtain a PPI regressor. For each subject, we set up a GLM that contained (for each of the four attention task sessions): the PPI regressor as well as eight other regressors of no interest, including the time series of the seed region (right amygdala), the psychological factor (threat versus neutral) convolved with the canonical HRF, and the six covariates modeling the temporal derivatives of realignment parameters. The model was then fitted to each brain voxel. Finally, at the group level, the contrast images of the PPI regressors (four different sessions) were compared across contexts using paired t-tests. This test revealed which brain regions showed significant changes in functional coupling with the amygdala due to the emotional or neutral context. We applied a liberal uncorrected threshold at 0.001.

**Results**

**Behavioral results**

Participants generally performed well in both the word completion task (mean ± SD = 88% ± 0.40 of items correctly classified; see Fig. 1b) and in the attention task (87 ± 0.05% of pairs correctly matched; see Fig. 1c). To determine whether the priming context influenced behavior during the subsequent attention experiment, we analyzed the mean recognition rates and response times (RT) in the latter task using repeated-measure ANOVA with the factors priming context (emotional, neutral), emotion expression of the face (threat, neutral) and attention condition (face attended, face unattended). For recognition rates, we used standard signal detection theory methods to compute a bias-free sensitivity index ($d’$) of performance (Green and Swets, 1966). This revealed a main effect of attention condition ($F_{1,19} = 41.5, p < 0.001$; see Fig. 1c), indicating that houses were generally better matched than faces. This effect was superseded by a context-by-attention interaction ($F_{1,19} = 5.1, p < 0.05$), driven by increased sensitivity to attended faces in the emotion priming context [mean $d’ = 2.36 ± 0.63$ versus $2.14 ± 0.65$ in the neutral context], together with decreased sensitivity to houses [mean $d’ = 2.95 ± 0.63$ versus $3.12 ± 0.65$ in emotion versus the neutral context, respectively]. This suggests that faces had a stronger impact in the emotion context and thus competed more when houses (rather than faces) had to be matched. RT were generally faster for houses than for faces [1034 ms ± 41 versus 1126 ms ± 44, $F_{1,19} = 23.6, p < 0.001$], but no other effect reached significance ($p’s > 0.05$).

Following behavioral work on semantic priming in similar paradigms (Aarts and Dijksterhuis, 2003), we assumed that the time taken to recognize real words in the letter-string task would reflect the ease of semantic access and hence indirectly the strength of activation of corresponding concepts. All subjects without exception recognized words more quickly than pseudo-words during the completion task (mean 1906 ms ± 150 versus 2641 ms ± 167, $F_{1,19} = 113.9, p < 0.001$;
For each subject, we therefore estimated a **semantic activation index** by subtracting the mean recognition speed of real words from the mean recognition-speed of pseudo-words within each context. Next we tried to relate this measure to the context-induced change in matching performance between houses and faces in the attention task (the context-by-attention interaction described above). The semantic index was negatively correlated with the difference between house and face matching performance (dprime) in the emotion context ($r_{\text{Spearman}} = -0.62, p = 0.004$, Fig. 1d), but not in the control context ($r = 0.11, p = 0.622$). This suggests that the effectiveness of semantic access observed in the priming task predicts how much subjects become sensitive to faces (and thus less efficient in house matching) in the emotion context specifically.

To ensure that the two priming conditions did not differ in terms of general difficulty, we also analyzed performance and RT in the priming task using repeated-measure ANOVA with the factors context (emotional, neutral) and lexical material (word, pseudo-word). Both contexts did not differ in terms of correct completion rates ($F_{1.19} = 0.03, p = 0.86$).

