



Effects of emotion regulation strategy on brain responses to the valence and social content of visual scenes

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ABSTRACT

Emotion Regulation (ER) includes different mechanisms aiming at volitionally modulating emotional responses, including cognitive re-evaluation (re-appraisal; REAP) or inhibition of emotion expression and behavior (expressive suppression; ESUP). However, despite the importance of these ER strategies, previous functional magnetic resonance imaging (fMRI) studies have not sufficiently disentangled the specific neural impact of REAP *versus* ESUP on brain responses to different kinds of emotion-eliciting events. Moreover, although different effects have been reported for stimulus valence (positive *vs.* negative), no study has systematically investigated how ER may change emotional processing as a function of particular stimulus content variables (i.e., social *vs.* nonsocial). Our fMRI study directly compared brain activation to visual scenes during the use of different ER strategies, relative to a “natural” viewing condition, but also examined the effects of ER as a function of the social *versus* nonsocial content of scenes, in addition to their negative *versus* positive valence (by manipulating these factors orthogonally in a 2×2 factorial design). Our data revealed that several prefrontal cortical areas were differentially recruited during either REAP or ESUP, independent of the valence and content of images. In addition, selective modulations by either REAP or ESUP were found depending on the negative valence of scenes (medial fusiform gyrus, anterior insula, dmPFC), and on their nonsocial (middle insula) or social (bilateral amygdala, mPFC, posterior cingulate) significance. Furthermore, we observed a significant lateralization in the amygdala for the effect of the two different ER strategies, with a predominant modulation by REAP on the left side but by ESUP on the right side. Taken together, these results do not only highlight the distributed nature of neural changes induced by ER, but also reveal the specific impact of different strategies (REAP or ESUP), and the specific sites implicated by different dimensions of emotional information (social or negative).

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1. Introduction

Emotions play a vital role in human life, shaping many personal and social processes. However, besides being influenced by emotions in our actions, we in turn have the ability to modulate our emotional responses by different mechanisms. The importance of emotion regulation (ER) capacities can be observed in various domains or situations, either in terms of increasing pos-

itive health outcomes when used appropriately, or by promoting mood disorders and anxiety when malfunctioning (Gross, 2002; Jackson, Malmstadt, Larson, & Davidson, 2000). Uncovering the neural mechanisms that can regulate affect and their influence on the processing of emotionally significant information is therefore of great importance, not only to gain insight into the determinants of well-being and adaptive emotional processing, but also to better understand the predispositions to affective disorders and the effect of specific therapeutic interventions.

Behavioral research on ER (Gross, 1998) has highlighted two major kinds of ER strategies, which are conceptualized to have their impact at distinct stages during emotion processing.

On the one hand, *cognitive reappraisal* (REAP) is thought to intervene at a relatively early stage of emotion processing by modulating the meaning of an emotional event. This typically involves the intentional (conscious) generation of alternative interpretations in response to an event, allowing one to modify (e.g., minimize)

Abbreviations: BASE, baseline; CON, control; ER, emotion regulation; ESUP, expressive suppression; INST, viewing instruction; INT, intensity; NAT, natural viewing; NEG, negative; NSN, nonsocial negative; NSOC, nonsocial; NSP, nonsocial positive; PLN, pleasantness; POS, positive; REAP, re-appraisal; SC, social content; SN, social negative; SOC, social; SP, social positive; VAL, valence.

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its emotional significance. Accordingly, REAP has been shown to alter subjective emotion experience (as measured by physiological arousal and verbal reports) to both negative and positive emotional stimuli, and for both up- and down-regulation of affect (Kim & Hamann, 2007). Moreover, studies using functional magnetic resonance imaging (fMRI) during REAP have shown increased activity in a widespread network of cortical frontal regions, together with simultaneous decreases in areas critical for emotion elicitation, such as the amygdala, the posterior cingulate cortex (PCC), and insula (Goldin, McRae, Ramel, & Gross, 2008; Kim & Hamann, 2007; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner, Ray et al., 2004).

