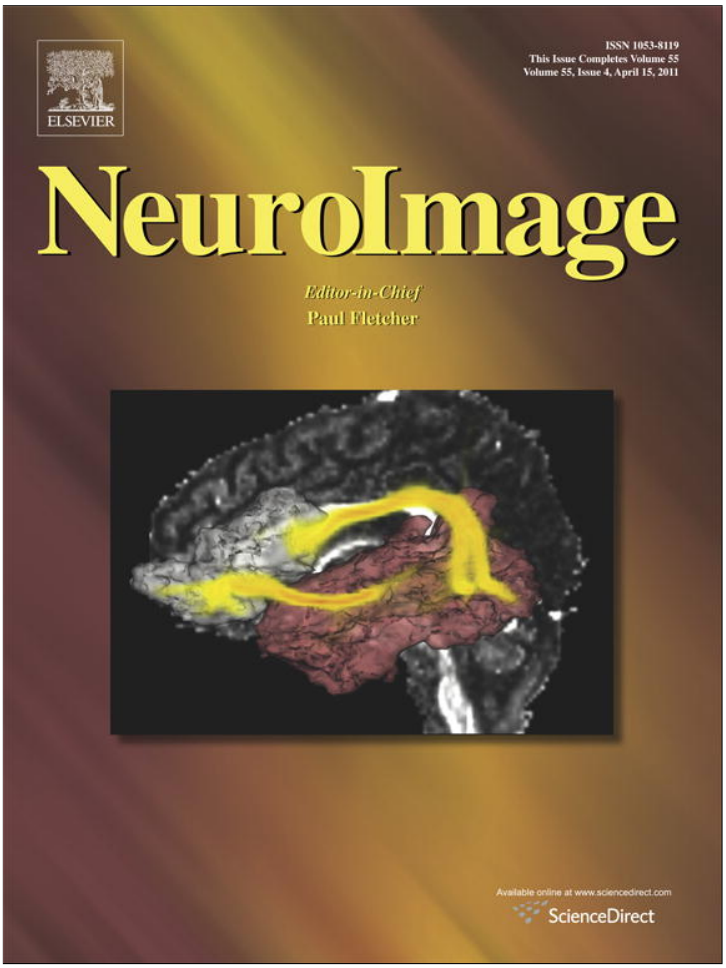

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Fear and stop: A role for the amygdala in motor inhibition by emotional signals

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ABSTRACT

Rapid interruption of ongoing motor actions is crucial to respond to unexpected and potentially threatening situations. Yet, it remains unclear how motor inhibition interacts with emotional processes. Here we used a modified stop-signal task including an emotional component (fearful faces) to investigate whether neural circuits engaged by action suppression are modulated by task-irrelevant threat-related signals. Behavioral performance showed that reaction times were prolonged in the presence of incidental threat information, and this emotional slowing was enhanced when incorrect responses were made following stop signals. However, the speed and efficacy of voluntary inhibition was unaffected by emotion. Brain imaging data revealed that emotional cues during stop trials interacted with activity in limbic regions encompassing the basal amygdala and sublenticular extended amygdala region, as well as with the supplementary motor area (SMA). In addition, successful motor inhibition to threat signals selectively recruited a region in lateral orbitofrontal cortex, distinct from areas in inferior frontal gyrus typically associated with voluntary inhibition. Activity in primary motor cortex was lower when incorrect responses were made on stop signal trials accompanied by a fearful face, relative to neutral, in parallel with the slower response times observed behaviorally. Taken together, our findings suggest that the amygdala may not only promote protective motor reactions in emotionally-significant contexts (such as freezing or defensive behavior) but also influence the execution of ongoing actions by modulating brain circuits involved in motor control, so as to afford quick and adaptive changes in current behavior.

Introduction

Unexpected changes in the environment may prompt the suppression of current or planned actions to afford adapted behavioral responses. Without efficient inhibition of ongoing actions, many ordinary situations would turn into catastrophes. Thus, emotions elicited by the perception of threatening stimuli are likely to exert direct influences on motor activity even without intentional control (LeDoux, 2000), allowing fast changes in current actions or plans prior to deliberate processing. On the other hand, rapid changes in motor behavior can also be voluntarily controlled in order to adjust to new sensory inputs or new goals. However, little is known about how the voluntary suppression of an ongoing voluntary motor behavior interacts with the more automatic response to emotional signals.

In the present functional MRI (fMRI) study, we designed a stop-signal paradigm with a task-irrelevant emotional component that allowed us to compare brain responses to stop signals and emotion signals, as well as any interaction of these two types of events. The stop-task is particularly suitable for investigating inhibitory control, both behaviorally and neurally, because it provides a measure of inhibition that is independent of motor execution (Aron and Poldrack, 2006; Li et al., 2006; Logan and Cowan, 1984). In this task, stimuli are presented in regular succession for speeded discrimination responses but occasionally appear with unpredictable stop signals that require withholding the response to the target. Critically, the stop signals occur with a variable delay after target onset, such that motor inhibition will be successful only when the delay is short enough to allow inhibitory processes to cancel the ongoing motor program; whereas inhibition will fail when the delay approaches the time of overt motor execution (e.g. actual key press). By systematically varying the stop signal delay (SSD) on a trial-by-trial basis, it is possible to calculate the time necessary for successful motor inhibition (stop signal reaction time, SSRT; Logan and Cowan, 1984; Aron et al., 2003b). Here, we designed an emotional version of the stop-signal task enabling us to assess how incidental emotional signals modulate inhibitory motor control in the human brain. Specifically, we examined whether inhibition processes would be

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differentially recruited when participants must withhold an action in response to faces with fearful expression (thereby signaling a potential source of danger; see Davis and Whalen, 2001; Ewbank et al., 2009). We hypothesized that threatening signals might promote inhibition mechanisms through some interaction with the same control pathways that activated by voluntary reaction to stop signals, or alternatively could act on motor action through the activation of (at least partly) distinct emotion-specific circuits.

In particular, because of its critical involvement in motor arrest or freezing behavior (LeDoux, 2000), the amygdala represents a key neural candidate to orchestrate a rapid integration between emotional inputs and motor output processes (Armony et al., 1997). In animals, direct electrical stimulation of the amygdala can provoke an interruption of ongoing motor behaviors together with manifestations of attentional orienting such as bradycardia and tachypnea (Applegate et al., 1983). Projections to the brainstem, ventral striatum, and ventro-medial prefrontal cortex are thought to mediate these motor effects. In humans, an influence of amygdala activity on attentional and perceptual processes has been well established for different sensory modalities (Grandjean et al., 2005; Vuilleumier, 2005; Vuilleumier et al., 2004), but emotional effects on motor processes and the possible role of the amygdala in such modulation remain unknown. Yet, adaptive motor behaviors and action tendencies are central features of emotions (Frijda, 1986; Scherer, 2005), concomitant with other changes in physiological bodily states and subjective feelings. Moreover, many behavioral studies have shown that fear-related stimuli lead to slower response times across a variety of tasks, even when emotion is task-irrelevant (e.g. MacLeod, 1991; Cacioppo and Gardner, 1999; Algom et al., 2004), a "negativity effect" that is often attributed to attentional capture and deeper processing for threatening information (Fox et al., 2002; Algom et al., 2004; Vuilleumier and Huang, 2009) or may reflect more general effects of negative vs positive affect on the speed of stimulus processing (Leppanen and Hietanen, 2004; Leppanen, 2006; Albert et al., 2010). In addition, studies using transcranial magnetic stimulation have shown a modulation of the motor cortex responses by induced emotions or concomitant emotional stimuli (Hajcak et al., 2007; Schutter et al., 2008). However, the neural circuits underlying the effects of emotion on motor action, and more generally the possible involvement of amygdala in motor control processes, still remain poorly known.

