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Negative emotions facilitate isometric force through activation of prefrontal cortex and periaqueductal gray

Rebekah L. Blakemore [a,b,*], Sebastian W. Rieger [b,c], Patrik Vuilleumier [a,b,c,d]

[a] Laboratory for Behavioral Neurology and Imaging of Cognition, Department of Neuroscience, University Medical Centre, University of Geneva, Geneva, Switzerland
[b] Swiss Center for Affective Sciences, University of Geneva, Geneva, Switzerland
[c] Geneva Neuroscience Center, University of Geneva, Geneva, Switzerland
[d] Department of Neurology, University Hospitals of Geneva, Geneva, Switzerland

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ABSTRACT

Emotions are considered to modulate action readiness. Previous studies have demonstrated increased force production following exposure to emotionally arousing visual stimuli; however the neural mechanisms underlying how precise force output is controlled within varying emotional contexts remain poorly understood. To identify the neural correlates of emotion-modulated motor behaviour, twenty-two participants produced a submaximal isometric precision-grip contraction while viewing pleasant, unpleasant, neutral or blank images (without visual feedback of force output). Force magnitude was continuously recorded together with change in brain activity using functional magnetic resonance imaging. Viewing unpleasant images resulted in reduced force decay during force maintenance as compared with pleasant, neutral and blank images. Subjective valence and arousal ratings significantly predicted force production during maintenance. Neuroimaging revealed that negative valence and its interaction with force output correlated with increased activity in right inferior frontal gyrus (rIFG), while arousal was associated with amygdala and periaqueductal gray (PAG) activation. Force maintenance alone was correlated with cerebellar activity. These data demonstrate a valence-driven modulation of force output, mediated by a cortico-subcortical network involving rIFG and PAG. These findings are consistent with engagement of motor pathways associated with aversive motivation, eliciting defensive behaviour and action preparedness in response to negative emotional signals.

Introduction

According to Frijda (2010), "emotions are intimately related to action; …they are causal determinants of action". As the word *emotion* comes from the Latin *emovere* (*ex*-, away, out; *movere*, to move), it is not surprising that an intimate association between affect and action (James, 1890; Dewey, 1895; Arnold, 1960) continues to influence modern theories of emotion. Frijda (1986, 2007) posited that a major feature of emotions is 'action readiness', which is most apparent in approach or withdrawal behaviour, where one moves towards life sustaining appetitive stimuli and away from aversive threatening stimuli.

The appetitive and defensive motivation systems have been investigated extensively using behavioural methods in humans. Particular emphasis has been placed on examining how direction (approach and withdrawal) of a movement is affected by emotional priming using positive or negative stimuli (Lang et al., 1998; Chen and Bargh, 1999; Bradley et al., 2001; Hillman et al., 2004; Rotteveel and Phaf, 2004; Marsh et al., 2005; Coombes et al., 2006, 2007). However, activation of these two motivational states can prompt a wide range of adaptive coping behaviours that are not necessarily direction-specific, including interruption of ongoing motor actions (Sagaspe et al., 2011). Such a perspective is consistent with that of Frijda, where "[e]motion, by its very nature, is change in action readiness" (Frijda, 2004, 2009). For example, action tendencies without a directional component but with adaptive functions to avoid threat and preserve survival (Lang and Bradley, 2013) include: change in facial expressions or body posture elicited by valenced stimuli (Frijda and Tcherkassof, 1997; Dimberg et al., 2000); animals demonstrating attentive immobility and 'freezing' in response to threat signals or predators (Blanchard and Blanchard, 1986); as well as similar freezing-like reactions involving muscle stiffness and reduced body sway during aversive picture viewing (Bradley et al., 2001; Azevedo et al., 2005; Roelofs et al., 2010).

Neuroimaging investigations on emotional processing in humans have rarely examined specific motor behaviours. Moreover, they generally highlighted common mechanisms engaged by both the appetitive and defensive motivation systems. Passive viewing of positive and negative images activates largely overlapping brain networks involving the amygdala, lateral and ventromedial prefrontal cortex (vmPFC),

* Corresponding author at: Department of Neuroscience, University Medical Centre, University of Geneva, 1 rue Michel-Servet, 1211 Geneva 4, Switzerland. Fax: +41 22 379 5402.
E-mail addresses: rebekah.blakemore@otago.ac.nz (R.L. Blakemore), sebastian.rieger@unige.ch (S.W. Rieger), patrik.vuilleumier@unige.ch (P. Vuilleumier).

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extrastriate occipital cortex, as well as various subcortical areas and thalamus (Sabatinelli et al., 2005, 2011; Kober et al., 2008). A few structures may however differentially activate depending on the appetitive or defensive context. Viewing pleasant images produce increased activity in the temporal and cingulate cortices (Aldhafeeri et al., 2012) and the nucleus accumbens (Sabatinelli et al., 2007), while activity in periaqueductal gray (PAG) is increased by viewing negative images (Pichon et al., 2012; Hermans et al., 2013). However, many of these studies employed passive viewing paradigms or tasks requiring directional approach or avoidance responses (Roelofs et al., 2009). Research specifically investigating how emotional states affect simple motor control unrelated to movement direction is scarce.

Two recent neuroimaging studies (Schmidt et al., 2009; Coombes et al., 2012) tested the effects of emotional valence and arousal on force production, providing some insight into the neural correlates of emotion-modulated motor behaviour. Coombes et al. (2012) used a pinch-grip task in which participants were trained to produce force pulses to a consistent level while viewing affective images. As expected, force performance was similar among the unpleasant, pleasant, and neutral conditions. However, neuroimaging results showed increased activity and connectivity between the dorsomedial prefrontal (dmPFC) cortex and contralateral premotor cortex for the highly arousing conditions compared with the neutral condition. On the other hand, Schmidt et al. (2009) reported increased force output associated with higher activity in bilateral ventrolateral prefrontal cortex (vlPFC) and primary motor cortex following the presentation of highly arousing images in a maximal power-grip force task. These partly diverging results may be due to differences in task requirements; dmPFC or vlPFC may differentially respond to emotional cues when force production is constant or variable, respectively. Nonetheless, both studies reveal a significant arousal-driven effect on brain activity and point to the prefrontal cortex as a crucial neural substrate underlying the integration of motor and emotional processes. These studies however, used tasks involving voluntary contractions generated over a brief time period. Thus little is known about the neural mechanisms underlying how affective state modulates more sustained force production, a functional motor control process inherent in many everyday activities.

To further elucidate cortical regions involved in the interaction of the emotion and motor systems, we conducted a functional neuroimaging study specifically examining how isometric precision-grip force control is affected by emotional state. To this end, we designed a task similar to that of Coombes et al. (2008) that included a broad range of arousing and valenced visual stimuli. Participants were required to produce grip force at 10% of their maximum force as accurately as possible. Visual feedback of force output was presented for a short time interval at trial onset, but then occluded and replaced with high arousing (pleasant or unpleasant), low arousing (neutral) or blank images. In line with previous motor control literature, it was hypothesised that force output would decay over time when feedback was removed (Vaillancourt and Russell, 2002; Vaillancourt et al., 2003). Importantly, based on behavioural findings by Coombes and colleagues (Coombes et al., 2008, 2011; Naugle et al., 2010, 2012), it was hypothesised that the magnitude of force decay would be attenuated during viewing of highly arousing images, relative to neutral or blank images. This prediction accords with observed alterations of motor behaviour in emotional contexts, which constitute adaptive mechanisms promoting survival and preparation for action. Furthermore, in light of the converging findings identifying the prefrontal cortex as a key region involved in emotional-modulated motor output and in memory guided force production (Vaillancourt et al., 2003), we anticipated increased activity in prefrontal regions during the highly arousing conditions. In particular we hypothesised involvement of vlPFC as this region has been highlighted in other studies on emotion-motor interactions where force output was modulated (Schmidt et al., 2009; Sagaspe et al., 2011), although an activation in dmPFC might also occur if force is held constant (Coombes et al., 2012). We also expected activations in subcortical structures of basal ganglia, thalamus, and brainstem associated with motor control.

Material and methods

Participants

Twenty-two healthy volunteers (25 ± 4 years; 11 females) participated in this study. All participants were right-handed as confirmed by the Edinburgh Handedness Inventory (Oldfield, 1971) with a mean laterality quotient of 83%, and were included if they had no upper limb pain or injuries, no prior or current neurological or psychiatric disorder, no history of drug use, normal hearing and speech, normal or corrected-to-normal vision and no contraindications to magnetic resonance imaging (MRI) scanning (claustrophobia, pregnancy, metallic implants). Participants completed the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983). Mean scores for the anxiety (6.3 ± 3.8) and depression (3.1 ± 2.7) sub-scales were considered to be within normal limits. Participants provided written informed consent to all procedures and received monetary compensation. This study was approved by the Geneva University and Hospital ethics committee, in accordance with the Declaration of Helsinki.

Apparatus and stimuli

Participants produced a sustained isometric precision-grip contraction by pinching a force-measuring device between their thumb and index finger. A commercially available load cell (LCM 4218, LCM Systems Ltd., UK; range 100 N) was adapted for use within a magnetic resonance (MR) environment, such that its aluminium construction was encapsulated within a plastic shell (5.5 cm wide). The load cell was connected to a differential bridge amplifier with reference voltage output (DA100C, BIOPAC Systems Inc., USA; DC-300 Hz, gain 200) in a Wheatstone bridge configuration. This amplified the output of the load cell (which was linearly proportional to the force produced) 200-fold and applied low-pass filtering at 300 Hz prior to analogue-to-digital conversion outside of the MR environment. The resulting force signal was continuously acquired using a 12-bit portable data acquisition module (Advantech Co., Ltd, USA) and recorded within Matlab (Mathworks Inc., USA), sampled at 100 Hz (resolution ± 0.036 N), allowing real time feedback of force output to be displayed back to the participant in the scanner.