On the other hand, *suppression of behavioral expression* (ESUP) is thought to operate only after emotion elicitation, and is directed towards the inhibition of emotional responses (e.g., facial expressions or physiological changes). Thus, the triggering event is typically appraised and elicits an emotion, but the overt behavioral manifestations are voluntarily suppressed. Unlike REAP, ESUP has been found to increase sympathetic activation, to produce little effect on negative emotion experience, and to even decrease positive affect and interfere with cognitive processes such as memory (Gross, 1998; Richards & Gross, 2000). Although brain imaging data on ESUP are still scarce, one study has reported an increase in prefrontal cortical activity during ESUP of negative emotions (either sadness or disgust; (Goldin et al., 2008)). The same investigation also found increased amygdala and insula responses during ESUP, but only in a late period of prolonged exposure to disgusting film-clips, contrasting with the decreases observed in these regions during REAP (Kim & Hamann, 2007; Ochsner et al., 2002; Ochsner, Ray et al., 2004). Finally, whereas the use of REAP has been linked to enhanced control of emotion, better interpersonal functioning, and higher psychological and physical well-being, the frequent use of ESUP is thought to result in diminished control of emotion, worse interpersonal functioning, and greater risks for depression (Gross & John, 2003).

Despite the fact that our knowledge regarding the neural correlates of ER has steadily increased during the last decade, several important issues still remain largely unresolved. Firstly, most of the previous brain imaging studies on ER have investigated only one type of ER strategy at a time (Beauregard, Levesque, & Bourgouin, 2001; Kim & Hamann, 2007; Koenigsberg et al., 2010; Levesque et al., 2003; Ochsner et al., 2002; Ochsner, Ray et al., 2004), except for one study (Goldin et al., 2008) that compared REAP and ESUP in a single experimental design but focused on difference in the time-course of ER effects. Hence, still very little is known about the *differential* impact of REAP and ESUP on brain activity during emotional processing, particularly in relation to different stimulus types. This does not only concern cortical brain areas exerting top-down control during ER, predominantly located within prefrontal cortex, where a functional segregation between behavioral (ESUP) and cognitive (REAP) control has already been suggested (Goldin et al., 2008); but also the lower-level areas in sensory cortices and subcortical regions that are crucially involved in emotional responses, such as the amygdala, striatum, or insula. Thus, it still remains to be elucidated whether insula activity during down-regulation of affect only decreases through REAP but increases during ESUP, as would be predicted by ER theory (Gross, 1998; Gross & John, 2003), or whether it can also be down-regulated during ESUP just like during REAP. Therefore, in our study, we examined both cognitive (REAP) as well as behavioral (ESUP) strategies of ER, in addition to a “natural” emotion experience condition (NAT; see Section 2) that served as a baseline condition.

Secondly, most previous fMRI experiments on ER only differentiated modulatory effects as a function of the valence (VAL; positive vs. negative) and/or arousal values (low vs. high intensity) attributed to emotional stimuli (Kim & Hamann, 2007; Mak, Hu, Zhang, Xiao, & Lee, 2009), but did not consider other important

aspects of the latter, such as their social versus nonsocial features. One exception is a recent investigation by Koenigsberg and colleagues where the authors used social negative images exclusively in a cognitive re-evaluation (REAP) paradigm (Koenigsberg et al., 2010). Yet, this study did not compare brain activations elicited by social negative to comparable nonsocial negative scenes. This lack of systematic investigation of ER as a function of the content of emotion-eliciting stimuli is regrettable given many other findings which point to major differences in emotional reactions (and their corresponding neural signatures) depending on the social versus nonsocial nature of information (Britton et al., 2006; Frewen et al., 2010; Goossens et al., 2009; Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002; Norris, Chen, Zhu, Small, & Cacioppo, 2004; Sander, Koenig, Georgieff, Terra, & Franck, 2005; Scharpf, Wendt, Lotze, & Hamm, 2010). In addition, there is evidence that the activation of some limbic brain areas (e.g., the amygdala) is more sensitive to social and thus interpersonal aspects rather than to nonsocial dimensions of emotion-eliciting situations (Killgore & Yurgelun-Todd, 2005; Vrtička, Andersson, Grandjean, Sander, & Vuilleumier, 2008). Likewise, the medial prefrontal cortex has also been linked with both emotion recognition and social cognition (Gilbert et al., 2007; Lane & McRae, 2004; Mitchell, Macrae, & Banaji, 2006; Peelen, Atkinson, & Vuilleumier, 2010). These differences in social and emotional content are likely to imply different mechanisms for successful ER strategies. As a consequence, in our study, emotional images were systematically varied according to both their affective valence (VAL: positive vs. negative) and their social content (SC: social vs. nonsocial), as separate experimental factors in a 2×2 design.

