Modulation of amygdala response to task-irrelevant emotion

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Abstract

It has been shown that as cognitive demands of a non-emotional task increase, amygdala response to task-irrelevant emotional stimuli is reduced. However, it remains unclear whether effects are due to altered task demands, or altered perceptual input associated with task demands. Here, we present fMRI data from 20 adult males during a novel cognitive conflict task in which the requirement to scan emotional information was necessary for task performance and held constant across levels of cognitive conflict. Response to fearful facial expressions was attenuated under high (*vs* low) conflict conditions, as indexed by both slower reaction times and reduced right amygdala response. Psychophysiological interaction analysis showed that increased amygdala response to fear in the low conflict condition was accompanied by increased functional coupling with middle frontal gyrus, a prefrontal region previously associated with emotion regulation during cognitive task performance. These data suggest that amygdala response to emotion is modulated as a function of task demands, even when perceptual inputs are closely matched across load conditions. PPI data also show that, in particular emotional contexts, increased functional coupling of amygdala with prefrontal cortex can paradoxically occur when executive demands are lower.

Key words: amygdala; prefrontal cortex; fear; emotion–cognition interactions; fMRI

Introduction

It is now generally accepted that automatic exogenous attention to emotional information interferes with concurrent task performance and activates key neural structures including the amygdala (e.g. see Carretié, 2014 for a review). However, the conditions under which exogenous attention is allocated to emotional stimuli, and under which amygdala activation is elicited, remain a matter of debate. Attentional load theory (Lavie, 1995) suggests that as task demands (i.e. difficulty) increase, there is reduced capacity for processing extraneous cues, because processing resources are occupied by the primary task. This principle also applies to situations in which the extraneous

cue is affective in nature (e.g. Erthal *et al.*, 2005; Junhong *et al.*, 2013).

Several studies have shown that amygdala response to task-irrelevant emotional cues are likewise modulated by task demands (e.g. Pessoa *et al.*, 2002, 2005; Bishop *et al.*, 2007; Mitchell *et al.*, 2007). The majority of these studies have used concurrent but distinct target-distractor paradigms, in which task-relevant targets and task-irrelevant emotional distractors appear simultaneously but are spatially segregated and comprise physically distinct objects or features. For example, in one of the first studies to investigate this effect, Pessoa *et al.* (2002) instructed participants to fixate on centrally-presented faces of varying

emotional valence. On 'attended' trials, participants judged the gender of the face, while on 'unattended trials', they judged the orientation of peripherally-presented bars. Amygdala response was reduced on the unattended trials relative to attended trials, despite central fixation, suggesting that amygdala does not always respond automatically to emotionally salient stimuli. More specifically, amygdala response appeared to depend on the availability of attentional resources in line with biased competition models (Desimone and Duncan, 1995). Further characterization of the effect has shown that amygdala response can be parametrically modulated by task difficulty (Pessoa *et al*., 2005), and with the visual focus of attention (Bishop *et al*., 2004). For example, this latter study found reduced amygdala response when participants focused on a house-matching task relative to a face-matching task in an array containing both stimulus types, although this modulation was seen only in participants with low anxiety.

Studies have also looked at whether manipulating the focus of attention modulates amygdala response even when emotional and neutral stimuli are not spatially segregated, but are still forced to compete for attentional resources. Alpers (2009) used superimposed pictures of birds and spiders and found that these mixed displays activated the amygdala in spider-phobic participants, only when attention was focused on the spider and not the bird. This again suggests that attentional focus may play a key role in modulating amygdala response, with increased amygdala response only seen when sufficient attentional resources are allocated to the emotion-inducing stimulus. However, Anderson *et al*. (2003) used images of faces superimposed upon buildings and found no increase in amygdala response to fearful faces when attention was directed to faces (gender decision) compared to buildings (location decision). One possible explanation for this discrepant result is that task demands did not sufficiently modulate attentional capacity. Bishop *et al*. (2007) used letter strings superimposed on fearful faces and manipulated task difficulty by varying perceptual load [search for an X or N among an array of only Xs and Ns (low perceptual load) or among an array of several non-target letters of different identities (high perceptual load)]. Right amygdala showed increased response to fear on low load trials relative to high load trials. Similar results have been seen when varying task cognitive load. Mitchell *et al*. (2007) used words superimposed upon faces of varying valence. Participants either made a gender decision (lowest cognitive load; attention paid to the face), or judged the words based on case (mid cognitive load) or syllable number (high cognitive load). Modulation of right amygdala response was seen, with increased response to fearful faces for gender decision relative to case and syllable judgments.