Respiratory effort was synchronously recorded together with the force output using a respiration belt (TSD221-MRI, BIOPAC Systems Inc., USA) positioned around the participants' thorax and BIOPAC's MP150 data acquisition system and AcqKnowledge software. Because both emotion and force production can induce changes in breathing (Homma and Masaoka, 2008), and thus create artifacts in MRI data (Birn et al., 2009), we recorded respiration to retrospectively correct for these effects. Gaze direction and pupillary size were also synchronously and continuously recorded at 60 Hz with an MRI compatible eye tracker (EyeTrac 6, Applied Science Laboratories, USA). Calibration of eye gaze position was performed using a standard 9-point calibration method prior to scanning.

The visual stimuli were presented using Cogent, a Matlab toolbox, displayed through a LCD projector onto a computer screen (1024 × 768 resolution; 60 Hz refresh rate) and viewed via a mirror positioned above the participants' eyes. A total of 96 images[1] were selected from

[1] Pleasant: 1650, 1710, 2300, 2347, 2389, 4220, 4599, 4641, 4643, 4645, 4650, 4653, 4660, 5260, 5450, 5480, 5700, 5825, 5833, 5910, 7405, 7451, 7499, 7501, 8030, 8163, 8190, 8206, 8380, 8492, 8500, 8501. Unpleasant: 2703, 2751, 2800, 2811, 3120, 3131, 3225, 3400, 3530, 6212, 6230, 6563, 7135, 9000, 9075, 9185, 9295, 9301, 9322, 9340, 9410, 9413, 9414, 9600, 9622, 9800, 9909, 9920, 9921, 9925, 9930, 9940. Neutral: 2036, 2038, 2102, 2200, 2210, 2221, 2393, 2396, 2397, 2411, 2513, 2850, 2870, 2890, 5510, 6150, 7000, 7003, 7004, 7010, 7012, 7017, 7031, 7041, 7056, 7170, 7175, 7179, 7233, 7255, 7493, 9260.

the International Affective Picture System (IAPS; Lang et al., 2008), comprising three emotional conditions (pleasant, unpleasant, neutral) based on their normative valence and arousal ratings (where, 1 = pleasant/low arousal; 9 = unpleasant/high arousal). Valence was significantly differentiated ($p < .001$) across each condition (pleasant, 2.7 ± 1.6; unpleasant, 7.8 ± 1.4; neutral, 5.0 ± 1.2), while arousal was matched between the pleasant and unpleasant conditions, but significantly differed ($p < .001$) from the neutral condition (pleasant, 6.0 ± 2.2; unpleasant, 6.1 ± 2.2; neutral, 2.9 ± 1.9). Each condition contained 32 unique images (1024 × 768 pixels) depicting an equal number of social and non-social scenes, included a range of image categories, and was exactly matched for luminance, contrast, and spatial frequency (Delplanque et al., 2007).

Experimental design and procedure

Participants completed one experimental session consisting of a maximum voluntary contraction (MVC) task performed outside the scanner, an emotional force control task performed during neuroimaging acquisition, and ratings of emotional stimuli (outside the scanner). Participants were provided written and verbal instructions and were familiarised with all three tasks at the beginning of the session.

The MVC task was used to determine, for each individual, the maximum isometric force that could be generated when pressing on the force device between the thumb and index finger using a precision-grip. Each hand was tested separately, and the order of hand was randomised and counterbalanced across participants. Participants held the force device with their left or right hand in a pronated position and resting in their lap. The other hand rested comfortably down the side of their body. This position was identical to the position adopted for the emotional force control task while participants lay supine inside the scanner. To begin each trial, a 3 second fixation cross appeared on the screen, followed by the word "ready" ("prêt" in French) displayed for 3 s. At the onset of the word "PUSH!" ("PRESSER!"), participants pressed the force device as hard as they could for 6 s. Verbal encouragement was provided by the experimenter. Three MVCs were performed with a 30 second rest between each trial. The maximum force for each trial was recorded as the mean of the greatest 10 force samples obtained over the 6 s. The grand mean MVC value for each hand was calculated as the mean of these three trials (Vaillancourt and Newell, 2003). The MVC values for each participant were then used as reference values for the target force in the emotional force control task. The MVC for the right (dominant) hand (56.0 ± 11.7 N) was significantly greater than left hand MVC force (49.6 ± 13.1 N; $t_{(21)} = 4.1$, $p = .01$), as expected in right-handed individuals.

Following the MVC task, participants completed 10 practice trials of the emotional force control task before entering the scanner. This task was adapted for neuroimaging from the paradigms used by Coombes and colleagues (Coombes et al., 2008, 2011; Naugle et al., 2010, 2012). Participants were instructed to continuously press on the force device at 10% of their maximum force (see Fig. 1). Each trial began with a fixation cross presented in the centre of the screen for a variable period (5–7 s). Two bars were then displayed on the screen, which indicated the initiation of force production. A white stationary horizontal bar located in the centre of the screen represented the target force, set at 10% of the participants' MVC force. A black bar, located at the bottom of the screen, represented the amount of force currently being produced. This bar could move vertically as participants pressed on the force device, thereby providing direct visual feedback of their force production. Participants were instructed to alter their force output to match the black bar with that of the white target bar. Following this feedback period (variable duration; 5–7 s) participants were presented with one of five conditions (for 6 s): Condition 1 (feedback) was a control condition in which the black and white bars remained on the screen for the remainder of the trial, providing continuous visual feedback of force output. In condition 2 (blank), the white bar remained on the screen but the black bar disappeared, occluding feedback. In conditions 3–5, visual feedback was also removed and the screen was entirely

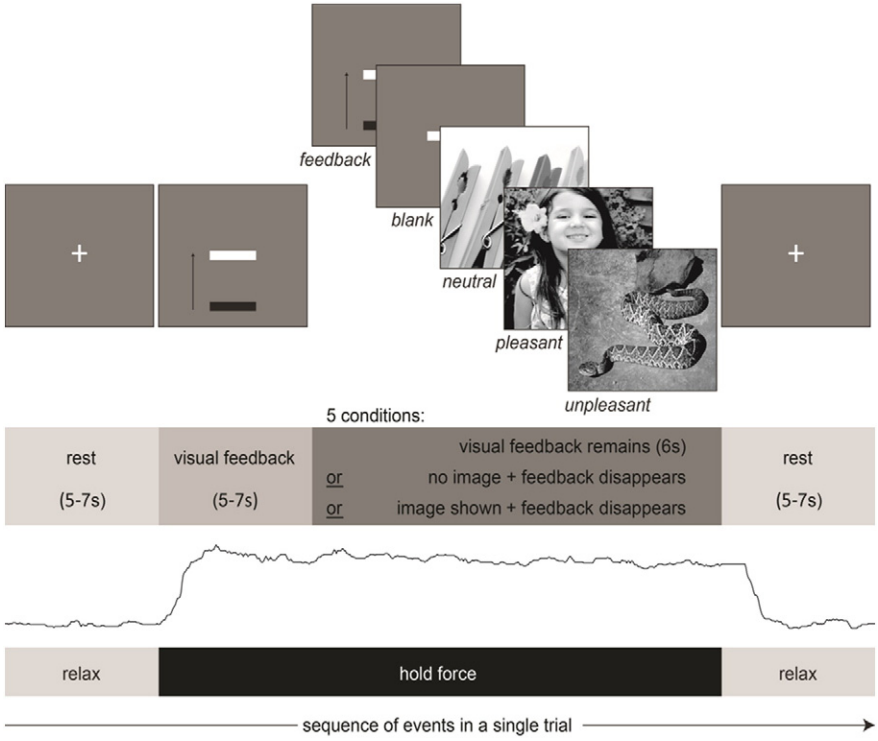

Fig. 1. Emotional force control task. The sequence of screens displayed for each trial is shown from left to right. A trial began with the presentation of a white bar (10% MVC force target level) and a black bar (actual force output) indicating to the participants to initiate force production with a precision-grip. Using this feedback, participants had to adjust their force output to match the target level as accurately as possible. Following a variable delay, one of five conditions was presented for 6 s: either feedback remained on the screen, feedback disappeared with no image presented, or feedback was replaced with a pleasant, unpleasant, or neutral IAPS image. An example force trace from a single trial is shown.

replaced with an IAPS image that was either high in arousal (condition 3, pleasant; condition 4, unpleasant) or low in arousal (condition 5, neutral). In all conditions, participants were instructed to maintain 10% force output as accurately and constantly as possible throughout the entire trial, until the onset of the next fixation cross that indicated relaxation (inter-trial interval).

Participants completed 144 trials of the emotional force control task, distributed as four blocks (~10 min each) of 36 trials (2 blocks for each hand; 72 trials per hand). The block order alternated between each hand and was randomised for each participant. A rest period was provided after completion of the first two blocks, enabling acquisition of the anatomical scan. Within each block there were 4 trials for condition 1, and 8 trials each for conditions 2–5, presented in a pseudo-random order.