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**Fig. 2.** Effects of emotion priming on brain activation in the visual attention task. (a) Whole-brain group analysis ($n = 20$) showing increased activity in right dorsal amygdala for threatening faces as compared to neutral ones across all task conditions ($p < 0.05$ FWE corrected, rendered on axial section of the average T1-weighted template brain of the group). (b) Mean group activation estimates in all experimental conditions of the attention task are shown for the right amygdala ROI as defined by the independent localizer task (a similar pattern was observed for mean group activation estimates when using the cluster as defined in (a)). These data show selective increases in amygdala response to attended neutral faces after exposure to the emotional context (significant context-by-emotion interaction, $p < 0.05$; red dashed line for emotion context, blue solid line for neutral context. Error bars correspond to the SE of the difference between fear and neutral trials in each condition). (c) Main effect of emotion priming (relative to neutral priming) in right basal amygdala and (d) corresponding mean group activation estimates ($p < 0.05$ SVC corrected, error bars correspond to the SEM), showing an increased response to faces in the emotion context. Note that this is consistent with behavioral data indicating that faces compete more after priming by the emotional context. (e) Scatter plot showing that the magnitude of induced bias in right basal amygdala after emotion priming (as shown in (d)) was predicted by the effectiveness of semantic access (and hence indirectly the strength of activation of corresponding concepts).
3.54, \( p = 0.075 \)), and neither the main effect of lexical material nor the context-by-lexical interaction reached significance (\( p's > 0.24 \)). Analysis of RT showed that, as expected, words were recognized more quickly than pseudo-words (1906 ± 150 ms versus 2641 ± 167 ms, \( F_{1,19} = 113.9, p < 0.001 \)), but we observed no difference between contexts (\( p = 0.42 \)) and only marginal context-by-lexical interaction (\( p = 0.053 \)). Completion was not faster for emotional than for neutral words (\( T_{19} = 1.75, p = 0.095 \)). These results rule out the hypothesis that any priming effect observed in the attention task results from a difference in difficulty of the priming tasks.

Finally, we debriefed participants after the experiment to verify whether they were aware of a potential link between the priming manipulation and the attention task. When asked so, none of the participant suspected any kind of relation between the tasks. Additionally, when asked whether they had noticed something particular about the words in the priming task, 60% of them reported nothing particular and only 40% reported that some words in the priming task were emotion-laden, but even those subjects denied noticing any relation between the two tasks when asked explicitly. When further asked whether they had noticed the presence of a specific semantic relation between words in the priming task, 35% still answered no. Finally, after having explicitly told them that some words were emotional, 15% of subjects reported they had not noticed their presence. Taken together, these data confirm that no subject established a causal link between the two tasks, in agreement with previous behavioral work using similar priming procedure (Bargh et al., 2001) and therefore suggest that any modulation by the context cannot be attributed to explicit emotional regulation or reappraisal of the situation.

fMRI results

Effect of emotion and priming in the amygdala

Using the whole-brain approach, we first determined the main effect of threat in the visual attention task by comparing all fearful to all neutral faces, independently of context and attention. As expected (Bentley et al., 2003; Vuilleumier et al., 2001), significant threat-related activations were found in the right dorsal amygdala (\( xyz = 16 - 8 - 18, Z = 4.85, \text{FWE corrected}, \text{Fig. 2a–b} \)).

More importantly, we then tested for the main effect of context, independently of the focus of attention and face expression. Task performance after exposure to the emotion context (versus neutral, pooled across all conditions) was associated with increased activity in the right amygdala, but with a peak in a more basal portion as identified on the average \( T_1 \)-weighted template brain of the group (Fig. 2c–d, \( xyz = 26 - 6 - 32, Z = 3.39, p < 0.05 \) corrected for the volume of interest; see Methods and Table 1). This effect was accompanied by increased activity in right fusiform gyrus (\( xyz = 36 - 68 - 18, Z = 3.3, p < 0.0001 \) uncorrected), in an area slightly posterior to the FFA peak identified in the face localizer (\( xyz = 44 - 50 - 22 \)). On the other hand, exposure to the neutral context (versus emotion, pooled across all conditions) was associated with greater activity in parietal and frontal cortices, including bilateral angular gyrus (\( xyz = - 44 - 76 26 \) and \( xyz = 50 - 74 32, Z = 3.84 \) and 3.53, \( p < 0.0001 \) and \( p < 0.0001 \) uncorrected), precuneus (\( xyz = 8 - 62 24, Z = 4.98, p < 0.05 \text{ FWE} \)), and medial prefrontal cortex (\( xyz = 4 50 - 18, Z = 3.46, p < 0.0001 \) uncorrected; see Table 1 for full results), all areas known to be often activated during resting state conditions (Raichle et al., 2001).