Therefore, the major aims of the present study were to investigate the influence of threat cues (fearful faces) on neural circuits mediating motor inhibition in response to stop signals, and to determine whether the amygdala would be implicated in any interaction between emotion and motor functions. We hypothesized that emotional processing in amygdala might contribute to motor inhibition, and that such inhibition might be further enhanced when stop signals are associated with threat cues. In addition, because recent human studies demonstrated that voluntary inhibitory processes during stop-signal tasks (with neutral stimuli) may involve a specific "hyperdirect" pathway between the right inferior frontal cortex (IFC), pre-supplementary motor area (preSMA), and subthalamic nucleus (STN) (Aron et al., 2007; Aron and Poldrack, 2006), we asked whether the same regions might constitute the critical neural sites where more automatic effects of emotional cues are integrated with motor inhibition processes. Alternatively, we could also test whether any emotional influence on motor control systems might be mediated by distinct neural pathways, unlike those implicated by motor inhibition in neutral or cognitive situations.

Based on past neuroimaging and neuropsychological work in humans, it remains debated whether similar neural systems for inhibition are shared across different domains and whether the right IFC recruited during cognitive and motor control is also responsive to emotional information (Dillon and Pizzagalli, 2007). Several recent studies have used fMRI (Berkman et al., 2009; Goldstein et al., 2007; Shafritz et al., 2006; Hare et al., 2005) or EEG (Albert et al., 2010; Putman et al., 2010; Chiu et al., 2008) to investigate emotion effects on response inhibition but provided divergent results, some supporting an involvement of the right IFC for inhibition within emotional contexts (e.g. Berkman et al., 2009; Shafritz et al., 2006) but others suggesting distinct inhibitory processes (e.g. Goldstein et al., 2007; Hare et al., 2005). However, all previous studies used go–nogo tasks, which typically require making keypresses to one stimulus category while withholding responses to another infrequent category, and thus potentially conflate inhibition with target detection and task switching (Aron and Poldrack, 2005). Moreover, most of these studies defined go and nogo trials based on the emotional valence of stimuli (positive vs negative), such that emotional information was task-relevant and response inhibition confounded with emotion recognition. By contrast, the stop-task used in our study is thought to be cognitively purer because it can probe the suppression of an ongoing (already started) response and thus provide a measure of inhibition that is independent of motor execution (Logan and Cowan, 1984; Aron and Poldrack, 2006; Li et al., 2006). In addition, in our study, emotional information was always incidental to the task and unrelated to stop signals. Finally, another advantage of the stop-task is that inhibition difficulty and frequency could be tailored to individual performance by using a dynamic algorithm that sets SSDs on a trial-by-trial basis and thus ensures a balanced rate of errors across subjects and conditions. In doing so, we could compare successful vs unsuccessful motor inhibition and thus distinguish brain activation related to stop signals and stop performance itself, as well as any emotional influence on these activations.

Materials and methods

Participants

Fourteen healthy volunteers (age range 18–25 years) participated in the study after giving informed consent according to the ethics regulation of the Geneva University Hospitals. All subjects were right-handed, had normal vision, and had no past or present neurological or psychiatric history. All were recruited among University students and collaborators, and were paid for their participation.

Stimuli and stop-signal task

Stimuli were gray-scaled fearful or neutral faces of 8 individuals (4 males) from the Ekman's series (adapted by D. Perrett and colleagues; see Calder et al., 1997). Each face subtended 2.15×2.15 degrees of visual angle and was surrounded by a blue frame (width: 0.125°; Fig. 1). During scanning, these stimuli were back-projected onto a mirror mounted on the head coil and presented centrally against a homogenous gray background. We used the E-Prime software (Psychology Software Tools, Inc., Pittsburg, PA) for stimulus presentation, timing of stimuli and response events, and synchronization with fMRI image acquisition.

Each trial started with a 500 ms fixation cross, immediately followed by the face stimulus that remained on the screen during 1 s. Subjects had to discriminate the gender of the face and answered by pressing the correct button of an MRI-compatible mouse as quickly and as accurately as possible during the 1-s presentation (go-trials; Fig. 1A). All subjects were right-handed and used their right hand to respond. Critically, they were also instructed to inhibit their response if the color of the surrounding frame briefly changed from blue to red (stop-trials, duration 100 ms; Fig. 1B). The blue and red colors were isoluminant. The interval between the face onset and the frame's color change (stop-signal delay; SSD) was adjusted online as a function of the subject's performance on the previous stop-trial with the same facial expression. Thus, stopping difficulty was kept under experimental control on a trial-by-trial basis, with longer SSDs corresponding to more difficult stop-trials. SSD was initially set at 250 ms (for each scanning block) and then

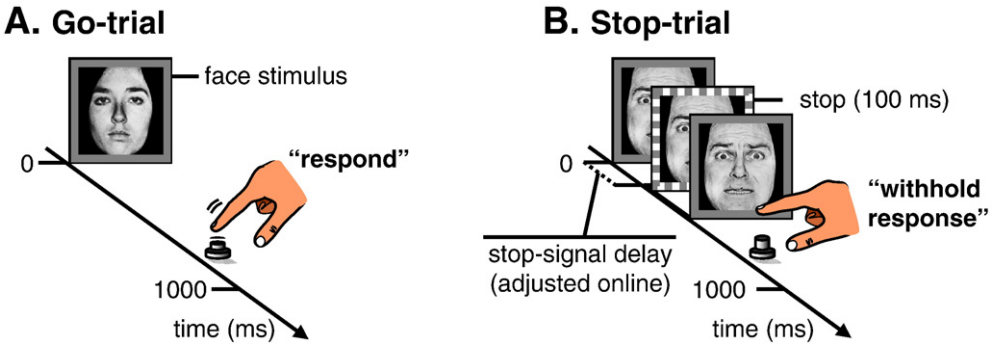

Fig. 1. Task trials, illustrating one neutral go trial and one emotional stop trial. Subjects performed a gender discrimination task on pictures of faces by pressing the correct key (go condition, A), unless the picture's frame briefly flashed from a blue color (plain gray frame) to an isoluminant red color (dashed frame), in which case subjects had to withhold their response (stop condition, B). Faces seen on Go or Stop-trials could display either a neutral or fearful expression (50% each), which was always irrelevant to the main task. An online tracking algorithm adjusted the stop-signal delay (SSD) according to the following rule: 50 ms added after successful inhibition (making it harder to inhibit on the next stop-signal trial) or 50 ms subtracted after unsuccessful inhibition (making it easier to inhibit on the next stop-signal trial). SSD was tracked independently for trials with fearful and neutral faces.

continuously adjusted according to separate staircase procedures for each emotional condition, in order to obtain a probability of stopping of 0.5 for both neutral and emotional trials. In this way, the tracking algorithm generated as many successfully stopped trials (StopInhibit) and failed stop-trials (StopRespond) in both emotional conditions. Subsequent analysis showed that this procedure generated a similar range of SSD values (from min. 50 ms to max. 400 ms) for StopInhibit and StopRespond trials in the neutral and emotional face conditions.

All RTs are reported for correct responses that were executed during the 1-s presentation of the face stimulus. Because we used the median of individual RTs in our analyses (see Aron et al., 2003a, 2003b; Aron and Poldrack, 2006), we did not remove any outlier data. The distribution of RTs was close to normality for all conditions (kurtosis range 1.53–2.50, skewness range 0.68–1.47). Based on the independence assumption of the horse-race model, we computed the stop-signal reaction time (SSRT) by subtracting the average SSD from the median Go RT, as described in previous studies (for a detailed explanation of the method, see Aron et al., 2003b; Aron and Poldrack, 2006; Logan et al., 1984, 1997; Williams et al., 1999). The resulting SSRT thus reflects the average time required to internally suppress the prepared motor response, and was estimated here independently for trials displaying neutral versus fearful faces.

Subjects performed one training run on the stop-signal task before scanning and then three additional runs during scanning. Each run comprised 80 Go trials and 40 Stop trials (mean inter-stimulus interval 3.2 s, range 2.6–3.8 s), plus 40 "null events" randomly distributed within each run to provide an appropriate baseline measure (Josephs and Henson, 1999). Half of the trials displayed an emotional face and the other half a neutral face. The experimental trials were delivered in a pseudorandom order with a maximum of two Stop trials in a row. The number of StopInhibit and StopRespond as well as the mean RT and SSRT were calculated automatically after each run to verify compliance with the task. After each run, subjects were reminded that they had to respond as fast as possible on each trial. All subjects were scanned at approximately 7.30 P.M. in order to control for possible time-of-day effects on attention level.