After scanning, a picture rating task was completed, where the 96 IAPS images were presented for a second time to obtain subjective ratings of valence and arousal. A computerised version of the 9-point Self-Assessment Manikin (SAM) scale (Bradley and Lang, 1994) was used. Following a fixation cross, each image was displayed first with the SAM-valence scale beneath. Participants rated valence by using the keyboard left and right arrow-keys that moved a cursor along the 9-point scale (1 = pleasant [agréable], 9 = unpleasant [désagréable]) without any time limit to answer. After confirming the rating, the valence scale was superimposed by the SAM-arousal scale; participants rated arousal in the same manner as valence (1 = low arousal [peu éveillé], 9 = high arousal [très éveillé]), and could advance to the next trial (image) at their own pace.

Behavioural data analysis

The force time series data recorded by Matlab were digitally filtered using a one-dimensional median filter (window of 20) to remove the MR gradient interference from the signal. The signal for each trial was epoched into 7 second segments, beginning 1 s before the onset of each condition (used to baseline correct the signal) until the end of image presentation, followed by further segmentation into seven 1 second epochs for data analysis. For each 1 second epoch, the mean force (expressed as a percentage of MVC) and coefficient of variation (CV; standard deviation/mean force) were calculated for each condition and hand, for each participant. The CV was included to quantify variability of force taking into account differences in the absolute magnitude of force. For the emotional stimuli ratings, the mean and standard deviation for subjective valence and arousal were calculated for each condition for each participant.

For statistical analyses, we first determined whether performance was similar among conditions in the 1 second period before image onset when visual feedback was provided for each trial (epoch 0; baseline). A two-factor repeated-measures analysis of variance (ANOVA) was performed to examine the effects of condition (pleasant, unpleasant, neutral, blank, feedback) and hand (left, right) on mean force and CV. Next, we examined the mean force and CV during each condition (epochs 1–6) by performing two separate two-factor repeated-measures ANOVA for condition × hand. Subjective valence and arousal were each analysed using a one-factor repeated-measures ANOVA to compare emotional conditions (pleasant, unpleasant, neutral). To explore whether emotional reactivity could predict the magnitude of force output, we conducted a multiple regression analysis with the subjective valence and arousal ratings for each trial as explanatory variables, and force as the outcome variable. The coefficients for each participant were obtained and the significance tested using one-tailed t-tests. All analyses were conducted using SPSS 22 (IBM SPSS Inc.), and the alpha set at .05. For the repeated-measures ANOVA analyses (including analyses of beta estimates obtained from the functional MRI (fMRI) data; see Section 2.7 below), the Greenhouse-Geisser correction was used when the assumption of sphericity was violated, and the Bonferroni degrees of freedom correction was applied for all multiple pairwise comparisons when a significant F statistic was obtained.

Eye-tracking data processing and analysis

Post-processing of pupil dilation and eye movement data (raw coordinates) were performed using ILAB 3.6 (Gitelman, 2002) and custom-written software. The data were filtered to remove blinks and other artifacts, and then epoched into 7 second segments, beginning 1 s before the onset of each condition until the end of image presentation. Trials were rejected if more than 15% of data were missing after blink correction; data for one participant were discarded due to excessive eye movement artifacts. For each trial and emotional condition, four parameters were extracted: pupil dilation, number of fixations, total duration of fixations, and scanpath length. Pupil responses were baseline corrected over the 1 second period before image onset and waveforms averaged. Viewing IAPS images typically results in an initial decrease in pupil diameter due to the light reflex, that lasts between 0.6 and 1.6 s after picture onset, followed by an increase in pupil diameter that is modulated by emotional content (Bradley et al., 2008). This increase in pupillary response rises steadily towards baseline and is sustained until the end of the viewing interval. Mean pupil dilation was therefore calculated from an average over the 2–6 second period post image onset (avoiding confounds due to the light reflex), consistent with other studies using IAPS images (Bradley et al., 2008; Hermans et al., 2013; Henderson et al., 2014). We found no affective modulation of the amplitude of the initial light reflex. Fixations were defined as the eyes staying fixed within a 0.5 × 0.5° area for at least 100 ms; the total cumulative duration of fixations was computed over the 6 second period of image presentation. Scanpath length was calculated as the sum of the distance between successive fixations. Each measure was then analysed using a one-factor repeated-measures ANOVA to examine the effect of emotional condition (pleasant, unpleasant, neutral). Planned comparisons were performed to determine differences between conditions using one-tailed paired t-tests.

Imaging data acquisition and processing

Magnetic resonance imaging was performed with a 3 T whole body MRI scanner (Trio TIM, Siemens, Germany) and 32 channel head coil. Earplugs were used to attenuate scanner noise and head movement was restricted using memory foam pillows. Functional images were acquired using a fast multiplexed echo-planar image (EPI) sequence (Feinberg et al., 2010) optimised for blood-oxygen-level dependent contrast (TR = 650 ms, TE = 30 ms, flip angle = 50°, 36 interleaved slices, 64 × 64 pixels, isotropic voxel size of 3 mm^3, and 3.9 mm slice spacing). The multiband acceleration factor was 4 and parallel acquisition technique (PAT) was not used. Structural images were acquired with a T_1-weighted 3D sequence (MPRAGE, TR = 1900 ms, TE = 2.27 ms, TI = 900 ms, flip angle = 9°, 192 sagittal slices, voxel dimensions = 1 mm isotropic, 256 × 256 pixels, PAT factor = 2).

EPI images were preprocessed and analysed using statistical parametric mapping software SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). To avoid T_1 saturation effects, image acquisition for each run started after ten dummy volumes had been recorded. Functional images were spatially realigned to the mean of the images, coregistered to the anatomical scan, spatially normalised to the standard Montreal Neurological Institute (MNI) EPI template, and spatially smoothed with an isotropic 8 mm full-width at half-maximum Gaussian kernel (Friston et al., 1995).

Imaging data analysis

Following image preprocessing, two complementary analyses were performed on the functional images: categorical whole-brain voxelwise analyses and parametric modulation analyses. In all first-level linear regression models, we implemented physiological noise modelling to model noise arising from respiratory fluctuations (Brooks et al., 2013). Nuisance regressors were created from the respiration data using

RETROICOR (Glover et al., 2000) and Respiration Volume per Time (Birn et al., 2006, 2008). Nuisance variables for each run therefore included six parameters for head motion estimated during realignment and nine respiration regressors.

For the whole-brain voxelwise analyses, data for each participant were concatenated across runs (2 runs for movements of each hand) in a single general linear model. Each run contained five separate regressors (for the five conditions), corresponding to the onset of target (i.e., force level bar) presentation, and convolved with a standard simulated hemodynamic response function. From this model, we generated parameter estimates of activity at each voxel, and the associated statistical parametric maps (SPM) for each experimental condition versus rest. A group analysis was performed on the ten contrast images (5 conditions × 2 hands) generated from each participant using a flexible factorial model. This model allowed for comparisons among conditions and between hands; however because we found no significant between-hand difference (or condition × hand interaction) for mean force or at the neural level[2] (see Sections 3.1.1 and 3.3.1, respectively), our results for all subsequent fMRI analyses were pooled over hand. The primary focus of whole-brain statistical analyses were to identify regions showing increased activity during the highly arousing conditions compared with the neutral condition (unpleasant and pleasant > neutral), and greater activity during the unpleasant compared with the pleasant condition (unpleasant > pleasant), and vice versa (pleasant > unpleasant). The resulting t-maps were corrected for multiple comparisons ($p < .05$; family-wise error [FWE] correction) and all significant clusters contained a minimum of 10 voxels.

Next we performed two parametric modulation analyses to specifically identify brain areas mediating the effect of emotion on the control of force production, using an approach previously described by Pessiglione and colleagues (Pessiglione et al., 2007; Schmidt et al., 2012). In both analyses, the first-level design matrices included two categorical regressors for each run: one containing trials from the pleasant, unpleasant and neutral conditions (emotional trials), and the other containing trials from the blank and feedback conditions. Each trial was modelled with one onset corresponding to the onset of target presentation (force level bar). Five different measures were added as parametric modulators. The first linear regression model included three parametric modulators: subjective valence and arousal ratings (for the regressor modelling the emotional trials), plus the actual force produced (for both regressors). The second model included two parametric modulators for each emotional trial, representing interaction effects of interest. Here we included variables obtained by multiplying force production by either the subjective valence or arousal rating (valence*force, arousal*force). For each model, the regressors were convolved with a standard simulated hemodynamic response function, and the regression coefficients of the linear contrasts for each modulator were computed for each participant. Random-effect group analyses were conducted on the subsequent contrast images using one-sample t-tests. Significant activations surviving a threshold of $p < .001$ (uncorrected) were retained, and all significant clusters reported contained a minimum of 50 voxels ($p < .05$; FWE corrected at the cluster level unless stated otherwise).

To examine activation levels in the significant clusters obtained from the parametric modulation analyses, we extracted beta estimates for each emotional condition from five regions of interest (ROI). ROIs were defined using the global maxima cluster of interest (Friston et al., 2006; Schmidt et al., 2009) identified for each parametric modulator in key brain regions: valence, right inferior frontal gyrus (rIFG) [Brodmann area - BA 44]; arousal, amygdala; force, cerebellum; valence*force, rIFG [BA 46]; arousal*force, PAG. Activity within each ROI was estimated for each of the six linear contrasts (3 emotional conditions × 2 hands) generated from the whole brain voxelwise analysis using Marsbar (http://marsbar.sourceforge.net). Mean beta estimates for each region and condition were extracted at the individual level and analysed using separate one-factor repeated-measures ANOVA for each ROI. These functional ROIs were defined with contrasts orthogonal to the emotion effects investigated in our subsequent ANOVAs, by identifying those voxels that correlated with each of the parametric modulators above (Friston et al., 2006). To further ensure location specificity, we also defined anatomical ROIs using masks from the automated anatomical labelling (AAL) atlas (Tzourio-Mazoyer et al., 2002) for all relevant brain areas reported below (e.g., IFG, amygdala, cerebellum), except for the PAG that was hand-drawn using MRIcron (www.mccauslandcenter.sc.edu/mricro/mricron) on individual *T1*-weighted images following Duvernoy's atlas (Naidich et al., 2009). Because all results were similar to those obtained with functional ROIs, we do not report these data in detail.