The amplified amygdala response to faces in the emotional context suggests that priming emotional representations in the previous word completion task produced higher emotional reactivity and increased amygdala sensitivity to these stimuli. This is consistent with behavioral data indicating that faces compete after priming by the emotional context. This might also reflect a general increase in arousal, rather than an effect specific to fear, as the amygdala has been shown to respond to the intensity more than to the valence of emotion-laden words, scents, or tastes (Anderson et al., 2003; Lewis et al., 2007; Small et al., 2003). On the other hand, priming by non-emotional concepts may have the opposite effect and promote rest, as suggested by increased activations in parts of the resting state network.

To further examine the effects of semantic priming on amygdala activity, without any sampling bias due to the task itself (Kriegeskorte et al., 2009), we performed an region-of-interest (ROI) analysis using right amygdala voxels defined by an independent localizer task (contrast neutral faces > houses). Note that the cluster observed in the main effect of threat overlapped with the cluster defined in the face localizer. However, this cluster was located in a more dorsal part of the amygdala, with only partial overlap with the basal amygdala cluster observed in the main effect of context. A three-way repeated-measure ANOVA on activation parameters (average across voxels) from the right amygdala ROI during the visual attention task confirmed a main effect of emotion (\( F_{1,19} = 8.53, p = 0.009 \)) with higher response to threat than neutral stimuli (\( t_{19} = 2.92, p < 0.01 \)), as well as a main effect of attention (\( F_{1,19} = 8.21, p = 0.01 \)) with higher amygdala responses to attended than unattended faces (\( t_{19} = 2.86, p < 0.01 \)). Contrary to basal amygdala, the dorsal amygdala did not show a main effect of context (\( F_{1,19} = 0.079, p = 0.78 \)). Critically, however, we found a significant context-by-emotion interaction (\( F_{1,19} = 4.76, p = 0.05 \)), driven by a selective increase in amygdala response to neutral attended faces (see Fig. 2a, b), which became indistinguishable from amygdala responses to fearful attended faces in the emotion context (\( p > 0.53 \)), unlike what was observed in the neutral context (\( t_{19} = 2.93, p = 0.009 \)).

Table 1

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<tr>
<th>R/L</th>
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<th>MNI coordinates ( x ) ( y ) ( z )</th>
<th>( Z ) value</th>
<th>Size in voxels</th>
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</table>

\( p < 0.001 \), uncorrected except for * which survived FWE correction (\( p < 0.05 \)) and mxyz corrected for the volume of interest (\( p < 0.05 \)). Cluster extent threshold > 10 except for the three a priori ROI (AMG, FFA, PPA)
observed in the attention task when comparing the emotional context to the neutral context (see Fig. 2d). This analysis revealed a significant correlation between both measures ($r_{\text{Spearman}} = 0.483$, $p = 0.016$ one-tailed, Fig. 2e). This suggests that the effectiveness of semantic access observed in the priming task predicts how much the right basal amygdala responds to faces in the emotion context of the attention task. Finally, we also observed a marginal correlation ($r_{\text{Spearman}} = 0.329$, $p = 0.061$ one-tailed) when the same analysis was performed using the bias magnitude observed in dorsal amygdala for attended neutral faces (Fig. 2b), in the emotional context relative to the neutral context.