To this aim, our study used a systematic approach combining whole-brain imaging with analysis of functionally defined regions of interest (ROIs) while participants were instructed to apply different ER strategies for different stimulus types. In previous work, activation differences related to ER have typically been derived from comparisons between REAP versus baseline or ESUP versus baseline, and this for a single emotional dimension (i.e., negative stimuli) (Goldin et al., 2008; Ochsner, Ray et al., 2004). To our knowledge, only two imaging studies so far also compared the *relative differences* in brain responses to positive versus negative images during ER (Kim & Hamann, 2007; Mak et al., 2009). Here, we set out to identify brain areas that were not only involved in processing a specific stimulus attribute (i.e., VAL or SC), but also significantly modulated by the different ER instructions (INST; either NAT, REAP, or ESUP). Therefore, we specifically tested for regions showing a significant $INST \times VAL$ or $INST \times SC$ interaction. To restrain our analysis to regions showing reliable effects of interest but ensure sufficient sensitivity across the different conditions, we first used a whole-brain random-effects (RFX) analysis to determine functional networks whose activity was significantly modulated by either VAL or SC, and then computed an additional second-level RFX analysis (using a paired *t*-test design in SPM) to identify voxels within these networks that displayed significant effects due to the different ER strategies (see Section 2). This approach allowed us to define regions of interest (ROIs) where the processing of specific affective cues (VAL or SC) was selectively modulated by the different kinds of ER.

We predicted changes in activations related to the differential encoding of valence (negative vs. positive) and/or stimulus content (social vs. nonsocial) in brain networks that are selectively tuned to social and affective information (Lieberman, 2007), including in particular the amygdala which has previously been shown to be sensitive to social cues (Britton et al., 2006; Frewen et al., 2010; Goossens et al., 2009; Hariri et al., 2002; Norris et al., 2004; Sander et al., 2005; Scharpf et al., 2010; Vrtička et al., 2008) and modulated by different ER strategies (Killgore & Yurgelun-Todd, 2005; Kim & Hamann, 2007; Koenigsberg et al., 2010; Levesque et al.,

2003; Ochsner et al., 2002; Ochsner, Ray et al., 2004). Other differences were expected in prefrontal cortical areas that have been implicated in controlling emotion processing during different ER strategies (Goldin et al., 2008; Kim & Hamann, 2007; Levesque et al., 2003; Ochsner et al., 2002; Ochsner, Ray et al., 2004).

2. Methods

2.1. Subjects

We recruited 19 healthy paid volunteers (all right-handed women, mean age 24.82 ± 4.0), who all had a normal or corrected to normal vision, no history of neurological or psychiatric disease, and gave informed written consent according to the local ethical committee regulation. Only women were included because of evidence that emotions are typically more intense and more prone to regulation in women (e.g., Fujita, Diener, & Sandvik, 1991), but also to increase comparability with previous emotion regulation studies that also included women only (Kim & Hamann, 2007) and to avoid any potential sex differences that could have modulated the regulation effects of interest. We did not record information about their menstrual cycle (see Limitations).

2.2. Experimental material and procedure

2.2.1. Stimuli

A total number of 360 emotional pictures were initially chosen either from the International Affective Pictures System (IAPS) or from the internet. All were in colors, and adjusted to obtain similar size, contrast, and pixel resolution. Half of the pictures displayed scenes with a clear social content, such as two people fighting or a mother interacting with her baby. The other half represented objects or landscapes (nonsocial), like a dead bird in industrial waste or a tropical island scene.