Amygdala modulation is also seen when task-relevant non-emotional and task-irrelevant emotional stimuli are temporally segregated within the same central focus. For example, Blair *et al*. (2007) used IAPS pictures sequentially interleaved with a numerical Stroop task, and found a greater bilateral amygdala response to negative stimuli on congruent (low load) Stroop trials compared with incongruent (high load) Stroop trials; while Kellermann *et al*. (2012) found reduced bilateral amygdala response to IAPS pictures presented sequentially within a high load working memory task compared with a low load control condition.

Taken together, these studies support the view that amygdala response to task-irrelevant emotion is susceptible to modulation depending on the attentional and cognitive demands, with reduced amygdala response typically seen when task demands are increased. This finding is important, as it demonstrates that emotional (and particularly fear-related) stimuli do not have universally privileged access to processing resources. However, it remains possible that this effect is driven by the processing of altered perceptual inputs rather than by variation in cognitive load. To date these factors have been confounded in all prior studies. In other words, all previous paradigms have had some degree of separation between task-relevant stimuli and emotional distractors. Even where the task stimuli are superimposed on emotional stimuli (e.g. Bishop *et al*., 2007; Mitchell *et al*., 2007), the task stimuli (e.g. letters) are distinct from the emotional stimuli (e.g. face) and require a separate focus of attention. It is, therefore, possible that amygdala modulation arises not only from changing task demands but also from altered perceptual input associated with those task demands. In order to determine whether amygdala modulation occurs as a direct result of varying levels of task difficulty, it is necessary to ensure that the perceptual inputs remain constant.

In the present study, we investigated whether reduced interference by emotion under high (*vs* low) cognitive load (conflict) occurs using a paradigm where perceptual inputs were matched across conditions. Using a novel cognitive conflict task where the requirement to scan emotional information was both necessary and held constant, we were able to assess whether the level of emotional responding varied across high and low levels of cognitive conflict as indexed by RTs and neural response. We manipulated cognitive conflict using the Simon effect of spatial compatibility (Simon and Wolf, 1963). On each trial, participants viewed a pair of faces appearing on the left and the right side of the screen simultaneously, one male and one female. They were asked to find the face of a target gender (e.g. the male face), and decide if it was tilted to the left or right. In compatible trials, the target face was located on the same side to which it was tilted (e.g. on the left and tilting left); while on incompatible trials the target face was on the opposite side (e.g. on the right and tilting left). Importantly, participants needed to scan the facial stimuli to the same extent on both compatible and incompatible trials, in order to identify the face of the target gender. This ensured that the perception of task-irrelevant emotional information contained in the face was matched across conditions.

Emotional processing was manipulated by presenting faces displaying fearful, angry and calm (neutral) expressions, as well as a scrambled face condition as a low level perceptual control to ensure participants were processing the faces as intended. Our primary hypothesis related to the contrast between fearful and calm faces, since the amygdala is particularly responsive to facial displays of fear (e.g. Fusar-Poli *et al*., 2009) and the majority of studies discussed above have found a modulatory effect for fear (although see Anderson *et al*., 2003). However, since threat more generally is also associated with amygdala response (Hoffman *et al*., 2007), we also investigated whether similar effects would be obtained for anger *vs* calm.

We had two main predictions. First, that emotion would cause greater interference (as measured by RTs) in the low *vs* high cognitive demand conditions. Second, that emotion would be associated with increased amygdala response in the low versus high cognitive demand conditions, even when perceptual inputs were matched. As discussed above, in the light of previous findings, we expected that the strongest modulation effects would be observed for the fear *vs* calm contrast. In addition, we wished to explore the pattern of functional connectivity with the amygdala using psychophysiological interaction (PPI)

analysis, particularly focusing on the role of prefrontal cortex (PFC) regions previously implicated in the implicit regulation of emotional conflict including medial and dorsolateral PFC and anterior cingulate cortex (Gyurak *et al.*, 2011). Specifically, we were interested to explore whether any increased amygdala response to emotion in low cognitive demand conditions would be associated with increased functional coupling with prefrontal regulatory regions (suggesting a need to regulate processed emotion) or decreased coupling (suggesting reduced regulatory efficacy). As this analysis was exploratory, we did not make a directional prediction.