MRI scanning

Scanning was performed on a 1.5 Tesla Intera Philips whole-body system (Philips Medical Systems, Best, NL) equipped with an eight-element head coil array (MRI Devices Corporation, Waukesha WI), using advanced parallel-imaging technology (sensitivity-encoded echo planar imaging; SENSE-EPI) that substantially increases speed of acquisition and spatial resolution in fMRI (by reducing spatial distortions and blurring; see Preibisch et al., 2003). Multi-slice T2*-weighted EPI images covered the whole brain except the lower part of the cerebellum, and were acquired continuously across three successive runs lasting 9 min each [TR (repetition time) = 2.15 s, TE (echo time) = 40 ms, flip angle = 80°, FOV (field of view) = 250 mm, matrix = 128 × 128 × 30, voxel size = 1.95 × 1.95 × 4 mm]. The scanning parameters were optimized during pilot testing to minimize susceptibility-related signal loss in the amygdala and orbitofrontal cortex. In addition to SPM masking procedures based on response maps derived from the experiment-specific statistics, we further excluded the presence of erroneous activation in amygdala regions by inspecting each individual data set for regional signal drop, using a half-maximum intensity threshold of the mean images over the whole experiment. Importantly, note that spatial distortion and signal loss in the lower temporal regions are generally less severe at 1.5 Tesla, as used here, while higher field at 3 Tesla mainly improves cortical signal (although recent technical developments should allow higher amygdala SNR at 3 T in the future; e.g. Robinson et al., 2008). Thus, altogether, our scanning parameters ensured optimal signal from amygdala and orbitofrontal cortex. For subsequent data processing, the four initial scans in each time series were discarded to ensure magnetization steady state, leaving 250 functional volumes for each of the three runs. In addition, a high resolution structural volume was obtained with a 3D GRE T1-weighted sequence (TR = 15 ms, TE = 5 ms, flip angle = 30°, FOV = 250 mm, matrix = 256 × 256, voxel size = 0.977 × 0.977 × 1.25 mm). The head was maintained fixed with a vacuum pillow to minimize motion during acquisition.

fMRI analyses

Data from twelve subjects were included in the final analyses (two subjects excluded due to technical problems in MRI acquisition). Functional images were analyzed using the general linear model for event-related designs using SPM2 (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm). All images from the three runs were realigned, corrected for slice timing, normalized to the MNI space (reslicing 3 × 3 × 3 mm voxel-size), and spatially smoothed with an 8-mm full width at half-maximum (FWHM) Gaussian kernel. High-pass frequency filter (cutoff 128 s) and corrections for auto-correlation between scans were applied to the time series. Individual events were modelled by a standard synthetic hemodynamic response function (HRF). Six event-types were defined, corresponding to each condition of interest: Go neutral, Go emotional, StopInhibit neutral, StopInhibit emotional, StopRespond neutral, StopRespond emotional. Success on each stop-trial (StopInhibit, StopRespond) was derived from each subject's individual responses. Seven covariates of no interest were added in the analysis, including one covariate for

unclassifiable keypresses [e.g. responses before or during the presentation of the stop-signal red frame (see Fig. 1B), and suspiciously short reaction-times <200 ms; 3.9% of all trials in total], as well as 6 covariates corresponding to head movement parameters derived from spatial realignment during image preprocessing.

The general linear model was used to estimate parameters of activity at each voxel for each condition and each participant across the whole brain. Random-effect group analyses were then performed using one-sample *t*-tests on contrast images obtained in each individual subject. The tables report the resulting statistical parametric maps (SPMs) of the *t*-statistic ($df = 11$) at a threshold of $p<0.001$ uncorrected, with a cluster-size threshold of 5 voxels (135 mm^3); but a threshold of $p<0.05$ corrected for multiple comparisons was used for all regions discussed in the main text. Post-hoc analyses were performed on selected regions of interest [ROIs] to directly compare the effects of the two emotion conditions (e.g. for a cluster identified by a separate main effect pooling across different trial types), by using *t*-test contrasts on the peak of activation defined by the previous analysis and then searching for the *z*-score maxima within a 6-mm sphere in SPM.

Results

Behavioral performance

Behavioral data collected during the three fMRI runs were included into repeated-measure ANOVAs with Emotion (neutral, fearful) and Run (first, second, and third) as within-subjects factors. There were no differences for correct gender discrimination responses on Go trials (mean 98.5% correct) and stop success rate on Stop trials (mean 50.8%) between the two emotion conditions and the three successive scanning runs (Table 1). These data show that our adaptive staircase procedure was effective to obtain a balanced number of trials across conditions, and that response execution and inhibition processes did not significantly vary over the course of scanning.

Analysis of RTs for correct Go responses revealed a main effect of Emotion ($F_{1,11} = 8.24$, $p = 0.015$) reflecting slower responses to fearful than neutral faces (Table 1). RTs for StopRespond also showed a significant effect of Emotion ($F_{1,11} = 13.15$, $p = 0.004$), with slower key-presses when erroneous responses were made on trials with emotional faces relative to erroneous responses made on trials with neutral faces. There was no main effect or interaction involving run number. The same ANOVA performed on the SSRT did not reveal any significant effect, indicating that the speed of voluntary inhibition was not modulated by emotion. Accordingly, this combination of longer total RTs with unchanged SSRT reflected longer stop-signal delay (SSD) values for trials with fearful faces than those with neutral faces (Table 1). Again, no effect of run was observed (for SSRT or SSD), indicating stable performance across the three successive scanning blocks. Consistent with the race-model assumption of independence of Go and Stop processes (Logan et al., 1984), there was no significant correlation between Go RT and SSRT, neither for neutral ($n = 12$ in each fMRI run: $r_1 = 0.42$, $r_2 = 0.55$, $r_3 = 0.15$, all n.s.) nor for emotional trials ($r_1 = 0.18$, $r_2 = -0.47$, $r_3 = 0.53$, all n.s.). Taken together, these behavioral data suggest that the slowing of responses on emotional trials was due to some processes activated prior to the onset of the stop signal, therefore affecting the SSD but not the SSRT.

Notably, however, emotional slowing was larger in StopRespond trials (where participants made erroneous keypresses) than in Go trials (19.8 ms vs 9.6 ms, respectively). This difference was formally verified by a repeated-measure ANOVA on RTs from both the correct (go) and incorrect (StopRespond) response conditions, which showed not only main effects of emotion and response condition (Fs>20, $p<0.001$) but also a significant interaction of emotion × response condition ($F_{1,11} = 11.29$, $p = 0.006$). Thus, as expected, average RTs were globally quicker in the StopRespond condition (since this corresponded to trials where motor execution was too fast to be overridden by inhibition), but this greater promptness to respond was attenuated when erroneous keypresses following stop signals were made to fearful compared to neutral faces (see Table 1). This result suggests that inhibition processes activated by stop signals could interact with emotional processing to further slow down motor responses in fear compared to neutral trials, even when such inhibition eventually failed to cancel motor execution.

Table 1
Behavioral performance on the stop-signal task for the 12 participants over the 3 fMRI runs.

Behavioral measure	Neutral	Fearful	Effect of emotion[a]
Median Correct Go RT (ms)	482.78 (6.70)	492.47 (7.13)	$F(1,11) = 8.24$; $p = 0.015$
Median StopRespond RT (ms)	441.29 (7.00)	461.13 (8.47)	$F(1,11) = 13.15$ $p = 0.004$
Percentage Go discrimination errors	1.06 (0.19)	1.50 (0.22)	$F(1,11) = 2.83$ $p = 0.121$
Percentage Stop Success	50.31 (2.97)	51.29 (2.85)	$F(1,11) = 0.51$ $p = 0.49$
Mean SSD (ms)	218.27 (12.34)	225.55 (11.82)	$F(1,11) = 4.13$ $p = 0.067$
Mean SSRT (ms)	264.51 (41.29)	266.29 (35.72)	$F(1,11) = 0.12$ $p = 0.732$

Abbreviations: SSD, stop-signal delay; SSRT, stop-signal reaction time.
[a] ANOVAs were performed with Emotion and Run as within-subject variables. No effect of Run and no interaction Emotion × Run were found for any of the measures.