Results

Behavioural

Mean force and coefficient of variation

Fig. 2A illustrates the mean force production in each condition for each 1 second epoch (beginning 1 s before the onset of each experimental condition), over the course of the trial. Analysis of the last 1 second epoch in which the target bars were displayed (epoch 0) revealed that initial motor output was similar across all conditions and hands ($p > .05$; overall mean force, 9.9 ± 0.4%). This result indicates participants successfully utilised the visual feedback to adjust their force to the 10% MVC target level before the onset of the experimental conditions; thus any differences in performance among conditions are not attributable to differences in baseline force production.

As seen in Fig. 2A, when feedback remained present throughout the entire trial, force output remained relatively consistent at the required target level. As predicted, force output decayed over time when feedback was occluded. Crucially however, this decay was modulated by the emotional content of the images. A slower decrease in force output was specifically seen in the unpleasant condition and persisted over the entire duration of image presentation. These observations were confirmed by statistical analyses, with a significant main effect of condition ($F_{(4,204)} = 77.4$, $p = .001$). Mean force was larger for the feedback condition compared with when feedback was occluded ($p < .001$), and larger for unpleasant images ($p < .000$) compared with pleasant and neutral images and the blank condition (Fig. 2B). There was no difference in force output among the blank, pleasant, and neutral conditions. This result provides evidence against a possible interpretation that the IAPS images were merely distracting, diverting attention away from the force control task. If this was the case, we would have expected the force decay to be greater for neutral, pleasant and unpleasant conditions compared with the blank condition. Finally, there was no significant main effect for hand or condition × hand interaction on the magnitude of force, indicating a consistent effect of condition regardless of the hand performing the precision-grip.

The coefficient of variation (CV) showed main effects of condition ($F_{(2,315)} = 8.0$, $p = .001$) and hand ($F_{(1,131)} = 41.8$, $p = .001$). CV was smaller ($p < .05$) when participants had visual feedback (3.7 ± 1.7%) compared with the emotional conditions, but with no difference among emotional conditions (Fig. 2C). Additionally, CV was smaller ($p < .001$) for the right (3.5 ± 1.8%) than the left hand (4.4 ± 2.8%).

Emotional stimuli ratings

The subjective ratings of IAPS images completed after scanning were analysed to determine the participants' affective experience. These post-scan ratings were similar to the normative IAPS ratings, indicating the images elicited the expected emotional response. A significant effect of condition was found for both valence ($F_{(1,27)} = 227.8$, $p = .001$, Fig. 2D) and arousal ($F_{(1,30)} = 23.6$, $p = .001$; Fig. 2E). Participants

[2] A between-hand comparison of cortical activity revealed differential activations in primary motor cortex, which were not modulated by emotion conditions.

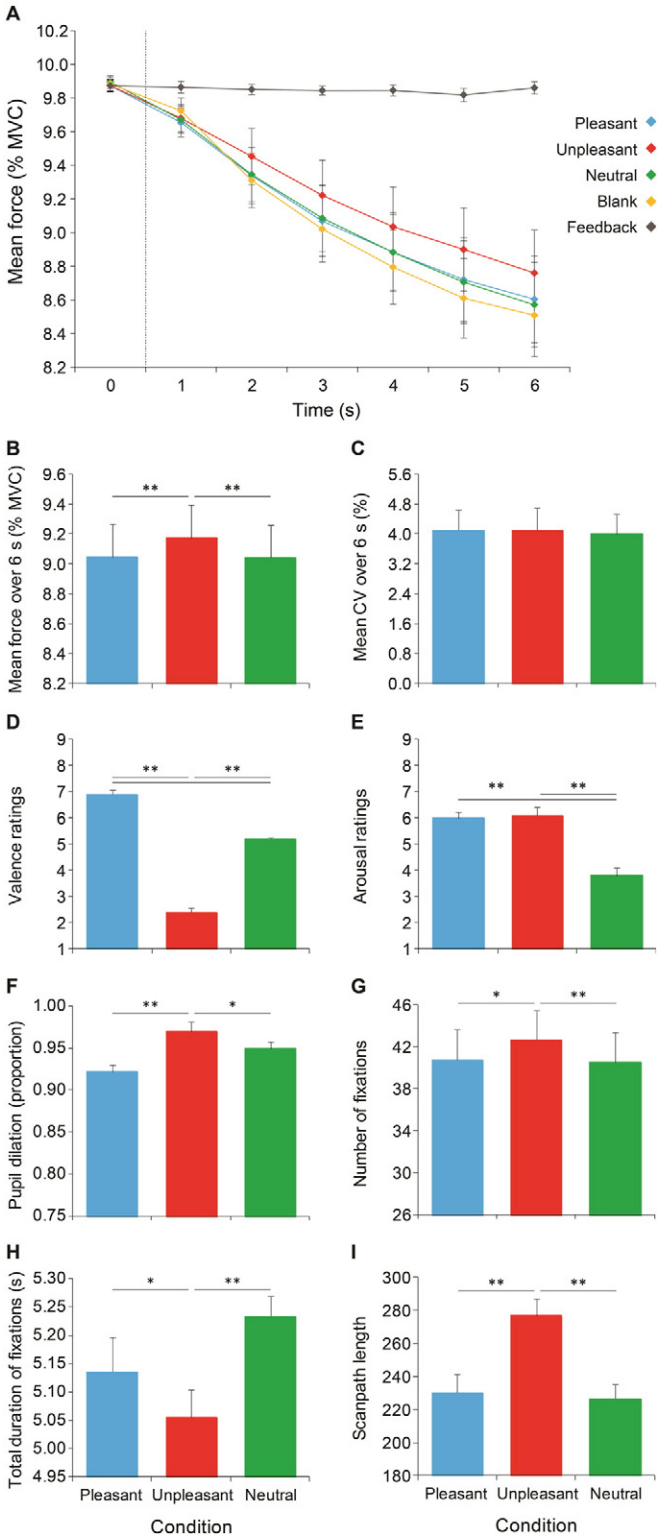

Fig. 2. Behavioural data. *A*, Mean force (expressed as % MVC) for each 1 second epoch for each condition, beginning 1 s before the onset of each condition (time = 0). *B*, Mean force (% MVC) and *C*, mean coefficient of variation, calculated over the 6 s of image presentation. *D*, Mean valence and *E*, mean arousal calculated from the post-scanning subjective ratings for each emotional condition. *F*, mean pupil dilation over 2–6 s of image presentation, expressed as a proportion of the baseline (computed over 1 s immediately before image presentation). *G*, number of fixations; *H*, total cumulative duration of fixations (seconds); and *I*, total scanpath length, all computed over 6 s of image presentation. Data from eye-tracking measures are based on 21 participants. Error bars in each graph represent standard error, $^{*}p < .05$, $^{**}p < .001$.

rated unpleasant images as more negative than neutral and pleasant images, and pleasant images as more positive than neutral images ($p < .001$). Additionally, the neutral images were rated as less arousing ($p < .001$) than unpleasant and pleasant images, which were not different.

We also performed multiple regression analysis of the individual subjective ratings against force. This revealed significant regression coefficients across participants for valence ($r = .08$, $t_{(21)} = 2.9$, $p = .004$) and arousal ($r = .02$, $t_{(21)} = 2.6$, $p = .009$); as the arousal and negativity of the image increased, the decay in force was attenuated. This result indicates that the individual subjective appraisal of the images' affective content was a key component in predicting the change in force control, i.e., the intensity of emotional reactivity was directly related to the modulation of overt motor output.

Pupil dilation and eye movements

Change in pupil dilation and eye movements while participants viewed the emotional images were assessed to index autonomic arousal and the degree of processing of emotional information, respectively. Significant main effects of condition were found for pupil dilation ($F_{(1,30)} = 15.79$, $p = .001$, Fig. 2F), number of fixations ($F_{(2,31)} = 4.97$, $p = .019$, Fig. 2G), total duration of fixations ($F_{(2,40)} = 10.97$, $p = .001$, Fig. 2H), and scanpath length ($F_{(2,40)} = 38.28$, $p = .001$, Fig. 2I). Pupil dilation was larger for the unpleasant condition compared with the pleasant and neutral conditions ($p < .05$). Eye movement analyses revealed a greater number of fixations ($p < .05$), but with a smaller total duration ($p < .05$), as well as a greater total scanpath length ($p < .001$) for the unpleasant than the pleasant and neutral images. Together these findings indicate that unpleasant scenes had significant impact on both autonomic responses and motor eye movements, consistent with a state of higher alertness elicited by negative emotional content.

Imaging

Whole brain voxelwise analysis

To examine regions significantly activated while participants produced an isometric force contraction and viewed emotional images, we contrasted the pleasant and unpleasant conditions together against the neutral condition (Table 1). As predicted, we found increased activity in emotional processing networks including large clusters centred on left temporal lobe that encompassed the middle occipital gyrus, fusiform gyrus, amygdala, thalamus (pulvinar), right inferior temporal gyrus, and right lingual gyrus, in addition to left precuneus and right superior parietal lobule. Furthermore, as hypothesised, we found increased activity in the vlPFC (specifically rIFG), but also in the right premotor cortex, bilateral vmPFC, and right dmPFC (lying more superior and lateral than dmPFC activity reported by Coombes et al. (2012), however we note some overlap in activation with their dmPFC cluster [conjunction analysis comparing arousing vs neutral images; x = 1.2, y = 53.8, z = 29.4] at a lower threshold of $p < .001$, uncorrected). Activations in rIFG predominated in the gyrus itself but extended slightly dorsally into the inferior frontal sulcus.