All 360 pictures were rated in a separate behavioral study (Vrtička et al., under revision) by 54 female students on three continuous rating scales (from 0 to 100), including PLEASANTNESS (PLN; from very negative to very positive), INTENSITY (INT; from low to high arousal), and CONTROL (CON; from absence to full presence of possible control over the emotional situation). According to the average rating results from this sample, 240 pictures were finally chosen for the fMRI study, and sorted by their SOCIAL CONTENT (SC; either social or nonsocial) and VALENCE (VAL; either positive or negative). This gave rise to four stimulus categories (60 pictures each): Social Positive (SP) or Negative (NSP), and Nonsocial Positive (NSP) or Negative (NSN). The final distribution of pictures in these four categories as a function of emotional rating scores (PLN, INT, and CON) showed that NEG images had significantly lower pleasantness scores as compared to POS images [$PLN_{NEG} = 20.67 \pm 6.02$ and $PLN_{POS} = 72.14 \pm 10.19$; $F(1,59) = 3919.25$, $p < .001$], but also higher intensity [$INT_{NEG} = 70.08 \pm 8.05$ and $INT_{POS} = 44.06 \pm 7.14$; $F(1,59) = 1554.01$, $p < .001$] and lower control [$CON_{NEG} = 35.91 \pm 8.14$ and $CON_{POS} = 55.49 \pm 9.25$; $F(1,59) = 452.97$, $p < .001$] scores. However, most importantly, there were no significant differences for all three rating scales between SOC versus NSOC images [$PLN_{NSOC} = 46.68 \pm 26.41$ and $PLN_{SOC} = 46.91 \pm 27.46$; $INT_{NSOC} = 57.17 \pm 14.46$ and $INT_{SOC} = 57.91 \pm 14.01$; $CON_{NSOC} = 45.53 \pm 11.96$ and $CON_{SOC} = 46.63 \pm 13.00$; $F_s(1,59) < 1.36$, $p_s > .25$], and no significant VAL \times SC interactions [$F_s(1,59) < 2.65$, $p_s > .11$] (as shown by a 2 [VAL] \times 2 [SC] repeated-measure analysis of variance [ANOVA]). Note that the differences in intensity between negative and positive stimuli could not be avoided in order to match pairs of social and nonsocial scenes in both valence conditions, because social material is otherwise typically judged as much more intense than nonsocial material (Ewbank, Barnard, Croucher, Ramponi, & Calder, 2009). Finally, we also selected 40 neutral images from the IAPS database (20 including humans, 20 without humans) to be used in a baseline control condition (see below), with average valence ratings of 49.7 ± 1.7 (on the same scale of 1–100).

The final experimental set of emotional images showed no differences in luminance across categories [$F_s < 2.83$; $p_s > .098$ in a 2 (VAL) \times 2 (SC) repeated-measure ANOVA], and all social images were comparable in terms of the average number of people depicted per image [complexity measure; SP versus SN: $F(1,59) = .468$; $p = .497$].

2.2.2. Experimental conditions

Before entering the fMRI scanner, all participants were told that the purpose of the experiment would be to investigate how the brain reacts to different types of images (e.g., real scenes, TV or movie scenes) and to which degree people can voluntarily influence the emotional impact of these images. Accordingly, the experimental layout comprised four different viewing instructions (INST), in which pictures were presented with different tasks to induce different emotion regulation strategies.

The first INST served a control baseline (BASE), and was introduced to the participants as “a photographic quality” judgment, where they had to indicate on each trial (by button press, using a 4-point scale—see below) whether the image was of good quality (e.g., well focused or properly lighted). All images in this condition were neutral, but could display either scenes with humans (i.e., social content) or inanimate settings and landscapes (i.e., nonsocial content). This viewing condition was later used to provide a baseline for general differences in brain activation to social vs. nonsocial stimuli, irrespective of emotional processing demands and valence. It

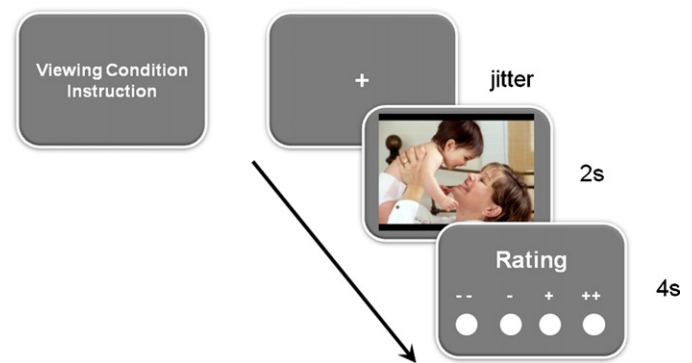


Fig. 1. Illustration of the within-block event-related fMRI paradigm. Each block for each viewing condition began with an instruction slide (7 s), followed by a series of pictures. Each picture was shown for 2 s, preceded by a central fixation cross (jittered between 790 and 1485 ms), and followed by an emotional rating display (4 s). Stimulus type (social vs. nonsocial, negative vs. positive) was pseudo-randomized within each of the different regulation condition blocks.

was presented as the first block of the first scanning run and the last block of the last run.