Methods

Participants

Twenty-two healthy right-handed adult males with no history of mental illness or contraindications for fMRI took part in the study. Two were excluded: one due to excessive error/missed trial rates and outlier mean RTs on the experimental task, and one due to an incidental MRI finding. Data from a final sample of 20 participants (mean age 30.25, SD = 4.31, range = 25–40) were analyzed. All participants provided written informed consent and were compensated at the institution's standard rate of £10 per hour. The study was approved by the local ethics committee.

Experimental task

Task: On each trial participants viewed one male and one female face presented simultaneously (Figure 1), and were asked to find the face corresponding to a target gender (e.g. the male face). Faces were tilted either to the left or to the right, and participants were instructed to make a key press with their right index finger if the face was tilted to the left, and with their middle finger if it was tilted to the right, i.e. the response key was spatially compatible with the direction of the tilt. On compatible trials, the target face was located on the same side to which it was tilted (e.g. on the left and tilting left); while on incompatible trials the target face was on the opposite side (e.g. on the right and tilting left). This set up a spatial incompatibility between the required response and its location.

Stimuli: Stimuli consisted of two male and two female identities each with four different facial expressions: fear, anger, calm and scrambled. A scrambled face condition was included as a low-level control to ensure participants were activating typical face processing regions (see Table S1). The three expressions were chosen from the standardized NimStim face set (Tottenham *et al.*, 2009). Several measures were taken to ensure that participants would need to scan the emotion-conveying regions of the face in order to make the gender decision required as part of cognitive task performance. An identical oval cut-out was placed on each face to remove obvious gender-specific information, such as hair. Additionally, a greyscale filter was applied, since this has been shown to reduce participants' ability to identify facial gender based on isolated cues such as lip color (Dupuis-Roy *et al.*, 2009). Participants must, therefore, rely on relational distance cues (Burton *et al.*, 1993) and luminance information in the eye-region (Dupuis-Roy *et al.*, 2009) for gender discrimination. Importantly, the eye-region is also important in the identification of fear (Adolphs *et al.*, 2005) and anger (Smith *et al.*, 2005). Scrambled face stimuli were created by phase scrambling calm face images (Sadr and Sinha, 2004), producing images with luminance and spatial frequency
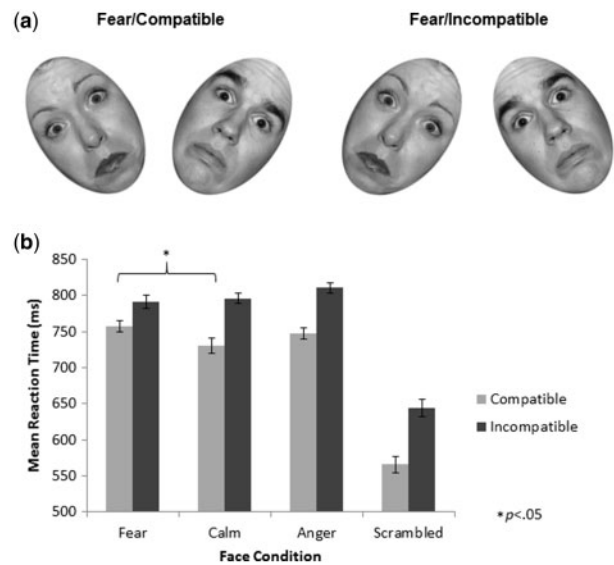

Fig. 1. (a) Example of the experimental task stimuli. Each stimulus consisted of two faces: one male and one female. Participants were instructed to identify the face of the target gender (counterbalanced across participants) and indicate with a left/right button press (index/middle finger respectively) whether it was tilted to the left or right. The location of the target face set up response conflict on 50% of trials, i.e. where the target face was located on the right but tilting left, or vice versa. Emotion shown: fear. Facial identities are those for which permission is given to publish, and differed from the identities used in the study. (b) Mean reaction times (RTs) showing an interaction between Compatibility and Face conditions. RTs were significantly slower on fear/compatible trials compared to calm/compatible, but did not differ between fear, anger and calm conditions on incompatible trials. RTs were significantly faster for scrambled than non-scrambled faces for both compatible and incompatible conditions. Within-subject error bars are shown.

comparable with the original face (Ishai, Schmidt, & Boesiger, 2005). Participants indicated the 'gender' of the phase scrambled images based on a small pink or blue cross presented in the middle of each oval.

All faces were rotated along the vertical axis by 35° to the left or right. Paired images of male and female faces with the identical expression were created, half with the female face on the left and half with the female face on the right (Figure 1). These images were paired such that there were eight possible paired images (each male with each female) for each expression at each level of task difficulty (stimulus-response compatibility), i.e. 64 images in total. Each stimulus array of two faces on a white background measured 606 × 349 pixels and each face oval measured 6×4cm.