Functional MRI data

Brain activation during imperative stop cues

We first identified brain regions recruited by imperative inhibition cues by comparing all trials with stop signals to go trials [(StopInhibit + StopRespond)>Go], independently of inhibition success and facial expressions. Stop-signals activated several regions previously reported to be involved in inhibitory control and error monitoring (Table 2; Fig. 2A, C, D), including the right superior, middle, and inferior frontal gyri, bilateral orbitofrontal lateral regions, and bilateral insula (see Aron et al., 2004; Casey et al., 1997; de Zubicaray et al., 2000; Garavan et al., 2002; Liddle et al., 2001; Ramautar et al., 2006; Rubia et al., 2001). In particular, there was a robust activation of the right inferior frontal cortex (IFC; see Fig. 2A). This region is critical for action monitoring and inhibition across a wide range of motor tasks, as shown by both imaging and lesion studies (e.g. Aron et al., 2003b, 2004; Li et al., 2006), but also suspected to play more general role in attentional reorienting and task switching (e.g. Corbetta et al., 2008; Hampshire et al., 2010). Activity in the right IFC (as identified by the main effect of Stop>Go) across the different emotion conditions is plotted in Fig. 2B. A region-of-interest (ROI) analysis centered on this cluster showed significantly larger increases during StopInhibit trials when the face was neutral, relative to when the face was fearful (StopInhibit neutral>StopInhibit fear, $t = 2.16$, $p<0.05$, SVC; Fig. 2B), while there was an equal activation to fearful and neutral faces on failed stop trials (StopRespond neutral>StopRespond fear, $t = -0.72$, n.s.). Moreover, there was no significant increase on fearful StopInhibit compared to fearful Go trials ($t = 1.11$, n.s.), suggesting that successful stopping might not depend on activation of the lateral IFC in the emotional condition.

The same contrast [main effect of (StopInhibit + StopRespond)>Go] further revealed that stop signals activated several other brain regions (Table 2), including bilateral parietal areas in the temporo-parietal junction (TPJ) and intraparietal sulcus (IPS) that are also involved in attention reorienting (Corbetta & Schulman, 2002; Corbetta et al., 2008), as well as regions that critically contribute to motor control such as the SMA/preSMA (Fig. 2C), premotor cortex, and a subcortical cluster compatible with the subthalamic nucleus (STN, Fig. 2D; see Aron and Poldrack, 2006; Aron et al., 2007). This STN activation (peak 3*x* −15*y*

Table 2
Brain regions showing a main effect of motor inhibition.

Brain areas	L/R	X Y Z (MNI coordinates)			T value	Cluster size (voxels)
Contrast: (StopInhibit + StopRespond) > Go						
Frontal sup.	R	27	9	60	8.14	255
SMA/preSMA	R	12	15	66	8.06	[a]
ACC	R/L	0	30	36	7.01	[a]
Cingulate med.	L	−3	−18	27	6.16	29
Frontal mid.	R	42	30	42	6.50	138
Premotor	R	45	6	45	6.22	[a]
Frontal mid.	R	36	45	15	6.45	15
Frontal sup. and mid.	R	24	60	30	5.81	34
IFC	L	−54	18	−6	6.28	10
IFC	R	54	18	−3	6.83	47
IFC	R	51	45	9	5.58	17
Frontal inf. orbital / insula	R	33	24	−9	4.77	15
Frontal inf. orbital / insula	R	42	21	−15	4.27	5
Insula	L	−33	21	−3	4.69	7
STS	R	54	−39	−3	7.03	25
Precuneus	R	12	−78	45	8.30	31
IPS	L	−39	−57	48	6.98	114
IPS	R	39	−57	39	5.70	9
Parietal inf.	L	−30	−63	42	5.34	7
Supramarginal gyrus	R	54	−48	39	6.82	142
TPJ	L	−57	−57	9	10.38	57
TPJ	R	66	−51	12	7.40	51
Occipital pole	L	−12	−99	6	5.53	7
Occipital pole	R	12	−102	6	5.04	8
Subthalamic nucleus (STN)	R	3	−15	−6	6.01	9

Abbreviations: ACC, anterior cingulate cortex; IFC, inferior frontal cortex; inf., inferior; IPS, intraparietal sulcus; mid., middle; SMA, supplementary motor area; STS, superior temporal sulcus; sup., superior; TPJ, temporo-parietal junction.
[a] Belongs to the same cluster as row above.

−6*z*) was corroborated by a ROI approach using a 6-mm sphere centered on the MNI coordinates reported for STN in a previous study using a stop task without emotional stimuli (10*x* −15*y* −5*z*; see Aron and Poldrack, 2006; $p<0.05$ corrected).

Brain activation during successful inhibition

To determine regions that might be more directly responsible for motor inhibition, we also compared successful relative to failed stops, irrespective of emotion conditions. This contrast (StopInhibit>StopRespond) activated a ventral portion of IFC, inferior to the main effect found for all stop trials (above) and extending into the lateral orbitofrontal cortex (OFC) bilaterally (Table 3; Fig. 2E). Activity in this cluster across the different task conditions is illustrated in Fig. 2F. As can be seen, the right ventral IFC/lateral OFC was not only activated during all successful inhibition trials, but also activated to fearful faces during StopRespond trials, where stopping actually failed (Fear>Neutral, $t=2.09$, $p<0.05$, SVC; see Fig. 2F). By contrast, it was equally activated on all successful stops, with no significant emotional modulation in this condition ($t=0.59$, n.s.). This pattern in ventral IFC/OFC was therefore distinct from the emotional effect observed in lateral IFC (see above and Fig. 2A), suggesting that inhibitory processes mediated by ventral IFC/OFC could be recruited by threat signals in the absence of any activation in lateral IFC on StopInhibit trials.

In addition, the same contrast (StopInhibit>StopRespond) indicated that successful inhibition also activated the left SMA/preSMA, as well as bilateral dorsolateral prefrontal and inferior parietal regions that are also typically involved in executive control and attention (Corbetta and Shulman, 2002). Inspection of activity in these clusters across all conditions indicated no differential effects as a function of emotional face expression.

Brain activation during executed movements

We also compared all trials where keypresses were executed (correct or incorrect) relative to those were no movement was made [i.e. (Go + StopRespond) > StopInhibit]. As expected, this revealed a highly selective activation of the left primary motor cortex (M1, −48*x* −21*y* 51*z*, $t=6.02$, $p<0.001$; Fig. 3A), plus left secondary somatosensory cortex (−45*x* −6*y* 9*z*, $t=8.62$, $p<0.001$) and left cerebellum (−3*x* −60*y* −6*z*, $t=7.12$, $p<0.001$). Activity in the left M1 cluster is illustrated in Fig. 3B for the different task conditions and demonstrated a significantly weaker increase on emotional than neutral StopRespond trials ($t=2.85$, $p<0.05$, SVC), whereas activation was similar for emotional and neutral trials in the Go condition ($t=-0.87$, n.s.).

Brain activation to fearful faces

Finally, we identified the main effect of emotional threat signals, irrespective of motor condition, by comparing all trials with fearful versus neutral face expressions (i.e. both go- and stop-trials). As expected, this contrast revealed an activation in the right lateral amygdala (27*x* 0*y* −24z, $t=4.02$, $p<0.001$; Fig. 4A, D), but also a more dorsal cluster in the extended sublenticular amygdala in substantia innominata (SI/SLEA). Additional increases were seen in other limbic regions, including posterior insula and ventral striatum (putamen and nucleus accumbens), as well as in bilateral premotor areas (Table 4). This pattern is consistent with previous studies on the processing of fear-related stimuli across different stimulus modalities (de Gelder et al., 2004; Pichon et al., 2009; Vuilleumier et al., 2004).