**Effect of priming in the visual cortex**

As described above, the whole-brain analysis showed that emotion context enhanced activity in right posterior fusiform gyrus with a peak just posterior to the FFA proper. Moreover, consistent with the attentional demands of the visual task (see Vuilleumier et al., 2001; Wojciulik et al., 1998), the whole-brain analysis also showed increased BOLD response in bilateral fusiform cortex when attention was focused on faces ($t_{\text{FWE}} = 29.04, p < 0.001$) with stronger responses when faces were attended relative to houses ($t_{\text{FWE}} = 5.47, p < 0.001$). Yet, contrary to the priming effect described earlier in right posterior fusiform gyrus, no significant main effect of context was observed in FFA proper. Instead, the effect of attention was superseded by a context-by-attention interaction ($F_{1,19} = 4.74, p = 0.05$; $F_{1,19} = 4.41, p = 0.05$; Fig. 3b), meaning that the attentional modulation within FFA proper was weaker after exposure to the emotion priming context. This is consistent with results by Egner et al. (2010) who reported that FFA responses to faces or houses become undistinguishable under high face expectancy. As developed later in the discussion, we propose that emotion priming could increase unconscious expectations of forthcoming emotional or social information. We did not detect any main effect of stimulus expression across context conditions ($p = 0.117$). No other main effect or interaction reached significance ($p's > 0.52$). Contrary to the FFA, attentional modulation in the PPA was unaffected by the priming manipulation (see Fig. 3c). Only the main effect of attention reached significance ($F = 197.57, p < 0.001$), with higher responses when houses were attended relative to faces ($t_{\text{FWE}} = 14.2, p < 0.001$). No other main effect or interaction reached significance ($p's > 0.09$).

**Effect of priming in orbitofrontal cortex (OFC) and amygdala connectivity**

Finally, we used functional connectivity (psycho-physiological interactions, PPI, see Methods) to investigate how priming context modulated the functional coupling between right amygdala and other voxels in the brain. Amygdala connectivity during responses to threat vs. neutral faces was estimated separately for each priming context, as the factor context was distributed across the different sessions (see Methods). To test whether the two different context conditions induced distinct connectivity patterns, we compared the two resulting PPI maps using a paired t-test. When contrasting the emotional context with the neutral context, we observed no increase in connectivity; but the reverse contrast (neutral > emotional) showed greater coupling of activity with the ipsilateral posterior part of the medial orbital sulcus ($xyz = 26 -32 -16, Z = 3.21$; see Fig. 4), a region highly interconnected with the amygdala. This effect was not significantly predicted by the semantic activation index. This result could not be explained by a general difference in the magnitude of BOLD activity between contexts, because the parameter estimates averaged over the OFC PPI peak did not differ ($p > 0.25$).

![Fig. 3. Effect of semantic priming in the visual cortex.](image-url)
(a) Emotion priming decreases connectivity between AMG & OFC

![Figure 4](image-url)

**Fig. 4.** PPI analysis showing how priming modifies connectivity between amygdala and OFC. Coupling of activity between the right amygdala and right OFC in response to threatening (versus neutral) faces was stronger during the neutral than the emotion context (sagittal section, p < .005 uncorrected for display purposes, ***p = 0.001).**

### Discussion

The present study investigated whether incidental exposure to negative emotion-laden semantic representations can bias emotion processing and modify attention control in a subsequent, unrelated, visual task. We found that prior exposure to negative words (relative to neutral words) led to subsequent increases in basal amygdala responses to both fearful and neutral faces, with the effect on faces being the strongest when presented in the focus of attention. Furthermore, this response bias was predicted by the efficiency of semantic access during the priming session (and hence indirectly the strength of activation of emotion concepts). The quickest the participants recognized the word in the priming task, the strongest the bias they showed in their amygdala response to faces. In addition, this enhanced responsiveness led to a diminished discrimination in amygdala between fearful and neutral pictures after emotional priming, relative to neutral priming. Finally, we also found that FFA modulation by attention was weaker after priming with emotional relative to neutral words and that connectivity between amygdala and orbitofrontal cortex was diminished, suggesting a reduced prefrontal inhibition on amygdala in the emotional context.