Task design and procedure: The 64 stimuli were presented in eight blocks of eight stimuli, one block for each Compatibility (compatible, incompatible) × Face (fear, anger, calm, scrambled) condition. These eight blocks were presented three times, in a different pseudorandom order each time (192 trials), and participants completed two task runs (384 trials in total). Block randomization was constrained to ensure that the there was a tolerance of up to only two back-to back repetitions for both compatibility (incompatible, compatible) and emotion (fear, anger, happy, scrambled) conditions. The same compatibility/emotion condition was never repeated back-to-back. Within each block, stimuli were pseudorandomized such that participants would never see all four 'left response' stimuli followed by all four 'right response' stimuli, in order to prevent the possibility of a fully predictable series of responses in the second half of a block. Each trial consisted of stimulus presentation for 2000

ms, followed by a fixation cross ISI presented for 500ms. Each block length was, therefore, 20 s (2500 ms × 8) in duration. A short break screen was presented after every 4 blocks, consisting of a fixation cross displayed for 15s. Participants completed the task in the MRI scanner using left/right button box responses and viewed stimuli via a projector system and mirror mounted on the head coil. Prior to scanning, participants completed a short practice task using calm faces of identities not seen in the main experiment, until >80% accuracy was attained.

MRI acquisition

A Siemens Avanto 1.5T MRI scanner with a 32-channel head coil was used to acquire a 5.5 min 3D T1-weighted structural scan, and two runs of 199 multislice T2*-weighted echo planar volumes with BOLD contrast (∼10 min per run). The EPI sequence was designed to optimize signal detection and reduce dropout in OFC and amygdala (Weiskopf *et al.*, 2006), and used the following acquisition parameters: 35 2mm slices acquired in an ascending trajectory with a 1 mm gap, $TE = 50$ ms; $TR = 2975$ ms; slice tilt $= -30°$ (T > C); flip angle $= 90°$; field of view $= 192$ mm; matrix size $= 64×64$.

Analysis

Behavioral data were analyzed using repeated measures ANOVAs on mean correct reaction times (RT) and percentage error data averaged across runs, after removing missed trials and extreme individual RTs (<200 or >1500 ms).

Imaging data were analyzed using SPM8 (www.fil.ion.ucl.ac.uk/spm). Pre-processing followed a standard sequence: the first five volumes were discarded; data were realigned; normalized via segmentation of the T1 scan with a voxel size of 2×2×2mm; and smoothed with an 8 mm Gaussian filter. Eight regressors of interest were modeled with block duration 20 s, corresponding to each of the Compatibility (compatible, incompatible) × Face (fear, anger, calm, scrambled) conditions. An additional regressor modeled baseline fixation with block duration 15 s. These nine regressors were modeled as boxcar functions convolved with a canonical hemodynamic response function. The six realignment parameters were modeled as effects of no interest. Images showing between-scan motion of >1 mm or 1° were individually inspected for distortion. For two participants, extra regressors were included to model a small number (one and five respectively, of 398 total) of corrupted images resulting from excessive motion. These images were removed and the adjacent images interpolated to prevent distortion of the between-subjects mask. Data were high-pass filtered at 128 s to remove low-frequency drifts.

At the first level, main effects of each factor (Compatibility and Face) were computed. To increase specificity in interpreting interactions between these factors, two separate interaction contrasts were calculated for fear *vs* calm and anger *vs* calm at each level of Compatibility. Interactions involving fear *vs* anger and face *vs* scrambled conditions were not conducted, as we had no specific hypotheses regarding these interactions. Contrasts were then taken up to second-level analysis as one-sample *t*-tests across the whole group.

For whole brain analyses, main effects were thresholded at $P < 0.05$ FWE-corrected at the cluster level, after initial thresholding at $P < 0.001$, uncorrected. Interaction contrasts were thresholded at $P < 0.005$, uncorrected, $k ≥ 20$, to avoid Type II error caused by reduced power in these interaction analyses (Lieberman and Cunningham, 2009). Therefore, results are

reported as exploratory, except for results in amygdala surviving small volume correction (SVC) as an a priori region of interest (ROI). ROI analyses in this region were conducted bilaterally using 10 mm radius spheres centered on anatomically defined central amygdala co-ordinates used in a previous study contrasting fearful and calm faces (Phillips *et al.*, 2001) (±20 −8 −16, after conversion from co-ordinates reported in Talairach space (±20 −8 −13)).