Because the amygdala was our main a priori region of interest for an interaction between emotional processing and inhibitory stop signals (see Introduction), we then specifically concentrated on this region and tested whether its response differed as a function of the different stopping condition (i.e., successful or unsuccessful stop). These analyses are described in the following section.

Integration of emotion and motor inhibition in the amygdala

Because we hypothesized that amygdala activity might contribute to automatic inhibitory effects on motor action in response to threat cues, and/or mediate their integration with concomitant stop signals when both appeared together, we expected that this region would be differentially activated by fearful faces during successful motor inhibition. We therefore tested for brain areas that were more strongly activated during successful inhibition in the presence of fearful faces by comparing emotional versus neutral StopInhibit trials (Table 5). This analysis revealed significant increases in the SMA-proper (9*x* 3*y* 54*z*; $t=6.35$, $p<.001$) and amygdala (18*x* −6*y* −30*z*; $t=5.36$, $p<0.001$). The amygdala peak (Fig. 4B, E) was located in a slightly more ventral portion than the main effect of fearful expression (see previous section), but another distinct cluster was again observed dorsally in the SI/SLEA (Fig. 4B). On the other hand, no amygdala activation reached the statistical threshold when comparing emotional versus neutral faces on failed stop trials (StopRespond; only weak subthreshold responses were found in the lateral portion [27*x* −3*y* −21*z*; $t=2.31$]).

This difference in amygdala responses to emotional faces as a function of inhibition success was confirmed by formally testing for an interaction between emotion and stop conditions ([fear minus neutral StopInhibit]>[fear minus neutral StopRespond]) using a whole-brain SPM analysis. This interaction revealed a selective activation in SI/SLEA (9*x* −3*y* −12*z*, $t=5.21$, $p<0.001$; Fig. 4C). These results therefore suggest that activity in SI/SLEA was sensitive to the combined effects of threat and stop signals, and specifically associated with successful inhibition. No significant interaction was found in the more lateral or ventral portions of the amygdala.

Finally, to further verify how the neural responses elicited by fearful faces in the amygdala differed as a function of the different inhibition conditions, we extracted the parameter estimates of activity (betas) from the three amygdala peaks identified by SPM contrasts above (lateral, ventral, and SI/SLEA; Fig. 4D, E, F). Animal studies suggest that electrical stimulation applied to different amygdala subregions have different effects on motor behavior (Applegate et al., 1983). For each peak, we therefore performed 2×2 repeated-measure ANOVAs with Face-Emotion (fearful, neutral)

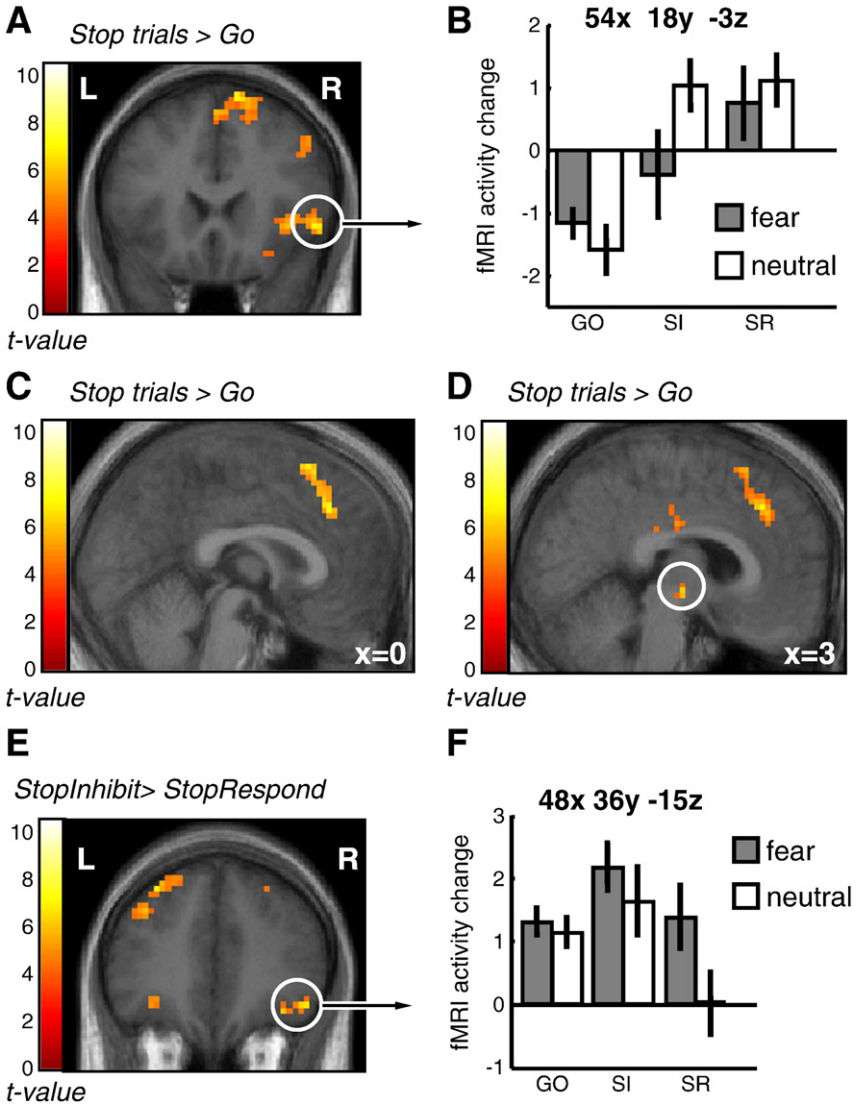

Fig. 2. Brain regions activated during stop-trials. (A) SPM map revealed increased activity in the right IFC. (B) Parameter estimates of activity extracted from the right IFC (depicted in A) showed increases in all stop conditions relative to go trials, but with a reduced effect for successful emotional stop-trials (compared to neutral stops), suggesting that additional neural mechanisms of inhibition might subserve successful inhibition in this condition (see main text). SPM maps showing increased activity in the (C) SMA/preSMA and (D) subthalamic nucleus during stops (irrespective of inhibition success) as compared with go trials. (E) Brain regions activated during successful versus failed stop-trials. (F) Parameter estimates of activity extracted from the right ventral IFC/lateral OFC show a main effect of stop success, but also a persistent increase in response to fearful faces even during failed stops, suggesting that some inhibitory processes mediated by ventral IFC/lateral OFC could be recruited by threat signals even during unsuccessful stops (see main text). GO = correct go trials, SI = stop-inhibit trials (successful inhibition); SR = stop-respond trials (unsuccessful inhibition). Clusters of activation are overlaid on the mean-normalized T1-weigthed structural scan from all participants.

and Stop-Success (StopInhibit, StopRespond) as within-subjects factors, for each peak separately. As expected, the ANOVA for the lateral amygdala peak showed a main effect of Face-Emotion ($F(1,11) = 15.1$, $p<0.01$), but no significant interaction of Stop-Success by Face-Emotion ($F(1,11) = 0.05$, n.s.). A main effect of Face-Emotion was also significant for the SI/SLEA ($F(1,11) = 12.5$, $p<0.01$), but not for the ventral amygdala peak ($F(1,11) \leq 3.16$, $p \geq 0.103$). Most importantly, the critical interaction of Stop-Success by Face-Emotion was significant for the SI/SLEA region ($F(1,11) = 9.24$, $p<0.05$), as well as the ventral amygdala peak ($F(1,11) = 5.54$, $p<0.05$; Fig. 4). No main effect of Stop Success was observed for any of the three peaks.

Discussion

In the present study, we used a modified stop-signal paradigm with concomitant (task-irrelevant) emotional signals (fearful faces), in order to examine how brain circuits involved in automatic reactions to threat might interact with those involved in the voluntary inhibition of motor action. Our results show that emotional cues effectively influenced motor responses and that their effect was modulated by concomitant stop-signals. However, the speed of voluntary inhibition was not changed by emotional cues. Taken together, our data demonstrate that threat perception may influence brain system involved in motor control in humans, through partly overlapping but also partly different pathways than those mediating voluntary inhibition.