Our findings have several important implications: first, they demonstrate that priming-dependent shifts in amygdala functioning are not only caused by voluntary top-down control or modulated by task difficulty or perceptual load, as it has typically been assumed (Ochsner and Gross, 2005; Pessoa et al., 2002). We show that implicit biases in attention and emotional processing can also arise as a consequence of incidental priming by prior processing of information unrelated to the present situation. This is in sharp contrast with the perceptual priming produced by subliminal stimuli which produces effects that are hardly detectable beyond the second (Dehaene and Changeux, 2011; Kouider and Dehaene, 2007). The persistent effects we observed might be related to changes in preparatory brain states, which may be implemented independently of consciousness and voluntary control, but nonetheless have a strong impact on neural activity and behavior. It is known, for instance, that changes in brain states related to high level of state anxiety or chronic stress can provoke amygdala hyper-responsivity and alter the modulatory role played by prefrontal cortex (Bishop et al., 2004a; Correll et al., 2005). Here, however, brain state was manipulated using an incidental exposure to emotion-laden concepts presented during another, unrelated task.

Secondly, our findings show that such priming occurs without deliberate strategy, since the priming task was antecedent and irrelevant to the attention task. Interestingly, our results resemble the findings from Kim et al. (2004), who investigated how the presentation of immediate contextual information (e.g., the sentence “she/he won/lost $500”) could modify subsequent amygdala response to a surprised face. These authors found that negatively cued surprised faces produced greater ventral amygdala activations as compared with positively cued surprised faces. They also observed that the negative sentences increased right orbitofrontal cortex (BA 47) activity. These results are consistent with emotion regulation studies showing that cognitive re-interpretation of an emotional or neutral stimulus can, respectively, down-regulate or up-regulate amygdala responses to this stimulus (Ochsner et al., 2009; Ray et al., 2005). However, our results further suggest that similar biases can be induced without volitional control or deliberate strategies. Notably, all of our participants considered the two tasks as independent, and some even failed to notice any emotional meaning of words in the priming task.

These results indicate that the pattern of emotional responses in amygdala and other regions can be implicitly modulated by incidental task contexts. One possible mechanism for this could be that the prior priming procedure could sensitize emotion processing by changing response thresholds of the amygdala and/or by increasing the recruitment of affective associations in response to novel stimuli. Although we can only speculate about this, these effects seem consistent with previous behavioral work suggesting that implicit conceptual priming procedures might activate particular representations which can then facilitate subsequent responses compatible with these representations and/or promote their access by attentional systems (Aarts et al., 2008; Bargh, 2005; Bargh et al., 2001; Custers and Aarts, 2010; Dijksterhuis and Aarts, 2010). We note however that we found no changes in lateral prefrontal or parietal areas typically associated with semantic or attentional functions.