Psychophysiological interactions were conducted to explore differences in functional coupling between the amygdala ROI and the rest of the brain during different task conditions. Decisions regarding the specific amygdala seed and psychological contrast of interest were taken following initial second-level analyses; therefore, further information on the PPI analysis are given below.

Results

Behavioral data

Reaction times: A Compatibility (compatible, incompatible) × Face (fear, anger, calm, scrambled) repeated measures ANOVA on mean RT data showed a main effect of Compatibility: $F(1,19) = 70.73$, $P < 0.001$, with RTs significantly faster on compatible ($M = 700$ ms) than incompatible trials ($M = 761$ ms); and a main effect of Face: $F(3,57) = 119.72$, $P < 0.001$. This was driven by significantly faster RTs for scrambled faces ($M = 605$ ms) compared with fear, anger and calm ($Ms = 774$, 779 and 763ms, respectively, all $Ps < 0.001$), as well as significantly faster RTs for the calm condition relative to anger ($P = 0.034$). There was also a significant interaction between Compatibility and Face: $F(3,57) = 3.42$, $P = 0.023$ (Figure 1b). While the difference between incompatible and compatible conditions was significant for all Face conditions, it was significantly smaller for fear than for anger ($P = 0.027$) and scrambled ($P = 0.002$) conditions, and was marginally smaller than for calm ($P = 0.079$). In contrast, calm, anger and scrambled conditions did not differ in terms of the RT difference between Compatibility levels ($Ps > 0.23$). Simple effects tests showed that this reduced difference effect for fear appeared to be driven by disproportionately slow RTs on the compatible condition. While there were no significant differences between RTs on fear, anger and calm conditions during the incompatible blocks, RTs were significantly slower on fear trials ($M = 757$ ms) than on calm trials ($M = 730$ ms) on compatible blocks ($P = 0.009$). This effect (RT interference relative to the calm condition on compatible trials only) was not seen in mean RTs for the anger condition, with no differences between anger and calm found for either compatible ($P = 0.18$) or incompatible ($P = 0.17$) trials.

Error rates: A Compatibility × Face-repeated measures ANOVA conducted on mean percentage error data showed a main effect of Compatibility: $F(1,19) = 9.43$, $P = 0.006$, with more errors on incompatible ($M = 1.56\%$) than compatible ($M = 0.42\%$) trials. There was no main effect of Face, or Compatibility × Face interaction ($Ps > 0.11$).

Missed trials: There were very few missed trials, totaling less than 1% of trials for each of the eight conditions.

fMRI data

We focused our fMRI analyses on the contrasts involving fear and calm stimuli, with main effects of task (Incompatible > Compatible and Face > Scrambled), and analyses contrasting anger *vs* calm reported fully in the supplementary materials (Tables S1 and S2).

Table 1. Contrasts involving Fear and Calm conditions

Brain region	BA	L/R	Peak voxel			k	t	z
Fear>Calm								
Inferior frontal gyrus	9	L	−62	6	28	32	4.58	3.72
Superior frontal gyrus	8	L	−14	50	44	47	3.77	3.22
	9	L	−6	56	42		3.68	3.16
Superior frontal gyrus	9	R	14	58	38	27	3.61	3.11
Calm>Fear								
Caudate	–	L	−8	24	4	20	4.06	3.40
Cerebellum, anterior lobe	–	R	8	−26	−20	27	3.61	3.11
(Fear/Compatible > Calm/Compatible) > (Fear/Incompatible > Calm/Incompatible)								
Amygdala	–	R	22	−2	−22	33	4.01	3.37
Superior temporal gyrus	38	R	46	4	−14	35	3.95	3.33
(Fear/Incompatible>Calm/Incompatible) > (Fear/Compatible > Calm/Compatible)								
Subgenual anterior cingulate cortex	25	R	10	18	−8	22	3.74	3.20
Anterior cingulate cortex	32	L	−10	24	38	25	3.53	3.06

BA, putative Brodmann area; Peak Voxel, peak voxel in MNI space; k, cluster size at $P<0.005$, $k \geq 20$, uncorrected. Overall main effects of Face and Compatibility, as well as contrasts involving Anger and Calm, are displayed in Table S1.

This focus was partly driven by the prior literature discussed above which has largely used fear-related stimuli relative to calm or neutral stimuli, and partly because our behavioral effect of interest (interaction between Compatibility and Face) was seen to be driven most strongly by the difference between fear and calm RTs.