The three other INST constituted the main experimental design and included emotional images only. To assess brain responses during “natural” or spontaneous emotion experience (NAT), participants were asked to watch and evaluate the depicted emotional scenarios as if they corresponded to real situations to which the participants would be personally exposed. To assess the effect of cognitive re-evaluation (RE-APPRAISAL instruction; REAP), participants were instructed to view the depicted emotional scenes as parts of a movie clip or TV show that displayed fake or artificially set-up situations created to give rise to emotions. The latter strategy (“pretend unreal”) has been one of the most often used in order to down-regulate emotional reactions to negative and positive images (Kim & Hamann, 2007). Finally, to assess the effect of behavioral inhibition of emotional expression (EXPRESSIVE SUPPRESSION instruction; ESUP), the participants were told to watch the pictures similarly to the NAT condition, but with the important difference that they were instructed not to display any felt emotions that could become visible on the outside (e.g., through breathing frequency, heart rate, skin conductance responses, and facial expression—which were told to the participant to be recorded via electrodes attached to the body and an eye-tracker camera). After each picture, participants were shown a rating display and asked to report the feeling state evoked by the preceding stimulus (“How did you feel while seeing the last image?”), using a 4-point scale (see below).

All emotional images were counterbalanced across participants, so that the same images seen in one INST condition by a given subject were seen in the other INST conditions by different subjects.

2.2.3. Procedure

The fMRI experiment was divided into three successive scanning runs. Each run included two of the three INST conditions, presented in blocks of 40 emotional images (duration = 294 s per block), whereas the first and the last run also included an additional block of 20 neutral images (BASE, duration = 151 s). Within each block, images were pseudo-randomized and equally probable for the different stimulus categories (social vs. nonsocial content, positive vs. negative valence). Hence participants could not anticipate an image from a given category. The first and the third runs lasted approximately 13 min, and the middle run 10 min.

Each block began with an INST display (7 s), followed by images in pseudo-randomized order. Every individual trial started with a fixation cross at the screen center (average duration = 1125 ms jittered between 790 and 1485 ms), followed by an emotional or neutral image for 2 s, and then a response display probing for emotion ratings (4 s; see Fig. 1). This brief presentation enabled us to focus on stimulus-drive responses, while the same emotion regulation strategy could be employed in a sustained manner throughout each block. While many studies on ER have used longer stimulus duration and manipulated the strategy instructions in randomly mixed succession, here we chose a blocked design for the different instruction conditions, allowing us to obtain a stable task-set over successive stimuli and avoid any prolonged carry-over effects of emotions from one scene to the next (Pitroda, Angstadt, McCloskey, Coccaro, & Phan, 2008; Richiardi, Eryilmaz, Schwartz, Vuilleumier, & Van de Ville, 2010).

Ratings were made on a 4-button response box, according to a 4-point scale ranging from very and slightly negative (buttons 1 and 2, respectively), to slightly and very positive (buttons 3 and 4, respectively). This 4-point scale does not allow for strictly neutral values, but forced participants to make emotional judgments and was previously found to provide reliable emotion discrimination measures (e.g., Peelen et al., 2010).

2.2.4. MRI acquisition

MRI data were acquired on a 3 T whole-body INTERA system (Philips Medical Systems), using standard head-coil configuration. For each participant, a structural image was obtained with a MPRAGE T1-weighted sequence (TR/TE/Flip = 2200 ms/30 ms/85°, parallel acquisition (GRAPPA) with acceleration factor 2, FOV = 235 mm × 235 mm, matrix = 128 × 84, resulting voxel size is 2.8 × 1.8 × 3.4 mm³). Functional images (TI/TR/TE/flip = 900/1900/2.32/9°, parallel acquisition (GRAPPA) with acceleration factor 2, FOV = 230 × 230 × 173 mm³, Matrix = 256 × 246 × 192) covered the whole brain, composed of 36 contiguous 4 mm axial slices parallel to the inferior edge of the occipital and temporal lobes, and acquired continuously for a total of 975 images per participant (two sessions with 350 and one session with 275 images). Image quality was verified to exclude prominent signal drop-out in orbitofrontal and mediotemporal areas.