At the behavioral level, threat signals caused a general slowing of motor responses that affected both Go and StopRespond trials (i.e. correct and incorrect keypresses), but did not change the average stopping latencies as estimated by SSRT. On the contrary, a facilitation of voluntary motor inhibition by emotion should have produced shorter SSRT—unlike what we found. This global slowing of RTs with unchanged SSRT for fearful face trials suggest that emotional processes activated by fearful faces could inhibit either the initiation or the execution of motor responses to target stimuli, prior to the activation of voluntary inhibition processes that were engaged by stop

Table 3
Regional activation during successful versus failed inhibition.

Brain areas	L/R	*X Y Z* (MNI coordinates)			*T* value	Cluster size (voxels)
Contrast: StopInhibit>StopRespond						
SMA/preSMA	L	−12	24	63	4.90	5
Frontal sup.	R	21	48	45	10.24	57
Frontal sup. medial	R	12	57	42	5.98	5
Frontal sup. and mid.	L	−30	36	48	6.72	35
Frontal mid.	L	−42	27	42	5.71	39
Frontal mid.	L	−39	12	54	5.29	5
Frontal mid.	R	36	15	36	5.34	8
Ventral IFC	L	−33	36	−15	4.83	6
Ventral IFC/lateral OFC	R	48	36	−15	6.47	16
OFC medial	R	9	54	−15	5.58	20
STS	R	66	−18	0	5.62	13
Angular gyrus	L	−48	−66	30	4.91	8
TPJ	R	51	−63	18	6.08	12
Amygdala (ventral)	R	24	−9	−27	4.38	20

Abbreviations: IFC, inferior frontal cortex; inf., inferior; mid., middle; OFC, orbitofrontal cortex; SMA, supplementary motor area; STS, superior temporal sulcus; sup., superior; TPJ, temporo-parietal junction.

signals (see Fig. 5). In keeping with these findings, many behavioral studies using emotional versions of the Stroop and go/no-go paradigms have also reported longer reaction-times for negative emotional material (e.g. MacLeod, 1991; McKenna and Sharma, 1995; Nigg, 2000; Williams et al., 1996). Slower discrimination responses to threat-related stimuli correspond to a classic "negativity effect" that is commonly attributed to stronger attentional capture and deeper processing for negative stimuli (e.g. Algom et al., 2004; Cacioppo and Gardner, 1999; Vuilleumier, 2005). Other studies have found slower processing speed for negative information or, conversely, facilitation of responses to positive information (e.g. Leppanen and Hietanen, 2004; Leppanen, 2006; Hare et al., 2005; Albert et al., 2010), which could reflect affective influences at the perceptual, attentional, and/or motor levels.

To our knowledge, only a single behavioral study directly investigated emotional effects on motor inhibitory systems by using a stop-task, in combination with a priming paradigm where each trial was preceded by a neutral or highly emotionally-arousing picture (Verbruggen and De Houwer, 2007). This study found prolonged reaction-times on emotional trials but together with longer stopping latencies, which was interpreted as evidence that highly-arousing stimuli could divert attention away from the current cognitive goals. The reason for this divergence with our own behavioral results is probably due to differences in task design, including different delays between emotional stimuli and stop signal onset. In our study, instead of modulating voluntary inhibition by the preceding emotionally-arousing context, we used an orthogonal manipulation of stop signals and threat signals (fearful faces) within the same event (Fig. 1), allowing us to probe for any convergence of incidental emotional processing and voluntary inhibitory control during ongoing motor behavior. Our behavioral results clearly show that emotional face expressions produced a significant slowing effect on motor execution, but no changes of inhibition latency (i.e. SSRT), suggesting that task-irrelevant fear-related cues could modulate brain pathways that directly control motor programming and execution but not those that mediate voluntary motor inhibition (Fig. 5). This lack of emotion effect on SSRT is unlikely to reflect a lack of statistical power given that significant effects were observed for RTs to fearful faces.

On the other hand, we found that the slowing of responses to fearful compared to neutral faces was significantly larger on erroneous responses (when inhibition to stop signals actually failed) than on correct Go responses. This suggests that stop signals interacted with emotion signals and could enhance their "braking" influence on motor execution in this condition, perhaps by converging on similar neural pathways that were modulated by both stop signals and emotion but insufficiently activated on the unsuccessful StopRespond trials (as compared with the successful StopInhibit). However, these pathways are likely to lie downstream to those initiating voluntary inhibition since SSRT were unaffected by emotion. Accordingly, activity in the left primary motor cortex paralleled this interaction pattern, with reduced activation on emotional compared to neutral StopRespond, consistent with a latent but inefficient suppression of motor responses in the former condition. Such modulation of the primary motor cortex converges with studies showing that emotional cues can influence motor excitability as directly measured by TMS (Hajcak et al., 2007; Schutter et al., 2008).

In line with these behavioral results, our neuroimaging data indicated that incidental threat signals modulated neural activity in several brain regions associated with motor function, and that the amygdala was involved in integrating these threat signals with the concomitant stop signals. Amygdala activation to emotional faces has previously been found to arise irrespective of selective attention or task-relevance (see Adolphs, 2008; Glascher et al., 2007; Vuilleumier et al., 2001; Winston et al., 2003), consistent with its responses to incidental emotional cues in the present study. Critically, here we observed a significant interaction of emotion with successful inhibition in the amygdala. When tested across the whole-brain, this interaction selectively implicated a dorsal cluster in the SI/SLEA, leading to greater activation in this region during StopInhibit relative

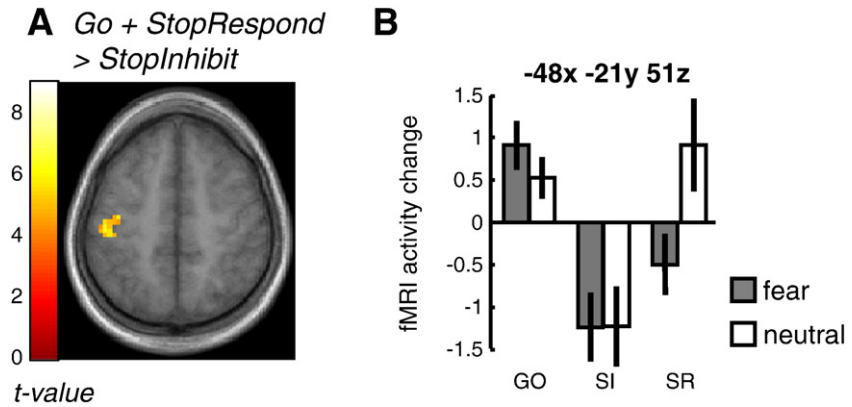

Fig. 3. Motor activation during movement. (A) The comparison of (Go + StopRespond) > StopInhibit trials showed selective increases in the left primary motor cortex, in a region probably corresponding to the hand area. (B) Parameter estimates of activity extracted from this motor cluster showed similar activation to keypress on go-trials and similar deactivation to successful stop-trials for both fearful and neutral faces, but weaker activation to fearful than neutral faces during incorrect keypress on failed stops. GO = correct go trials, SI = stop-inhibit trials (successful inhibition); SR = stop-respond trials (unsuccessful inhibition). Clusters of activation are overlaid on the mean-normalized T1-weigthed structural scan from all participants.