Next, we examined activations during force production in the presence of unpleasant relative to the pleasant images, as our behavioural results showed a selective valence-driven facilitation of force control for the unpleasant condition (Table 1). Here we also found an increase in rIFG and medial frontal gyrus, indicating that the effect in rIFG was not caused only by globally arousing stimuli. Additional significant activations were also found unique to the unpleasant condition including in the amygdala, cingulate gyrus, fusiform gyrus, cerebellum, and the PAG. No significant clusters were found for the reverse contrast (pleasant > unpleasant).

These data show that emotional contexts activate several brain areas associated with emotional appraisal and regulation, with distinctive increases in the unpleasant condition that involved motor and executive

Table 1
Whole brain voxel wise activations. Significant clusters and their MNI coordinates (centre of mass), voxels, and *Z*-score for the two primary contrasts obtained while participants produced force and viewed emotional visual stimuli: main effect of emotion (arousal; pleasant and unpleasant > neutral); effect of negative valence (unpleasant > pleasant).

	MNI coordinates (mm)			Effect of arousal U + P > N		Effect of valence U > P	
	x	y	z	Voxels	*Z*-score	Voxels	*Z*-score
Frontal lobe							
R inferior frontal gyrus	54	38	4	97	7.10		
R inferior frontal gyrus	36	32	−20	104	6.77		
R inferior frontal gyrus	39	32	−17			465	7.82
R inferior frontal gyrus	39	14	25	16	5.11		
R middle frontal gyrus	48	−1	43	40	5.37		
L medial frontal gyrus	−9	47	−14	13	4.93		
R medial frontal gyrus	6	38	−17	10	4.90		
R medial frontal gyrus	6	41	46			187	7.63
R superior frontal gyrus	6	56	37	49	5.22		
L insula	−27	20	−14			103	6.08
Temporal lobe							
L middle temporal gyrus	−51	−67	7	8133	65535		
L fusiform	−24	−70	11				
L middle occipital gyrus	−42	−85	13				
L amygdala	−18	−4	−17				
R pulvinar	18	−28	−2				
R lingual gyrus	3	−79	−5				
R inferior temporal gyrus	42	−55	−14				
R middle temporal gyrus	51	−1	−23	45	5.95		
Parietal lobe							
L precuneus	0	−49	49	95	6.21		
R superior parietal lobule	33	−49	61	59	5.78		
Limbic lobe							
R amygdala	18	−1	−20			34	5.87
R middle cingulate gyrus	6	−1	34			13	5.58
Cerebellum							
L posterior lobe Crus I	−18	−76	−32			16	5.24
Occipital lobe							
L fusiform gyrus	−27	−67	−11			396	7.54
R fusiform gyrus	27	−49	−14			205	7.10
Midbrain							
R periaqueductal gray	9	−25	−8			350	7.34

Clusters listed had a minimum of 10 voxels ($p < .05$; FWE corrected). Coordinates of significant peak-level activations ($p < .05$; FWE corrected) within the large left temporal cluster are also listed (with *Z*-scores identical to the primary cluster). No significant clusters were found for the pleasant > unpleasant contrast. P, pleasant; U, unpleasant; N, neutral; L, left; R, right.

Table 2
Main activations for each parametric modulator. Significant clusters and their MNI coordinates (mm; centre of mass), voxels, and *Z*-score for positive correlations with each parametric modulator obtained while participants produced force and viewed emotional visual stimuli.

	MNI coordinates (mm)			Effect of each parametric modulator	
	x	y	z	Voxels	*Z*-score
Negative valence					
R inferior frontal gyrus [BA 44]	51	14	28	327	4.97
Arousal					
R amygdala	21	−1	−23	3854	5.10
L medial frontal gyrus	−3	50	−5	773	4.94
L middle temporal gyrus	−54	−64	1	689	4.94
R cerebellum anterior lobe nodule	12	−58	−38	133	3.97
R superior frontal gyrus SMA	6	14	55	125	3.88
Force					
R cerebellum pyramis	6	−79	−32	277	3.44
*Negative valence*force*					
R Inferior frontal gyrus [BA 46]	51	29	16	157	4.25
*Arousal*force*					
L midbrain (PAG)	−6	−31	−17	4486	5.25
L superior frontal gyrus	−6	59	1	342	5.14
R fusiform gyrus	39	−49	−23	81	4.95
R anterior cingulate cortex	6	26	16	111	4.53
R thalamus	6	−7	1	66	4.30

All activations surviving a threshold of $p < .001$ (uncorrected) were retained. Clusters listed had a minimum of 50 voxels ($p < .05$; all FWE corrected at the cluster level except cerebellar activation which was uncorrected at the cluster level). No significant clusters were found for the reverse correlations of positive valence or positive valence*force. L, left; R, right.

control. However, given that these effects could potentially reflect neural processes involved in the production and maintenance of force, in emotional visual processing, or a combination of both, it is difficult to disentangle the contribution of these areas to the specific (e.g., motor) processes. Therefore, to further identify brain regions demonstrating a specific valence-, arousal-, and/or force-related modulation of activity, we conducted parametric modulation analyses on the fMRI data (see Pessiglione et al., 2007; Schmidt et al., 2012).

Parametric modulation analysis

We searched for brain regions showing a positive correlation between change in brain activity and individual parametric variables associated with different components of the task, each considered separately (Table 2, Figs. 3A, 4A). Negative valence ratings were selectively correlated with increase in the rIFG [BA 44]. No significant effect was found for the reverse correlation using positive valence ratings. Higher emotional arousal was correlated principally with the right amygdala, but also additional areas in temporal cortex and medial prefrontal cortex, including the right supplementary motor area (SMA), as well as the cerebellum. Finally, the production of force closer to the target level, across all emotional conditions, was associated with increased activity of the cerebellum.

However, our main interest concerned how the different emotional contexts modulated neural pathways engaged by force production. To more specifically identify regions mediating the effects of valence and high arousal on force control, we defined specific interaction modulators by computing the multiplicative regressors of valence*force and arousal*force, which were then used as parametric modulators in a second analysis. Similar to the effect of negative valence alone described above, the interaction of negative valence*force correlated with increased activity in rIFG [BA 46]. Again, no significant effect was found for the reverse correlation testing for an interaction of positive valence*force. On the other hand, the neural correlates of the arousal*force interaction were found in the upper midbrain region, overlapping with the PAG (Fig. 4C), plus other regions in superior frontal gyrus, rostral cingulate cortex, fusiform gyrus, and thalamus. These data suggest that the modulation of force output by negative valence and high arousal relies on partly distinct sites within prefrontal cortex and midbrain.[3] The maxima cluster obtained for each modulator in this analysis (Table 2) was then used as a functional ROI, from which mean beta estimates for each emotional condition were extracted and compared (see Pessiglione et al., 2007; Schmidt et al., 2009).

As illustrated in Figs. 3B and 4B, there was a significant main effect of emotion for both rIFG ROIs (BA 44, $F_{(2,86)} = 23.0$, $p = .001$; and BA 46, $F_{(2,86)} = 26.1$, $p = .001$), but also amygdala ($F_{(2,86)} = 13.8$, $p = .001$) and PAG ($F_{(2,86)} = 29.3$, $p = .001$), however not for the cerebellum ($p > .05$). Post-hoc analyses confirmed that the unpleasant condition yielded higher beta estimates compared with the pleasant and neutral

[3] Additional parametric fMRI analyses using pupil dilation as an index of arousal showed no significant effect, but were likely underpowered due to missing eye-tracking data on several trials (see Section 2.5).