Image processing was performed with SPM2 (www.fil.ion.ucl.ac.uk) using standard procedures for realignment of the time-series, slice-timing correction, normalization to a standard brain template in MNI space, and smoothing with an 8 mm FWHM Gaussian kernel. Statistical analysis was performed using the general linear model implemented in SPM2, with a separate regressor for each event type convolved with a canonical hemodynamic response function. Twelve event types from the emotion regulation task (4 image categories: SP, NSP, SN and NSN; for each of the three INST: NAT, REAP, and ESUP), plus two additional event types (social and non-social) from the baseline condition (BASE) were modeled for each participant as separate regressors, using the three scanning runs in a fixed-effect analysis at the single-subject level. Movement parameters from realignment corrections were entered as additional covariates of no interest for each scanning run, in order to account for residual movement artifacts after realignment. Statistical parametric maps were then generated from linear contrasts between the different conditions in each participant.

A first second-stage random-effect (RFX) analysis was performed using one-sample *t*-tests on contrast images obtained in each subject for each comparison of interest. All contrasts were performed across the whole brain using standard threshold criteria (Worsley et al., 1996) of significant activation at a voxel-level of $p < .001$ uncorrected (except for bilateral amygdala, $p < .005$ given a priori predictions), and a cluster size greater than 5 voxels (135 mm³). Average parameter estimates of activity (betas) for each condition were extracted from all voxels in regions of interest (ROIs), defined by the full-extent clusters showing significant activation at a voxel level of $p < .001$ (T -value > 3.61 ; except for bilateral amygdala: $p < .005$, T -value > 2.88) in the SPM group analysis (random-effect contrasts). These beta values were then used for subsidiary repeated-measure ANOVAs and *t*-tests performed in SPSS with the factors of stimulus content, valence, and viewing condition, when appropriate.

Additional whole-brain RFX contrasts were also performed to reveal regions that showed differential responses to SOC versus NSOC and/or POS versus NEG images (and vice versa) as a function of the viewing conditions (e.g., $[NAT_{SOC} - NAT_{NSOC}] > [REAP_{SOC} - REAP_{NSOC}]$), and thus identify the selective effect of different emotion regulation strategies on different aspects of stimulus content (i.e., stimulus × viewing condition interactions). These comparisons were made using a stepwise paired *t*-test procedure applied to second-stage contrasts, as previously described elsewhere (Lazar, Luna, Sweeney, & Eddy, 2002; Ritchey, Dolcos, & Cabeza, 2008), which allowed us to assess specific non-crossed interactions between the factors of interest (unlike unconstrained interaction tests in SPM that typically probe for the two sides of an interaction in a single whole-brain contrast). Thus, the paired *t*-tests between relevant contrasts (e.g., NAT vs. REAP) were first inclusively masked with the SOC versus NSOC contrast or POS versus NEG contrast (at $p < .025$), and vice versa (to ensure that the interactions concerned the ROIs found to activate in the main effects of our initial RFX analysis), and then thresholded using a T -value > 3.61 ($p < .001$), and a cluster size of $k > 10$ voxels [270 mm³]. Even though probabilities may not be completely independent, this procedure results in an effective statistical significance that approaches the joint probability estimate of $p < .000625$ (Lazar et al., 2002; Ritchey et al., 2008), which is more stringent than the conventional statistical threshold of $p < .001$ at the voxel level.

3. Results

3.1. Behavioral data

During fMRI scanning, participants rated their emotional feeling in response to each picture on a four point scale (from very negative to very positive, see Section 2). These rating scores confirmed that positive images were significantly more pleasant and negative images less pleasant than neutral images, across all viewing conditions [average = $3.28 \pm .17$, $2.43 \pm .21$, and $1.52 \pm .15$ for positive, neutral, and negative, respectively; all pairwise comparisons $t \geq 14.44$, $p \leq .001$]. This difference was found regardless of stimulus categories [main effect of VAL, $F(1,18) > 6.24$, $p < .001$], without any effect of the social content for any of the emotional conditions [SP vs. NSP: $t(18) < 1.84$, SN vs. NSN: $t(18) < 1.47$, $ps > .05$, paired