Fear vs Calm: Results are displayed in Table 1. Across both compatible and incompatible trials, a greater response to fear than calm faces was seen in left dorsolateral and bilateral dorsomedial PFC, while a greater response to calm than fear was seen in left caudate and right cerebellum. Several regions showed a significant interaction between Compatibility and Face for fear *vs* calm conditions. We first looked at the direction '(fear/compatible > calm/compatible) > (fear/incompatible > calm/incompatible)', i.e. looking for regions where there is a greater effect on brain activity in the fear/compatible condition compared to fear/incompatible (relative to the equivalent calm conditions). This contrast looks for results in the same direction as the behavioral effect, where interference by fear was greater on compatible than on incompatible trials. Activations were seen in right amygdala and superior temporal gyrus. The cluster in the amygdala survived small volume correction: peak $= 22$ $−2$ $−22$, $k = 16$, $t = 4.01$, $z = 3.37$, FWE-SVC, $P = 0.033$). Inspection of the mean contrast estimates across the cluster (extracted with Marsbar; Brett *et al.*, 2002) showed that this effect was driven by significantly greater amygdala response on fear/compatible than fear/incompatible blocks, but no difference between calm/compatible and calm/incompatible blocks (see Figure 2). For the interaction in the reverse direction, i.e. greater response to fear/incompatible than fear/compatible relative to equivalent calm conditions, responses were seen in right subgenual cingulate cortex and left dorsal anterior cingulate cortex.

Psychophysiological interactions: To understand the connectivity profile of the right amygdala during activation on fear/compatible relative to fear/incompatible trials (relative to calm conditions), a psychophysiological interaction (PPI) analysis was performed using the right amygdala as a seed region. For each participant, neural response across the time course was extracted from a volume of interest defined as an 8 mm radius sphere around the peak amygdala co-ordinate from the above interaction analysis (22 $−2$ $−22$), corrected for effects of interest. This activity comprised the physiological variable, while the contrast (fear/compatible > calm/compatible) > ('fear/

incompatible'> calm/incompatible) comprised the psychological variable. The interaction between these factors (controlling for main effects of each) shows regions for which functional coupling with the amygdala varied across conditions. In order to constrain our analysis to regions of greatest theoretical interest, results were then masked by a similar PPI analysis run with the same seed region but taking the 'fear/compatible *vs* fear/incompatible' simple effect as the psychological variable of interest. This allowed us to interrogate regions in which connectivity with the amygdala showed an interaction effect in the relevant direction, i.e. (fear/compatible > calm/compatible)> (fear/incompatible> calm/incompatible), *and* in which connectivity was driven by the simple effect of greatest interest, i.e. 'fear/compatible > fear/incompatible', as opposed to being driven by the calm conditions. Using an exploratory threshold of $P < 0.005$, $k \geq 20$, this analysis yielded activation in a single cluster in middle frontal gyrus, BA 10 (peak $= 28$ $−50$ $−10$, $k = 35$, $t = 3.84$, $z = 3.26$; Figure 3). For the interaction in the reverse direction (masked by the simple effect fear/incompatible > calm/incompatible), clusters were seen in the right cerebellum and bilateral superior temporal gyrus. However, no clusters in PFC were seen.

Discussion

In the current study, we investigated cognitive load-dependent modulation of amygdala response to task-irrelevant emotion using a novel and stringently-controlled paradigm. There were two main findings. First, greater amygdala response to fear under low (relative to high) cognitive conflict occurs even when perceptual demands are held constant across conditions. Second, PPI analysis further showed that greater amygdala response to fear under low cognitive conflict was associated with increased functional coupling with a region of middle frontal gyrus previously implicated in the cognitive control of emotion.