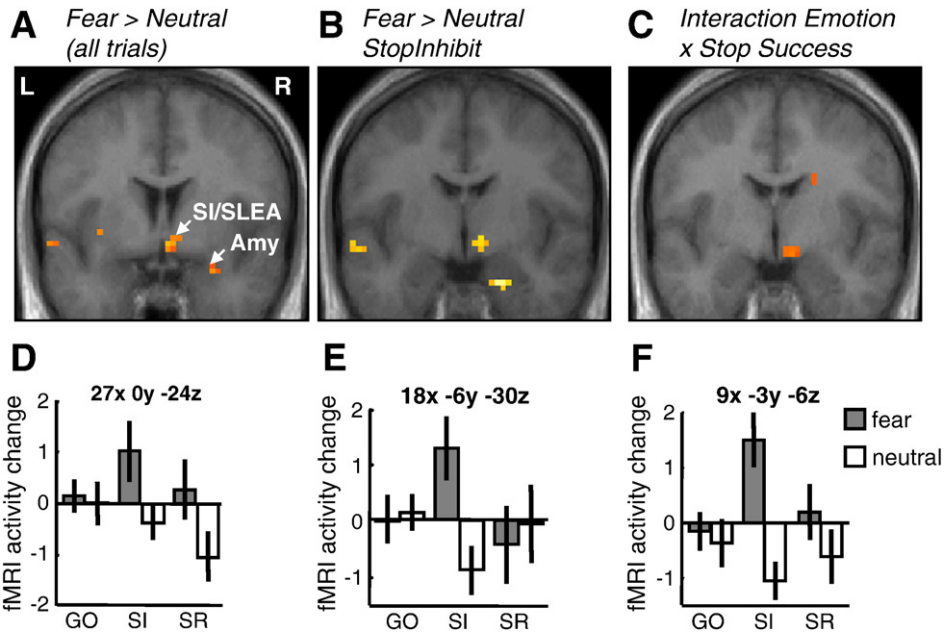

Fig. 4. Modulation of amygdala activity by emotion and motor inhibition. Different peaks were identified by different contrasts. (A) The lateral amygdala and SI/SLEA were activated when comparing fearful to neutral faces irrespective of motor response condition. (B) A more ventral peak and a similar dorsal region in SI/SLEA were activated when specifically comparing emotional StopInhibit to neutral StopInhibit. (C) Only the SI/SLEA region was found when testing for an interaction of emotion × inhibition success in a whole-brain analysis. Parameter estimates of activity extracted from activated clusters are shown for each of these regions (D: lateral peak; E: ventral peak; F: SI/SLEA), suggesting different effects of emotion and inhibition success in the different peaks, but a combined of both factors specifically implicating the SI/SLEA (and to a lesser degree the ventral subregion) rather than the lateral subregion (see main text). Clusters are overlaid on the mean-normalized T1-weigthed structural scan from all participants.

to StopRespond trials when the stop signals were paired with fearful faces (Fig. 4), but not when paired with neutral faces. These results point to a preferential role for the dorsal SI/SLEA portion of the amygdala complex (Aggleton, 2000) in the integration of emotional information with goal-relevant stop-signals, consistent with a key position of this region as one of the main output pathways of amygdala that control the expression of emotional behaviors (Davis and Whalen 2001; Liberzon and Sripada, 2008). A similar interaction between emotion and stop success was also significant (in post-hoc ROI analysis) for a more ventral region of the amygdala proper (see Fig. 4B). This could tentatively correspond to the basal nucleus where inputs from sensory (e.g. visual) areas and prefrontal areas are thought to be integrated (Aggleton, 2000).

By contrast, we note that a more lateral peak in the amygdala was found to activate to emotional faces but irrespective of stop success (showing a main effect of facial expression with no interaction with motor inhibition). Although we must remain extremely cautious when interpreting this pattern of distinct activations across amygdala subregions due to the limited resolution of fMRI, it is intriguing that this functional segregation of distinct subpeaks would be broadly consistent with anatomical studies of intra-amygdala circuitry in rodents (LeDoux, 2000; Stefanacci and Amaral, 2002), which indicate that the lateral nucleus of the amygdala is the primary site receiving emotionally relevant inputs from sensory areas, whereas the ventral/basal nucleus has dense reciprocal connections with ventro-medial prefrontal cortex that can modulate the subsequent output responses expressed through the central nucleus and SI/SLEA regions (Hariri et al., 2003; Morris et al., 2001). Moreover, in subsidiary analysis, we also found distinct pattern of functional connectivity for the lateral amygdala and SI/SLEA (see Supplemental material). However, even though our scanning parameters provided good signal within medial temporal regions (see Methods) and the distance across amygdala/extended amygdala peaks was reasonably high with respect to native and resliced voxel-sizes, such anatomical segregation in the human amygdala needs to be confirmed and further refined by appropriate studies using high-resolution techniques (Hurlemann et al., 2008).

Emotion signals in our modified stop-task also modulated activity in other brain regions known to be associated with behavioral inhibition. In particular, we found that activation of the inferior and ventral prefrontal cortex showed a distinctive pattern of interaction

Table 4
Brain regions showing a main effect of face expression.

Brain areas	L/R	*X Y Z* (MNI coordinates)			*T* value	Cluster size (voxels)
Contrast: Fear>Neutral						
Premotor cortex	L	−27	−21	54	4.20	5
Premotor cortex	L	−36	−6	60	4.66	6
Motor and premotor cortex	R	30	−18	51	5.86	7
Frontal sup.	L	−21	12	45	8.59	69
Frontal sup.	R	24	−3	66	4.77	5
Temporal sup./temporal pole	L	−54	9	−9	4.27	12
Temporal mid.	R	54	−39	0	5.01	6
Amygdala (lateral)	R	27	0	−24	4.02	9
Ventral striatum (putamen)	L	−27	9	−3	5.10	22
Ventral striatum (nucleus accumbens)	R	12	6	−6	4.77	20
SI/SLEA	R	3	0	−9	4.66	[a]
Insula	L	−33	3	−3	4.21	22

Abbreviations: SI/SLEA, substantia innominata/sublenticular extended amygdala; SMA, supplementary motor area.
[a] Belongs to the same cluster as row above.

Table 5
Regional activation during successful inhibition to fearful versus neutral faces.

Brain areas	L/R	*X Y Z* (MNI coordinates)			*T* value	Cluster size (voxels)
Contrast: StopInhibit Fear>StopInhibit Neutral						
SMA	R	9	3	54	6.35	14
SI/SLEA	R	9	−3	−6	6.06	31
Amygdala (ventral)	R	18	−6	−30	5.36	7
Insula	L	−48	0	0	5.06	6
Middle frontal gyrus	L	−30	42	15	4.56	8

Abbreviations: SI/SLEA, substantia innominata/sublenticular extended amygdala; SMA, supplementary motor area.

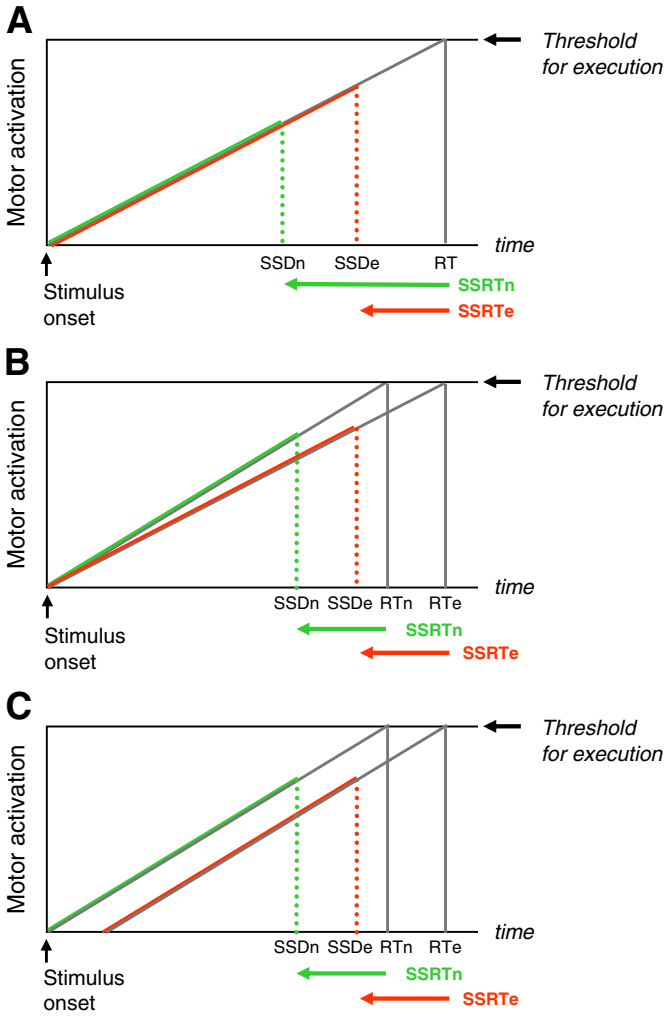

Fig. 5. Schematic illustration of the possible interactions of emotion with motor execution and inhibition. Motor activation is depicted as a linear function (continuous lines) increasing from stimulus onset until execution threshold is reached and a keypress is made with the corresponding reaction time (RT). Stop signal onset can occur with varying delays following stimulus onset (stop signal delay = SSD) but must be sufficiently early prior to RT for inhibition to be successful (stop reaction time = SSRT). Neutral and emotional trials are designated by green and red colors, respectively (and with corresponding abbreviations "n" and "e"). Average SSD for each emotion condition is indicated by doted lines. (A) If emotion cues act by enhancing inhibition efficacy after stop signal onset, average RTs may remain similar, but SSRTs should be shorter for emotion compared to neutral trials. (B) If emotion cues selectively reduce the speed of movement execution, RTs will be longer but SSRT similar for emotion compared to neutral trials. (C) Likewise, if emotion cues retard the initiation of movement, RTs will also be longer and SSRT similar for emotion compared to neutral trials. Our results support hypotheses depicted in panels B and C, but not A, while they cannot distinguish between B and C.