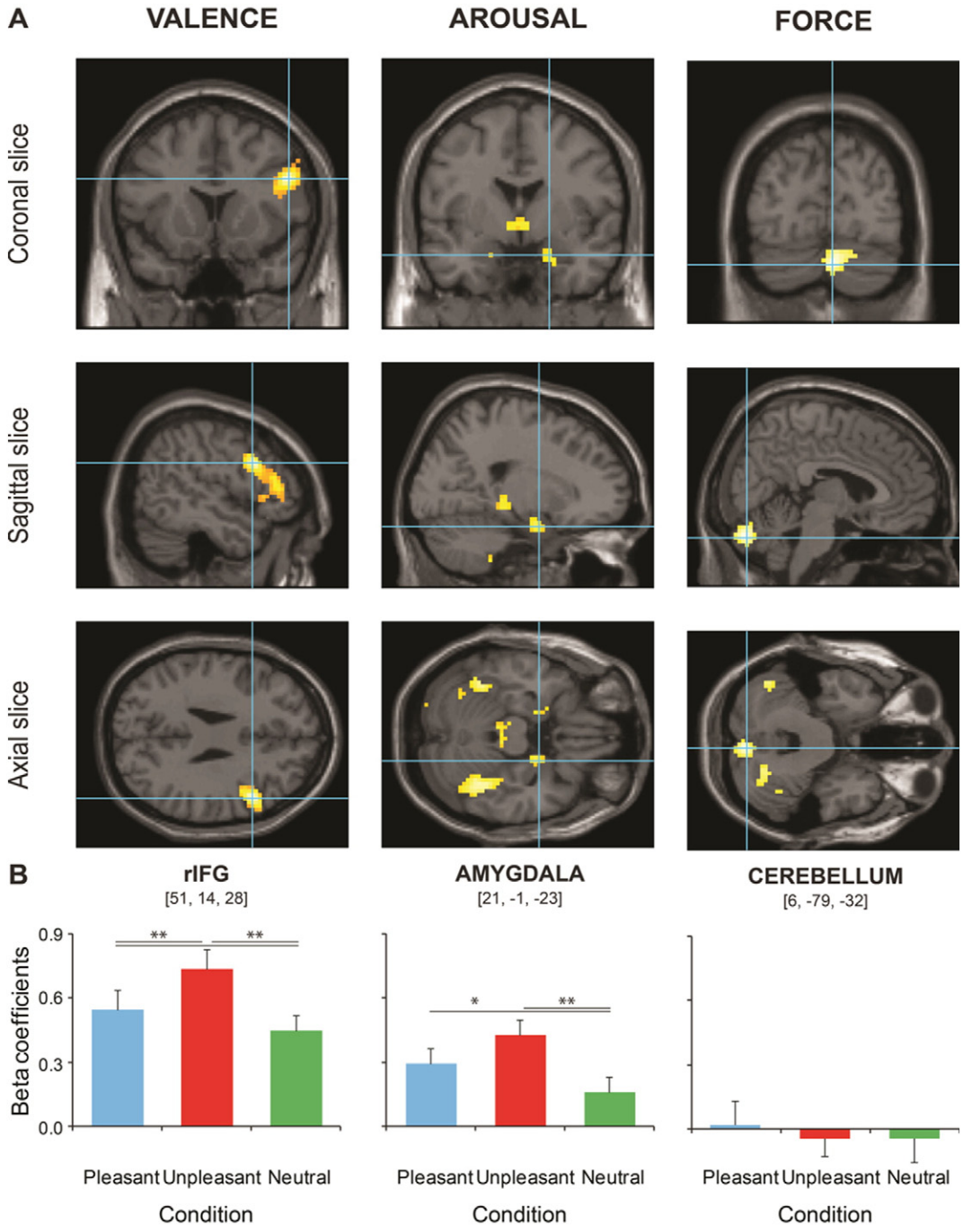

Fig. 3. Neuroimaging results for parametric analysis of emotion and force variables separately. *A*, Activations during force maintenance correlating with negative valence ratings (left column), higher arousal ratings (middle column), and actual force output (right column). SPMs illustrate significant activation clusters for each parametric modulator that survived a threshold of $p < .001$ (uncorrected). Each cluster had a minimum of 50 voxels ($p < .05$; FWE corrected at the cluster level). Slices are taken at the maxima of interest, with the respective MNI coordinates (x, y, z; mm) shown below the axial slices. The maxima cluster of interest for each parametric modulator was used to define a functional ROI to compare relative activations across conditions. *B*, Mean beta coefficients determined by the ROI analysis for each region in *A*, for each emotional condition. Error bars in each graph represent standard error; $^{*}p < .05$, $^{**}p < .001$.

conditions in the rIFG ($p < .001$ for both ROIs), whereas both pleasant and unpleasant beta estimates for the amygdala were higher than the neutral condition ($p < .05$), but not significantly different from each other. For the PAG, beta estimates were significantly higher for the unpleasant condition compared with the pleasant and neutral conditions ($p < .05$), and higher for the pleasant condition compared with the neutral condition ($p < .001$). Together, these results confirm the results of the whole-brain voxelwise analyses and point to the rIFG, PAG, and amygdala as being key regions mediating the specific effect of negative emotional contexts on the control of force production.

Discussion

Our study aimed to determine how emotion modulates motor force control during a precision-grip task. Here we show that viewing unpleasant images resulted in significantly attenuated force decay during force maintenance as compared with pleasant and neutral images, indicating a negatively valenced-driven modulation of motor control. Subjective valence and arousal reports reliably predicted this effect. No significant modulation of motor output control was produced by viewing pleasant images. Concomitant increases in autonomic arousal

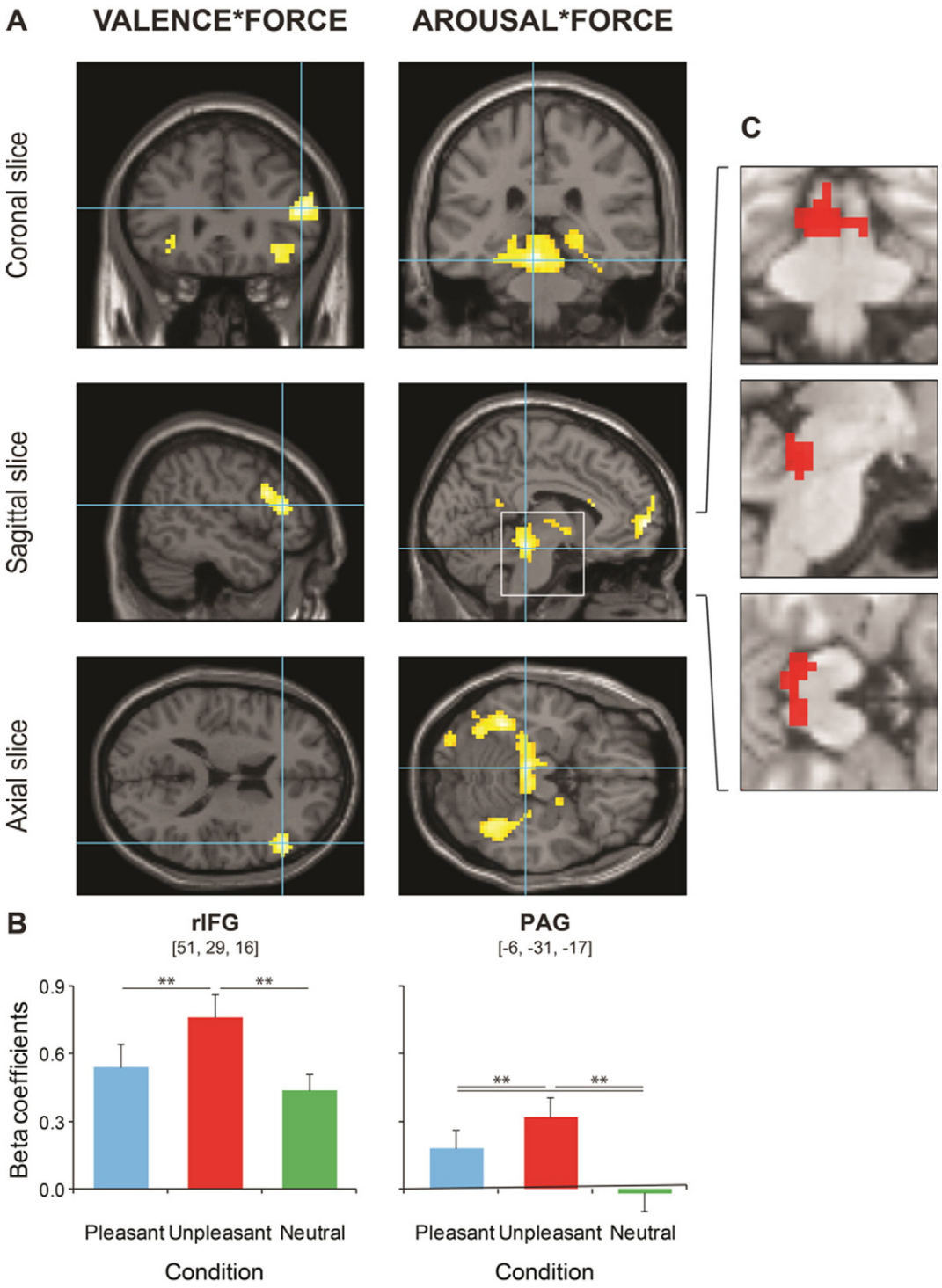

Fig. 4. Neuroimaging results for the interaction effects of force with valence and arousal. *A,* Activations correlating with the product term for negative valence × higher force output (left column), and for arousal × higher force output (right column). SPMs illustrate significant activation clusters for each parametric modulator that survived a threshold of $p < .001$ (uncorrected). Each cluster had a minimum of 50 voxels ($p < .05$; FWE corrected at the cluster level). Slices are taken at the maxima of interest, with the respective MNI coordinates (x, y, z; mm) shown below the axial slices. The maxima cluster of interest for each parametric modulator was used to define a functional ROI to compare relative activations across conditions. *B,* Mean beta coefficients determined by the ROI analysis for each region in *A*, for each emotional condition. *C,* Significant activation in PAG zoomed and illustrated at the same coordinates as above (right column). SPMs are thresholded at $p < .05$, FWE corrected. Error bars in each graph represent standard error; $^{*}p < .05$, $^{**}p < .001$.

and eye movement behaviour unique to the unpleasant condition were also observed, even though the unpleasant images were matched with the pleasant images in terms of arousal ratings and physical properties of the images (see methods). Neuroimaging results revealed the alteration of force output by unpleasant stimuli was mediated by a cortico-subcortical network including the rIFG and PAG, but also cerebellum, SMA, and amygdala. Further, our data point to partly dissociable effects of valence and arousal on the recruitment of rIFG and PAG, respectively. These results are consistent with engagement of motor pathways associated with the aversive motivation system, eliciting defensive behaviour and action preparedness in response to negative emotional signals (Frijda, 2004, 2009).