Task behavioral results showed a main effect of compatibility on both mean RT and error data. Trials in which the correct response was in conflict with the spatial location of the target stimulus were found to be more difficult, in line with the Simon effect (Simon and Wolf, 1963). Thus, we were able to manipulate cognitive load while matching perceptual inputs. Since the task-relevant targets also contained the task-irrelevant
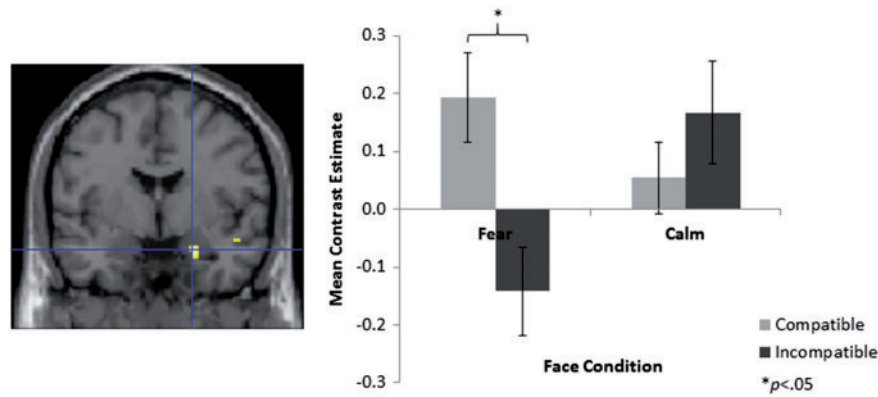
Fig. 2. Interaction between fear/calm and compatible/incompatible conditions in the amygdala. Responses were greater on fear/compatible compared with fear/incompatible conditions, but there was no difference between compatible and incompatible calm conditions. The SPM is displayed at a threshold of $P < 0.005$, $k \geq 20$, uncorrected. Bar chart shows mean contrast estimates across the cluster shown ($k = 33$). Part of this cluster with the same peak ($k = 16$) survived small volume correction.
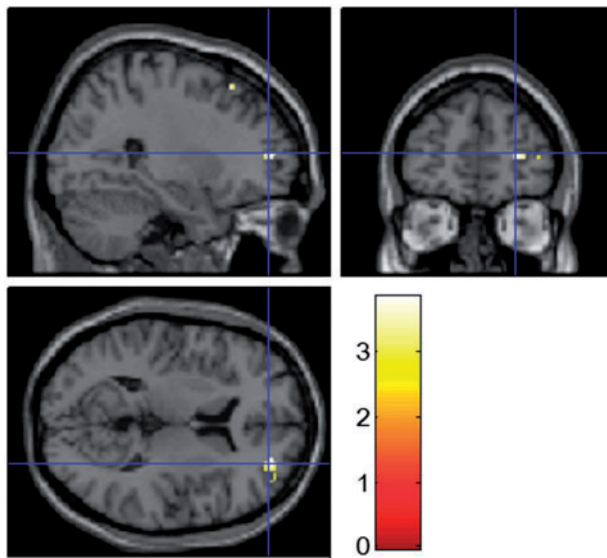

Fig. 3. Right middle frontal gyrus shows increased functional coupling with the right amygdala seed region on fear/compatible trials compared with fear/incompatible (relative to calm conditions). The SPM is displayed at a threshold of $P < 0.005$, $k \geq 20$, uncorrected.

emotionally distracting information, we were also able to set up a direct conflict between cognitive and affective domains. This resulted in an interaction effect, in which mean RTs were disproportionately slowed by the presence of fearful faces in the low conflict condition. While RTs were slower overall in the high conflict condition, they did not appear to be modulated by either fearful or angry faces.

This pattern of results is in line with the biased competition model of attention (Desimone and Duncan, 1995). In the high conflict conditions, greater top down executive control was required, biasing the allocation of attentional resources towards resolving the cognitive conflict, and leaving fewer processing resources available for emotional information. However, on low conflict trials, greater attentional capacity was available, leading to processing of the emotional information and interference with cognitive task performance. While many paradigms report such effects (Carretié, 2014), it is interesting that the effect holds even when, as discussed above, visual processing demands are ostensibly held constant across conditions.

The interaction effect in the mean RT data was largely driven by the contrasts between fear and calm. Looking at the equivalent fMRI data, a parallel effect was seen in the right amygdala. Namely, right amygdala response was greater on 'fear/compatible than on fear/incompatible' trials, but there was no difference between compatibility conditions for calm faces. In line with previous studies (e.g. Pessoa *et al.*, 2002, 2005; Bishop *et al.*, 2007; Mitchell *et al.*, 2007; Alpers, 2009, Kellermann *et al.*, 2012), this finding suggests that amygdala response to emotional information (in this case fearful faces) is susceptible to modulation by task demands.