It is intuitively accepted that complex mental states such as emotions can have lingering effects on brain activity that influence the processing of subsequent information through perceptual or memory biases (Dolan, 2002; see also Eryilmaz et al., 2011). Here, we demonstrate that prior exposure to emotion-laden representations can increase amygdala sensitivity to faces, while at the same time decreasing its selectivity for threat-related faces (see Fig. 2). Remarkably, van Marle et al. (2009) reported a similar increase and reduced differentiation in amygdala responses after acute stress induction: activation by emotional faces was drastically increased, but less discriminative across emotional expressions (i.e., becoming similar to fearful and happy faces, unlike prior to stress induction). Our results are also consistent with the observation that exposure to anxiogenic contexts produce exaggerated responses of the amygdala to negative pictures (Somerville et al., 2012). We speculate that such sensitization may at least be partly similar to observations in rodents showing increased sensitivity of amygdala to emotionally arousing stimuli after prolonged exposure to chronic stress or pain (Correll et al., 2005; Neugebauer and Li, 2003), as well as with stress-related disorders in humans such as PTSD (Hendler et al., 2003; Rauch et al., 1996; Shin et al., 2005) or anxiety (Bishop et al., 2007; Etkin and Wager, 2007). Unsafe environments, where subjects expect to receive electrical shocks, increase amygdala responses to task-irrelevant fearful faces, even during high attentional load and without receiving any electric shocks (Cornwell et al., 2011). These emotional biases arise implicitly when anticipating threatening situations. Taken together, these data therefore suggest that exposure to emotion-laden material may lead to increased sensitization through enhanced affective associations mediated by the amygdala and, as a by-product, results in overgeneralization of fear responses (van Marle et al., 2009). Critically, however, our findings go beyond these ideas by showing that emotion representations influencing amygdala responses are not limited to sensory features (LeDoux, 2000) or neurohormonal factors (van Marle et al., 2009) but encompass more abstract semantic associations that are presumably held in high-level cortical networks. These effects may also explain why some emotional biases in perception are modulated by selective attention to semantic meaning of visual stimuli (Huang et al., 2008).
We also note that this general sensitization to faces observed in right basal amygdala after exposure to emotion concepts is consistent with the context-by-attention interaction observed in behavioral results during the visual matching task. After emotion priming, we observed a slight improvement in face matching but a slight decline in house matching. This pattern suggests that faces had a stronger impact in the emotion context and thus competed more for attention when they had to be ignored and houses had to be matched instead. Although we did not observe a global change in sensitivity in FFA proper, emotion priming enhanced visual responses in the right fusiform gyrus, just posterior to the FFA proper (see Table 1). This enhancement of attention-independent responses to faces in fusiform may possibly explain the context-related effect on behavioral performance during the visual matching task (see Fig. 1c). It is well established that the perception of emotional information enhances visual processing (Pourtois et al., 2010; Sabatinelli et al., 2009; Vuilleumier et al., 2001). This effect is under a direct influence of the amygdala (Vuilleumier et al., 2004), which sends projections to all cortical stages of the visual stream (Amaral et al., 2003). Here we suggest that a persistent sensitization in both amygdala and visual responses may reflect changes in preparatory brain states induced by the preceding priming manipulation. Likewise, increases in visual processing may occur following emotional arousal due to acute stress (van Marle et al., 2009) or in mood disorders such as social anxiety and specific phobias (Etkin and Wager, 2007; Sabatinelli et al., 2005).

Contrary to predictions, we found no increase of activity in FFA proper following exposure to emotion concepts. Instead, we found that the effect of attention in FFA proper was weaker after emotion priming (or conversely, stronger after neutral priming; see Fig. 3b). Although this effect is modest, a possible explanation could be that, rather than increasing voluntary attention, emotion concepts might boost expectation of forthcoming emotional information. Unlike attention which prioritizes stimuli processing on the basis of task relevance, expectations constrain visual interpretation on the basis of what is likely to occur (Summerfield and Egner, 2009). Both mechanisms often coincide but can have different neural consequences: expectation decreases neural processing (Egner et al., 2010) whereas attention has the opposite effect (Maunsell and Treue, 2006). Thus, Egner et al. (2010) recently reported that FFA responses to faces or houses became indistinguishable under high face expectancy. In the same way, responses to attended faces may become less distinguishable under high emotion expectancy.

This pattern in FFA proper also indicates that increased amygdala responses in the emotion context are not a direct consequence of enhanced voluntary attention leading to differential visual processing. Instead, the amygdala showed increased activity independently of attention effects on visual cortex. Nonetheless, the amygdala also showed greater over-generalization to non-emotional (neutral) faces when these were attended and task-relevant. This effect may reflect the fact that primed representations were more strongly or easily activated by the current task-relevant (i.e., attended) faces (Dijksterhuis and Aarts, 2010), but less recruited when faces were unattended. An alternative explanation might also concern the role of the amygdala in processing ambiguity (Kim et al., 2004; Whalen, 1998). Previous exposure to emotional concepts may lead to treat neutral attended faces as more ambiguous than emotional attended faces and therefore explain why amygdala response to attended neutral faces is most impacted by context manipulation.