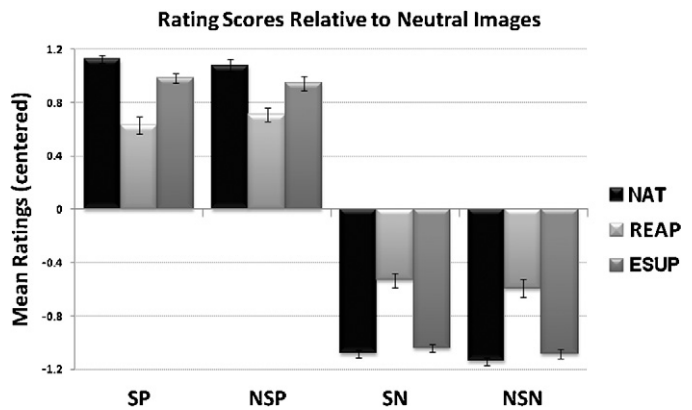


Fig. 2. Behavioral rating results. Subjects rated each image on a 4 point scale (from −2 and −1 for very and slightly negative, to +1 and +2 for slightly and very positive, respectively). While there was a clear main effect of picture valence, emotion regulation effects were stronger during REAP than during ESUP and significant (relative to NAT) for all four stimulus categories during REAP [$p < .001$], but only for POS stimuli [$p < .020$], not NEG stimuli [$p > .17$], during SUP. All values represent the average of individual means displayed with ± 1 S.E.M. Abbreviations: SP = Social Positive, NSP = Nonsocial Positive, SN = Social Negative, NSN = Nonsocial Negative, NAT = Natural Viewing, REAP = Reappraisal, ESUP = Expressive Suppression.

t-tests], and no interaction (VAL × SC × INST repeated-measure ANOVA).

More critically, however, the emotional rating of pictures was significantly modulated by the INST conditions induced by the different ER tasks (even though pictures were counterbalanced across participants and equally presented in each condition). As compared with the NAT condition, ER was successfully achieved during both REAP and ESUP conditions, leading to less intense emotional rating scores for all four stimulus categories during REAP [$t(18) > 4.35$, $p < .001$], and for POS stimuli during ESUP [$t(18) > 2.56$, $p < .020$]. There was no significant difference for NEG stimuli in the latter condition: $t(18) < 1.45$, $p > .17$. Moreover, as shown in Fig. 2, the effects of REAP on emotional ratings were stronger than those of ESUP for all four picture categories [paired *t*-tests, $ts(18) > 2.72$, $ps < .014$]. This pattern is consistent with predictions that REAP is a more efficient regulation strategy than ESUP.

3.2. fMRI data

The main aim of our study was to orthogonally vary ER (represented by INST) and stimulus content to test for any specific interactions within the whole brain. To achieve this goal, we first computed the main effects (Section 3.3 below) of scene content (SOC > NSOC, and vice versa; Section 3.3.1 and Fig. 3) and emotional valence (POS > NEG, and vice versa; Section 3.3.2 and Fig. 4), across all INST. Because only one study so far directly compared REAP and ESUP strategies (Goldin et al., 2008), we then also contrasted these two instruction conditions (REAP > ESUP, and vice versa; Section 3.3.3 and Fig. 5), across all picture types. All findings are summarized in Tables 1–3.

More critically, in a second step, we performed a random-effect SPM analysis using a stepwise *t*-test design on specific contrasts of interest (see Section 2), allowing us to test for the differential effects of each instruction condition as a function of emotional valence (INST × VAL interaction; Section 3.4.1) and social content (INST × SC interaction; Section 3.4.2) of scenes. Parameters of activity (betas) were then extracted from each region showing such interactions in the whole-brain analysis, and submitted to a full 3 (INST) × 2 (VAL) × 2 (SC) repeated-measure ANOVA to identify the specific sources of interaction. All findings for significant effects are summarized in Table 4.