Our task design further allows us to shed light on potential mechanisms which may underlie this effect. In previous studies employing concurrent but distinct target-distractor paradigms (e.g. Pessoa *et al.*, 2002; Bishop *et al.*, 2004; Pessoa *et al.*, 2005), amygdala modulation may have resulted from the spatial distinction between task-relevant non-emotional and task-irrelevant emotional information. In tasks which have used an overlapping display of emotional/non-emotional and task relevant/irrelevant information (e.g. Bishop *et al.*, 2007; Mitchell *et al.*, 2007; Alpers, 2009), spatial allocation of attention cannot explain the effect, but attention is still directed towards featurally distinct non-emotional aspects of the display (e.g. superimposed letter strings) on conditions in which amygdala modulation is seen. The current results demonstrate that reduced amygdala response to fear under high cognitive load still occurs even when task-relevant non-emotional features (gender) and task-irrelevant emotional features (fearful expression) are conveyed by the same stimulus. Specifically, gender decisions from greyscale photos and facial fear perception both rely on information in the eye region (Adolphs *et al.*, 2005; Dupuis-Roy *et al.*, 2009), while the task was designed such that perceptual requirements were ostensibly matched across low- and high-load conditions.

Since perceptual inputs were well-matched across conditions, it is likely that top-down mechanisms are implicated in mediating the effects seen. Indeed, regions showing greater activation to fear/incompatible than fear/compatible trials (relative to equivalent calm conditions) included subgenual and dorsal anterior regions of anterior cingulate cortex, albeit at uncorrected levels; regions implicated in resolving emotional conflict and regulating responses in emotional contexts (Etkin *et al.*, 2006, 2011). It is possible that the blocked presentation of stimuli facilitated the implementation of top-down strategies for incompatible trials, such that these regions prevented a

potentially costly attentional bias to emotion on these more demanding trials. In contrast, on compatible trials, it was perhaps unnecessary to implement such strategies (the task was easier overall as indexed by RTs and errors), with the result that attention was captured by emotional aspects of the stimuli. We hypothesize that this led to disproportionately slow RTs on the fear/compatible condition (which were nonetheless still significantly faster than on the fear/incompatible condition due to the relative ease of the task), as well as increased right amygdala response.

A PPI analysis using the right amygdala as a seed region found stronger connectivity with right middle frontal gyrus (dorsal BA10) on fear/compatible trials compared with fear/incompatible trials, relative to calm conditions. This overlaps with the region identified by Blair *et al.* (2007) as specifically responding during emotion–cognition interactions on a Stroop-like task. It has further been identified as being involved in the voluntary down-regulation of emotional reactivity (Kohn *et al.*, 2014). It is, therefore, plausible to assume that this connection mediates a regulatory function, for example, it is possible that this connection provided amygdala downregulation to maintain focus on the instructed task on fear/compatible trials; connectivity that was reduced on fear/incompatible trials because amygdala response was already low. An alternative interpretation (which the present study cannot disambiguate) is that the MFG could be mediating an attentional bias towards fear on compatible (relative to incompatible) trials, since this region has been suggested to mediate the dynamic control of attention between top-down goals and bottom-up sensory stimulation in response to changing task demands (Vossel *et al.*, 2014). Taken together, the current findings suggest that even when perceptual inputs are matched, task demands alter the dynamic interplay between bottom-up and top-down processes involved in emotion reactivity and regulation.

A number of outstanding questions still remain. While task instructions required participants to scan the face stimuli in ostensibly the same way on compatible and incompatible conditions, it would have been helpful to use eye-tracking measures to provide confirmation of this. It would also be useful to confirm whether participants did indeed chiefly use features such as the eye region, for gender decision, i.e. features which also convey maximal emotional information. In addition, the amygdala modulation effect was found only in the comparison between fear and calm conditions. While anger does signal threat, some studies have shown that fearful faces elicit a stronger amygdala response than angry faces (Whalen *et al.*, 2001), and that fear elicits amygdala responses while anger does not reliably do so (Blair *et al.*, 1999; Fusar-Poli *et al.*, 2009). The current data are in line with these studies, suggesting that the effects observed may be stronger for fear than anger, although they do not conclusively show fear specificity. It is also worth noting that we did not see an association between behavioral performance and neural response. Finally, the current data pertain to typically developing males only; future studies could investigate whether the same effects are seen in females and in groups with atypical emotion processing profiles.

In conclusion, we show that attenuated amygdala response under high processing load (in this case cognitive conflict) can be shown to occur even when visual inputs are closely matched across conditions, including a requirement to scan emotional information. In contrast, fear processing under low load was associated with RT interference, increased amygdala response and increased functional coupling between the amygdala and the middle frontal gyrus. Results, therefore, suggest that under certain conditions, prefrontal-amygdala connectivity may paradoxically increase when task demands are reduced.

Supplementary data

Supplementary data are available at *SCAN* online.

Conflict of interest. None declared.

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