Conversely, we found that regions known to activate during awake resting state showed decreased activity after priming with emotional words. Our finding is in line with studies that show that transient emotional episodes reduce subsequent activity in regions of the “default network” (Eryilmaz et al., 2011; Pitroda et al., 2008). The so-called “default network” (Greicius et al., 2003; Raichle et al., 2001) is thought to reflect intrinsic brain activity (Raichle, 2010) and possibly introspective processes such as mind-wandering (Mason et al., 2007) or social cognition (Amodio and Frith, 2006). Intriguingly, comparable results (Jang et al., 2011) have shown that practice of self-focused meditation techniques (increasingly used in the medical management of stress and psychiatric disorders) enhances functional connectivity between the default mode network and the ventromedial prefrontal cortex, close to the peak observed after priming with neutral words (xyz = 3 39–21 and present coordinates xyz = 4 50–18).

Importantly, the present PPI analysis suggests that primed emotional concepts could operate through changes in functional connectivity between amygdala and posterior OFC in the form of a selective reduction during the visual attention task following the emotion priming task. Posterior regions in OFC are in a key position to regulate emotion pathways, as they entertain, together with anterior cingulate cortex, strong connections with amygdala, hypothalamus, and peri-acueductal gray (An et al., 1998; Barbas et al., 2003; Carmichael and Price, 1995; Ongur et al., 1998). Monkey posterior OFC hosts a high-density inhibitory GABAergic (calbindin-containing) interneurons that surround projection neurons directed to the amygdala (Ghashghaei et al., 2006). These interneurons have been associated with focusing attention on relevant features and suppressing distracting stimuli (Wang et al., 2004). Moreover, OFC has direct reciprocal connections predominantly with the basal amygdala (Carmichael and Price, 1995), possibly corresponding to the basal amygdala activation by emotion context in our study (Fig. 2c, d). Interestingly, connections between OFC and basolateral amygdala are thought to be involved in context dependent modulation of amygdala responsiveness (Barbas et al., 2010; Schoenbaum et al., 2003), a function that would accord with the selective influence of priming context in our study. A possible interpretation of our result could be that the functional coupling between the amygdala and posterior OFC is disrupted following exposure to the emotional context. Reduced prefrontal inhibition could explain the global heightened sensitivity of amygdala to facial stimuli and the diminished capacity to discriminate between fearful and non-fearful attended stimuli.

To conclude, the present findings show that priming by negative emotion-laden concepts can alter emotion processing in the amygdala during a subsequent task by sensitizing its responses to socially relevant or ambiguous information. Nevertheless, this sensitization may also lead to a loss in functional selectivity for threat signals. These results add to the emerging notion that some degree of emotion (dis)regulation operate at little cost and automatically (such as those learned through cultural norms) may involve implicit processes that can be primed by appropriate procedures without explicit awareness or deliberate strategy (Mauss et al., 2007; Schweiger Gallo and Gollwitzer, 2007; Williams et al., 2009). Automatic (dis)regulation processes are thought to be effective because they are supposedly antecedent to the emotional response (Mauss et al., 2007). Hence, not all forms of emotion regulation require effortful cognitive control (Ochsner and Gross, 2005). These findings also call for a refinement of theories on (un)consciousness in order to better account for the existence of involuntary and long-lasting sources of implicit biases induced by conceptual priming. More generally, these results contribute to a better understanding of how emotional states sensitize or desensitize specific neural circuits in the long term, as it is observed after a stressful experience or prolonged exposure to violent media (Kelly et al., 2007; Strenziok et al., 2011; van Marle et al., 2009). Finally these findings have practical implications regarding the potential confounding effects of incidental task manipulations prior to an experiment. Indeed, they may activate covert representations and induce significant biases in patterns of neural responses to emotional and/or neutral information, reflecting a complex interaction between controlled experimental factors and other neglected environmental variables and unconscious expectations of the participants.