The selective effects of emotional valence on motor behaviour accords with previous work showing direction-specific movement responses to negative versus positive stimuli (Chen and Bargh, 1999; Hillman et al., 2004; Rotteveel and Phaf, 2004; Marsh et al., 2005; Coombes et al., 2007). Coombes et al. (2006) reported greater maximal force during exposure to unpleasant images compared with pleasant and neutral images, in a sustained wrist extension (upwards) movement. The latter task was specifically chosen to avoid any directional movements towards or away from the body. Here we observed a unique effect of negative emotional information on force output during submaximal isometric precision-grip contractions. This indicates the effect of unpleasant stimuli on force output is not limited to directional movements or the absolute magnitude of force exerted. Previous work also shows that exposure to an aversive stressor (threat of shock) may enhance fluctuations (standard deviations) in force output during a submaximal sustained pinch-grip task, both with visual feedback of the force output (Noteboom et al., 2001) and without (Christou et al., 2004; Christou, 2005). In these studies however, there was no effect on the magnitude of force, and highly arousing but pleasant stimuli were not included so it is difficult to determine whether the change in force variability was driven by the emotional valence or arousal. Our behavioural results thus only partially agree with this research as we found no effect of emotion on force variability. The modality of aversive stimuli (physical stressor versus emotional images) may account for these differences.

Of particular interest is the discrepancy between our behavioural findings and previous research reporting an increase in force production when participants were exposed to arousing stimuli, irrespective of the valence (Coombes et al., 2008, 2011; Schmidt et al., 2009; Naugle et al., 2010, 2012). In our study, the lack of change in force output in the pleasant compared with the neutral condition cannot be due to differences in arousal between these conditions as arousal was carefully matched (according to both normative values and individual subjective ratings). Although we used a similar experimental protocol to the behavioural studies of Coombes and colleagues, several distinctions might account for this discrepancy. First, the average normative arousal ratings of our emotional conditions were lower than those used by Coombes and colleagues, who actually speculated that "high levels of emotional arousal may mask potential valence effects" (Coombes et al., 2009). However, upon additional inspection of our data we found that even when segregating our stimuli within the pleasant and unpleasant conditions into those with relatively higher or lower arousal levels (while matching for valence; based on normative values), we obtained the same pattern of results; only the negatively valenced stimuli had an effect on force output, regardless of arousal. This indicates the valence-driven effect on force output is not dependent on the overall magnitude of arousal. Second, diverging results could be due to the content of stimuli. Here we used a broad range of images within each emotional condition, rather than specific categories such as erotica or mutilation for the pleasant and unpleasant conditions, respectively, as done by Coombes and colleagues. Interestingly, when we performed another split on the data within the pleasant condition, isolating only those stimuli considered as erotic, we found a pattern of results resembling the findings of Coombes et al. (where only erotic images were used). This was despite no difference in arousal between the erotic and non-erotic images (again based on normative values, as well as subjective ratings). Again, this indicates that arousal level does not drive the effect on force output in this task, and further that different modulations may arise as a function of the particular motivational significance of affective stimuli.

We therefore surmise that affective influences on isometric force might primarily be sensitive to the "motivational mobilisation" (Lang and Bradley, 2010) evoked by emotional stimuli, and more particularly, the degree to which they engage appetitive or aversive systems (Bradley et al., 2001). In this view, it appears the broad variety of unpleasant stimuli used here had greater motivational significance than those comprising the pleasant condition. Thus a stronger engagement of action tendencies mobilised by the aversive motivational system resulted in higher force generation during the picture interval. Furthermore, given the lack of effect with pleasant emotions, our findings indicate that conclusions regarding a generalised effect of positive stimuli on force output should be interpreted cautiously.

The idea that the unpleasant stimuli altered motor behaviour due to greater levels of motivational significance and stronger motor mobilisation by the aversive motivation system is consistent with the defence cascade model posited by Lang et al. (Lang et al., 1997; Bradley et al., 2001). This model proposes that changes in physiological reactions and adaptive behaviour (e.g., freeze-fright-flight) occur as a function of the degree of defensive system mobilisation (akin to predator imminence in animal models; Fanselow and Lester, 1988). When activation of the defensive system is low (early post-encounter phase), animals demonstrate orienting, heightened attention, and freezing behaviour that enables preparation for possible overt behaviour. Freezing is a passive defensive reaction with a distinct evolutionary advantage, whereby animals reduce body motion when threat of a distant predator is perceived (Blanchard and Blanchard, 1986; Marks, 1987; Blanchard et al., 2001). This "attentive immobility" serves to orient attention to stimuli, avoid detection, and mobilise the organism for overt defence (flight or fight; circa-strike phase) if the distance of the threat is reduced (McNaughton and Corr, 2004; Mobbs et al., 2007). In humans, it has been suggested that viewing unpleasant images also prompts focused attention and immobility, typically manifested as slower response latencies to negative stimuli (Sagaspe et al., 2011), analogous to freezing in animals (Lang et al., 1997; Bradley et al., 2001).

Thus one plausible explanation for our data is that exposure to unpleasant stimuli produced some degree of immobility, a freezing-like response that attenuated the force decay and maintained muscular effort closer to the target level.[4] Such an interpretation is in line with human studies showing freezing-like reactions in postural sway accompanied by bradycardia (a typical physiological index of freezing) when viewing unpleasant images depicting physical injury (Azevedo et al., 2005; Stins and Beek, 2007; Hagenaars et al., 2012) or social threat (Roelofs et al., 2010).

Although we did not measure cardiac responses, we recorded concomitant changes in eye-tracking and found specific effects in the unpleasant condition. First, pupil size was largest when viewing aversive stimuli. Increased pupil dilation is typically observed when people process emotionally engaging stimuli, an effect regulated by autonomic sympathetic activity (Bradley et al., 2008), most notably mediated by the locus coeruleus in the brainstem (Samuels and Szabadi, 2008). However, in contrast to the findings of Bradley et al. (2008) in which both pleasant and unpleasant images resulted in larger pupillary changes, our data reveal a selective effect of emotional *valence* on pupil dilation. Valence effects on pupillary responses were also reported by Tamietto et al. (2009), who found greater dilation following fearful compared to happy faces and bodily expressions. These stimuli, like those in the present study, may have been perceived as having greater motivational significance and thus elicited a more pronounced effect on sympathetic activity, increasing the arousal response. Increased

[4] Our interpretation that engagement of the defensive motivation system facilitated force control does not preclude a similar conclusion from being drawn regarding appetitive motivation engagement had we yielded the same pattern of results in the pleasant condition as we did for the unpleasant condition (e.g., if the pleasant condition was solely comprised of erotic images). Lang et al. (1997) suggested that "aversively motivated attending does not fundamentally differ from appetitive orienting at lower levels of activation" during the early post-encounter phase. Furthermore, they hypothesised that "a similar immobility, which may involve the same neural mechanism, is also found in predators when a potential prey first appears in their field of view". In this view, the findings of Coombes and colleagues may reflect engagement of the appetitive motivation system and a comparable "appetitive cascade" — inhibiting movement and heightening vigilance for life-sustaining rewards Löw et al., (2008).

pupil dilation is also observed concomitant to bradycardia and motor arrest (Applegate et al., 1983; Hermans et al., 2013). Second, we found that unpleasant images generated more fixations of briefer duration and increased scanning, consistent with the notion that motivationally-relevant stimuli engage attention, elicit orienting behaviour, and enhance information-seeking and stimuli processing (Aston-Jones et al., 1999; Bradley et al., 2011). Taken together, our pupillary and eye movement data add to the notion that the unpleasant condition had a greater motivational impact on both autonomic and motoric aspects of action tendencies.

Our neuroimaging data provide additional support linking the negatively valenced-driven effect on force control to a freezing-like response. Emotional influences on motor performance appeared to be mediated by a cortical–subcortical–cerebellar network consisting principally of the rIFG (vlPFC), PAG, cerebellum, and amygdala, but with differential sensitivity of these structures to valence or arousal. Neural activity correlating with increased force in proportion to *negative valence* (valence*force interaction) was found selectively in the rIFG, an area commonly associated with response inhibition in motor, cognitive, and affective contexts (Aron et al., 2003, 2004; Shafritz et al., 2006; Berkman et al., 2009). However, the rIFG frequently activates in paradigms with no overt inhibitory requirement, for example in target detection tasks when the targets are highly relevant to the current task (Hampshire et al., 2009, 2010), when re-orienting of attention is required (Corbetta and Shulman, 2002), and when attention must be sustained over time (Shallice et al., 2008). These data suggest a more general role of the rIFG in executive function that includes both attentional filtering and inhibitory control (Cojan et al., 2009). In our study, a response of rIFG to unpleasant stimuli that evoked stronger force output is therefore consistent with a role of this region in the focussing of attentional resources on motivationally significant events and heightened control of goal-oriented behaviour. It is possible that the rIFG may then modulate motor pathways and lower brain regions, including the PAG, to trigger freezing-like behaviour and prepare for motor action. This is plausible given direct anatomical connections between the PAG and vlPFC have been identified in humans (Hadjipavlou et al., 2006). The rIFG is also well connected to limbic areas in orbitofrontal cortex as well as striatum and amygdala (Sagaspe et al., 2011), through direct reciprocal connections (Amaral and Price, 1984; Ghashghaei and Barbas, 2002; Ghashghaei et al., 2007), indicating that this region is well placed to integrate emotional signals with action planning and task-related goals.