between stop signals and emotional signals, suggesting a functional dissociation between these two areas. A lateral region in the right IFC exhibited significant increases during stop-trials, supporting a critical role of this region in motor inhibition as proposed in many studies using go/nogo or stop paradigm with neutral or abstract stimuli (Aron et al., 2003a, 2003b, 2004; Aron and Poldrack, 2005). Importantly, however, the right IFC responses were reduced on successful stops when the face expression was fearful (Fig. 2A), as compared to successful stops with neutral faces (or unsuccessful stops), suggesting that activity in the right IFC might not be directly responsible for effective inhibition in this condition, and that other neural mechanisms are recruited to produce successful inhibition in response to emotional stimuli. Accordingly, we found concomitant increases in a more ventral region of the right IFC, abutting the lateral OFC, which arose not only during all successful stop-trials relative to failed stops, but also in response to fearful faces even when inhibition actually failed (see Fig. 2E, F). This increase to fearful faces on failed inhibition trials might reflect an automatic activation of inhibitory processes mediated by OFC in response to threatening stimuli, which could be responsible for the significantly prolonged latencies of incorrect keypresses in the emotional StopRespond condition, but insufficient to successfully withhold motor execution on these trials. Importantly, this ventral prefrontal region receives major inputs from limbic areas such as the amygdala and ACC (Cavada et al., 2000; Pandya et al., 1981). It might therefore constitute a critical node for the integration of unexpected emotional signals with cognitive goal-related information represented in more lateral prefrontal regions, and thus mediate emotional influences on executive control processes and motor function. These data converge with other imaging results in neuropsychiatry disorders (Cojan et al., 2009a) suggesting that the right IFC commonly recruited during voluntary inhibitory control is not modulated by affective factors that promote more "reflexive" or even unconscious influences of emotions on motor behavior, while the right lateral OFC is more critically implicated in such cases (Marshall et al., 1997).

Our results partly contrast with a recent study of Berkman et al. (2009) who suggested that regions in the right lateral IFC that are recruited during motor inhibition might also be involved in emotion regulation. These authors used a go–nogo task (based on face gender) and found that the right IFC activation to nogo trials correlated with reduced amygdala responses to negative emotional expression of faces, relative to the same faces in go trials. However, this study did not directly test for the effect of negative emotion on motor inhibition but rather indicated that action inhibition can automatically "spill over" into the affective processing pathways. Moreover, besides IFC, an activation in right OFC was also selectively observed for negative nogo trials, somewhat similar to our findings. Other fMRI studies using go–nogo tasks showed that motor inhibition in response to emotionally salient stimuli activate the right IFC together with subcortical limbic structures (amygdala and ventral caudate), but in conditions where emotional information was task-relevant for motor decision and stimuli of different valence were mixed (Shafritz et al., 2006; Hare et al., 2005). On the other hand, a common fronto-limbic network (including OFC and amygdala) was shown to be activated by both response suppression and emotional processing during a go–nogo task with task-irrelevant emotional stimuli (Goldstein et al., 2007). These findings are broadly consistent with the idea that limbic structures might contribute to modulate motor inhibition in emotional contexts, but do not reveal the exact neural sites where emotional signals interact with inhibitory processes. Moreover, nogo tasks do not provide a direct measure of inhibition for ongoing (already programmed) action, unlike the stop-task used here (Aron and Poldrack, 2005). Therefore, our study goes beyond previous work in several ways, allowing us not only to test for the impact of incidental threat cues on inhibitory processes, but also to compare conditions of successful and failed inhibition in different emotional contexts. More generally, our findings that activity in right lateral IFC did not correlate with stop success in emotional trials also provide novel evidence that neural systems for inhibitory control are not uniform (Dillon and Pizzagalli, 2007), and that inhibition does not depend on the right IFC alone (Hampshire et al., 2010). Accordingly, the right IFC might also serve more general functions related to attention reorienting, state switching, and monitoring (e.g. Corbetta et al., 2008; Cojan et al., 2009b; Hampshire et al., 2009).

Our fMRI results also revealed differential responses in SMA, preSMA, and several premotor regions. In particular, the right SMA-proper was not only activated during stop relative to go trials (together with other prefrontal regions and STN), but also significantly more activated during successful than unsuccessful stops when associated with emotional faces (Table 5). These findings converge

with the elegant functional and anatomical work of Aron et al. (Aron et al., 2007; Aron and Poldrack, 2006), demonstrating a tight link between IFC, SMA/preSMA, and STN for efficient motor inhibition in stop tasks. This set of interconnected regions is thought to play a critical role in programming and shifting motor plans (Aron et al., 2007; Garavan et al., 2002; Li et al., 2006; Mostofsky et al., 2003; Nambu et al., 2002). Taken together, these data suggest that the SMA/preSMA (and their projections to motor cortex and/or STN) provides a plausible neural pathway through which both emotion and stop signals may influence ongoing actions. Such modulation of SMA/preSMA could arise under the influence of IFC and OFC, but perhaps also more directly via inputs from the amygdala and SI/SLEA (Oliveri et al., 2003; Morecraft and Van Hoesen, 1998; Ferrer et al., 1987).

In conclusion, our new data suggest that incidental, task-irrelevant emotional cues interact with stop signal processing in the human amygdala (possibly in both the dorsal SI/SLEA and more ventral/basal subregions), as well as in the ventrolateral sectors of prefrontal cortex (lateral OFC). We propose that the amygdala response might contribute to the automatic effects of negative emotion on motor actions, by inhibiting the initiation or execution of movements in response to threat-related stimuli, through direct or indirect functional interactions with the SMA and interconnected motor pathways (such as STN; see Aron et al., 2007; Aron and Poldrack, 2006; Nambu et al., 2002). Partly similar pathways might be recruited by voluntary inhibition mechanisms and thus contribute to successful inhibition when stop signals are paired with threat information, as demonstrated by the selective interaction of emotion with stop success in SI/SLEA and ventral/basal amygdala. However, emotional responses in the amygdala do not modify the speed of voluntary motor inhibition, as shown by the lack of changes in SSRT. Furthermore, whereas voluntary inhibition is known to recruit the right IFC (Aron et al., 2004), successful motor inhibition to threat signals appears to depend on a more ventral region in lateral OFC which has strong bidirectional connections with amygdala (Cavada et al., 2000). Hence, the amygdala may not only trigger unspecific defensive or protective motor arrest in emotionally-significant contexts, through its connections with lower-level brainstem circuits and motor pathways (LeDoux, 2000; Applegate et al., 1983), but also contribute to modulate ongoing motor programs in higher-level cortical areas. More generally, by uncovering neural mechanisms that subserve interactions between emotion, motor behavior, and inhibitory control, our findings provide important insights for understanding the mechanisms of executive deficits that are frequently observed in psychiatric diseases and emotional dysregulations (Halligan and David, 2001; Vuilleumier, 2009; Cojan et al., 2009a, 2009b).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2011.01.027.

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