This result also converges with a recent fMRI study (Hermans et al., 2013) where rIFG activity during passive viewing of unpleasant images was found to correlate with cardiac deceleration, a physiological change commonly associated with freezing responses (Lang and Davis, 2006). Activation of inhibitory control circuits in prefrontal and subthalamic nuclei together with concomitant autonomic inhibition (cardiac deceleration) have been described during attentive motor preparation (Jennings et al., 2009). In our task, recruitment of inhibitory control networks when force had to be maintained at a constant level in a negative emotional context presumably reflects fine-tuned modulation of inhibitory action control during covert motor planning. Indeed, when comparing conditions with no IAPS images (feedback > blank), we still found clusters of activation in rIFG, as well as SMA and dorsolateral prefrontal cortex, though to a lesser degree than for the unpleasant condition (unpleasant > blank; unpleasant > pleasant). With the addition of emotional stimuli, the motor task presumably required greater cooperation between stimulus-driven and goal-directed processing, where the IFG is considered to lie at the intersection (Hampshire et al., 2009). This cortical region may thus implement rapid emotion-action regulation mechanisms; through increased inhibitory control signals, the rIFG may alert the motor system and PAG, which could attenuate force decay in our task, and more generally, alter ongoing action in order to respond adaptively to behaviourally salient information (Tops and Boksem, 2011).

On the other hand, correlations between brain activity and force in proportion to subjective *arousal level* were found predominantly in the PAG, extending to amygdala, medial prefrontal regions including SMA, and cerebellum. The finding that arousing stimuli activated the amygdala, with a linear relationship between arousal intensity and amygdala activity, is consistent with many neuroimaging studies of emotion (Taylor et al., 2000; Sabatinelli et al., 2005, 2011; Kober et al., 2008; Coombes et al., 2012). On the other hand, Schmidt et al. (2009) reported a correlation between arousal and IFG activity, whereas amygdala responses were associated with monetary incentives reflecting an effect of motivation on force output. Discrepancies regarding the motor task, timing of image presentation, and possibly image content may potentially account for this difference. Regardless, the arousal- and motivation-related cortical regions implicated in the facilitation of force output reported by Schmidt et al. were also activated in our task, as we found the greatest amygdala and IFG engagement for the motivationally-salient unpleasant stimuli. Increased activity in SMA and cerebellum, two regions critically involved in motor control (Picard and Strick, 1996; Kawato et al., 2003), is consistent with previous findings demonstrating their involvement in force production during emotional compared with neutral contexts (Coombes et al., 2012).

Here however, a selective neural correlate for the combined effects of arousal and force was found in the PAG, where activity was globally greater for unpleasant than pleasant and neutral images (main valence effect), but also increased in parallel to the arousal-dependent modulation of force output (arousal*valence interaction). This pattern lends further support to the interpretation of our behavioural findings that unpleasant stimuli induced a degree of immobility that attenuated force decay, as the PAG is a key brainstem region known to be critically involved in defensive, survival-related responses during threat and stress. Direct stimulation of the PAG evokes stereotyped motor behaviours and body postures, including freezing (Brandão et al., 2008; Satpute et al., 2013). In rodents, different sub-regions of the PAG have discrete functions underlying responses to threat: the ventrolateral and dorsolateral PAG are associated with passive-coping (freezing, bradycardia) and active-coping (flight-fight, tachycardia) strategies, respectively (Bandler and Shipley, 1994; Bandler et al., 2000; Linnman et al., 2012). These functional distinctions have similarities with the changes in adaptive behaviour that occur as a function of defensive system mobilisation (Fanselow and Lester, 1988; Lang et al., 1997). We note that our result might also reflect additional increases in the superior colliculi to unpleasant stimuli, since this oculomotor structure has been linked to freezing behaviour in rats, and to visual processing of negative stimuli in humans (Vuilleumier et al., 2001; Schenberg et al., 2005; Van den Stock et al., 2011). However, this remains speculative as our fMRI parameters limit the ability to precisely isolate activity of the PAG from adjacent brainstem nuclei (Wall et al., 2009; Satpute et al., 2013). Despite centrality of the PAG in non-human affective research (Panksepp, 1998, 2005), less is known about its role in human emotions and defensive behaviours (Buhle et al., 2013; Satpute et al., 2013). A recent study using high resolution fMRI indicated a rostrocaudal functional subdivision of the PAG with respect to emotional processing of aversive images, mirroring neurobiological observations in non-human animals (Satpute et al., 2013). Interestingly, activity in dorsal PAG was also demonstrated using fMRI when the perceived threat proximity of a virtual predator became closer (Mobbs et al., 2007, 2009), and when threatening facial expressions (e.g., anger) evoked covert defensive behaviour with concomitant activation of premotor cortices (Pichon et al., 2012). Our results therefore add to this literature, providing novel support for the role of the human PAG in attentive immobility, and point to a direct functional relation to subjective arousal.

The amygdala also lies at the interface between emotional appraisals and coordinated changes in bodily and physiological activity. Although its role in fear processing and fear-conditioning in humans and non-humans is well documented (LeDoux, 2000; Rosen, 2004; Armony and Vuilleumier, 2013), there is only scarce evidence in humans for its

involvement in modulating motor control processes in emotional contexts. In a recent study using an emotional stop-signal task, Sagaspe et al. (2011) showed heightened amygdala activity during successful motor inhibition in the presence of fearful faces. They suggested the amygdala might trigger defensive motor arrest in emotional contexts and modulate cortical preparatory activity through coupling with SMA and right inferior prefrontal regions. Likewise, in the study by Hermans et al. (2013), bradycardia evoked by unpleasant images was also correlated with increased functional connectivity between the amygdala and PAG. In agreement with these studies, and with animal studies showing cessation of motor behaviour and attention orienting upon amygdala stimulation (Applegate et al., 1983; Davis and Whalen, 2001), our data provide new evidence for a direct role of the amygdala in the modulation of force control in response to negative emotional information. However, unlike the PAG, the amygdala activity did not parametrically vary with force magnitude, consistent with the idea that it may lie upstream to the PAG and drive motor circuits in the latter, as well as other motor regions, when activated by emotional events. This notion accords with a recent DTI study demonstrating direct structural connections between the amygdala and motor cortex in humans (Grèzes et al., 2014). Importantly, the amygdala also has extensive direct descending projections to both the PAG and cerebellum (Rizvi et al., 1991; Linnman et al., 2012), making these two structures well placed to mediate amygdala-driven subcortical motor outflow (Brandão et al., 2008). Thus these connections conveying emotional information from the amygdala to IFG and PAG (reflecting subjective valence and arousal, respectively), as well as to other subcortical and cortical motor-related areas (Grèzes et al., 2014), may provide a mechanisms through which the amygdala can facilitate appropriate motor responses such as attentive immobility or defence. Rapid amygdala responses are thought to partly depend on subcortical visual inputs from the superior colliculus and pulvinar, which are part of the extrageniculostriate pathway. In the present study we found increased activity in the pulvinar, and possibly superior colliculus during emotionally arousing stimuli, possibly reflecting such relay of affective visual signals to the amygdala for further appraisal of threat-related information (Vuilleumier et al., 2003; Liddell et al., 2005).

To promote defensive behaviour, the PAG must engage spinal motor circuits, whose control may further involve sensorimotor circuits connecting the PAG to cerebellum. For example, in rodents the cerebellar lobule VIII (pyramis) is a key node within a chain of connections linking the ventrolateral PAG to the spinal cord, required to elicit fear-evoked freezing behaviour (Koutsikou et al., 2014). Interestingly, we found that several cerebellum areas activated during our task. A correlation with force output was observed in the cerebellar pyramis, an area implicated in sensorimotor control (Stoodley and Schmahmann, 2009), but also responding to negative emotions (Schraa-Tam et al., 2012). Although we found no significant effect of emotion on cerebellar pyramis activity in our ROI analysis, the whole-brain analysis revealed increased activity in area Crus I, the 'limbic cerebellum', specifically for the contrast comparing unpleasant to pleasant stimuli, consistent with previous findings (Stoodley and Schmahmann, 2009). Additionally, Crus I activation has been shown to scale with isometric precision-grip force amplitude and rate of force development (Spraker et al., 2012). In our study, it is therefore likely the cerebellum acted to control force amplitude in the presence of negative emotional stimuli and covertly prepare passive defensive behaviour.

In summary, we show an attenuation of isometric force decay by negative emotional information and link it with neural substrates in a cortical–subcortical–cerebellar network associated with the defensive motivation system. Increased activity in rIFG and PAG during motor performance correlated with the impact of valence and arousal on force production, respectively. Additionally, we demonstrate engagement of the amygdala, SMA, and cerebellum with subjective arousal during the force task. Together, these findings reflect a state of increased attentional focus and motor immobility leading to augmented force control, triggered by motivationally-relevant stimuli. Consistent with Fridja's notion that emotions are action tendencies (Frijda, 2009), we suggest the unpleasant images triggered a passive defensive coping mechanism that heightened attention and motor preparation to promote adaptive responses. This study provides new knowledge about the neural circuitry underlying emotion modulated force control, and identifies the rIFG and PAG as key nodes involved in the integration of negative emotional input and motor output processes. Moreover, by exploiting measures of motor output in parametric analyses of fMRI activity, this study sheds new light on the role of the human PAG in aversive emotional contexts and reveals a direct association between PAG activity and overt motor performance. Further research could refine this approach with simultaneous electromyographic recordings. It has recently been shown in rats that the ventrolateral PAG increases α-motorneurone excitability, which may drive increased muscle tone associated with fear-evoked freezing (Koutsikou et al., 2014). Electromyographic analyses of muscular co-contraction for example would permit stronger conclusions about the elicitation of a freezing-like response in humans. Finally, investigating the neural mechanisms underpinning how emotions can modulate motor performance may be important to our understanding of defensive reactions implicated in psychiatric disease, such as anxiety, post-traumatic stress disorder, or motor conversion disorders.

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