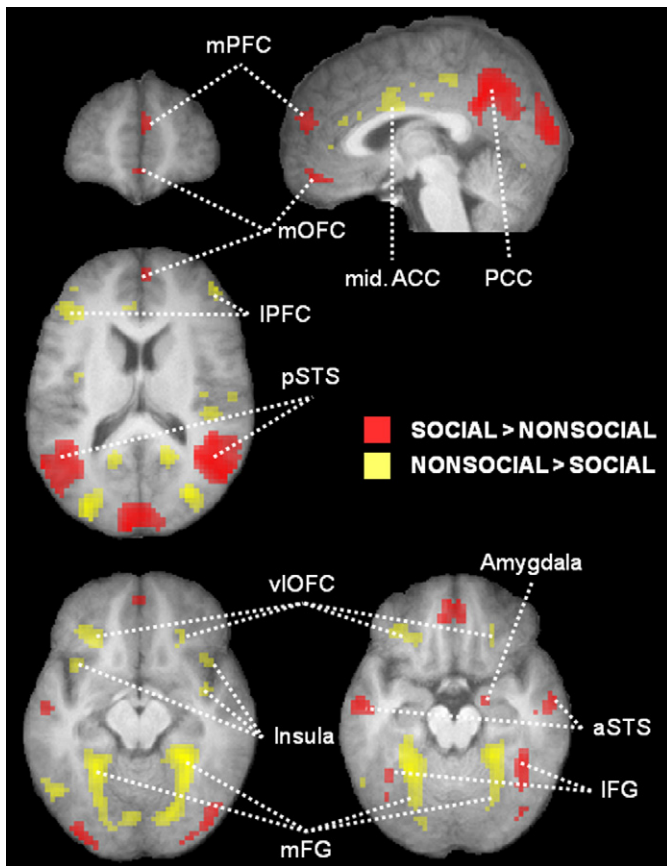


Fig. 3. Main effects of scene content. Statistical parametric maps (threshold $p = .001$) are illustrated for the contrasts SOC > NSOC (red) and NSOC > SOC (yellow), pooled across all viewing conditions. Abbreviations: mPFC = medial prefrontal cortex, mOFC = medial orbito-frontal cortex, vIOFC = ventro-lateral OFC, lat. PFC = lateral PFC, mid. ACC = middle anterior cingulate cortex, PCC = posterior cingulate cortex, pSTS = posterior superior temporal sulcus, aSTS = anterior STS, FG = fusiform gyrus, m = medial, l = lateral. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

3.3. Main effects

3.3.1. Comparison of social and nonsocial pictures

As expected, social scenes produced greater activation in widespread brain networks including extrastriate visual cortex, temporal lobe, and ventromedial prefrontal areas, all previously associated with face and body perception, person recognition, mentalizing, and/or social cognition (Britton et al., 2006; Goossens et al., 2009; Harris, McClure, van den Bos, Cohen, & Fiske, 2007; Norris et al., 2004; van den Bos, McClure, Harris, Fiske, & Cohen, 2007). Conversely, nonsocial scenes produced greater activation in visual regions associated with object and place recognition, as well as insula, anterior cingulate, and more lateral areas in prefrontal cortex (see Table 1 and Fig. 3).

3.3.2. Comparison of negative and positive pictures

Negative images (compared to positive) increased activity mainly in right insula, prefrontal and parietal cortex, dorsal anterior cingulate, and extrastriate visual cortex, all brain areas known to be involved in arousal, attention, and object recognition (Critchley, Melmed, Featherstone, Mathias, & Dolan, 2002; Kim & Hamann, 2007; Vuilleumier, Armony, Driver, & Dolan, 2001; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004). Positive images produced greater activation in subgenual anterior cingulate cortex, hippocampus, and occipital regions (see Table 2 and Fig. 4).

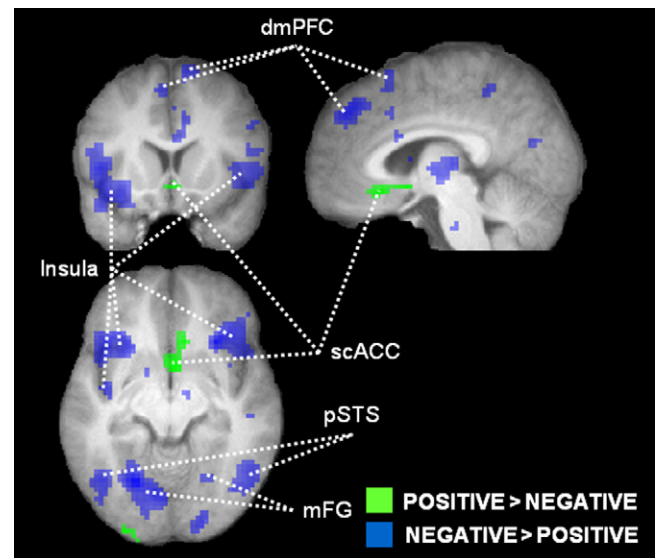


Fig. 4. Main effects of valence. The statistical parametric maps (threshold $p = .001$) are illustrated for the contrasts POS > NEG (green) and NEG > POS (blue), pooled across all viewing conditions. Abbreviations: dmPFC = dorso-medial prefrontal cortex, pSTS = posterior superior temporal sulcus, scACC = subcallosal ACC, mFG = medial fusiform gyrus. Note that when compared to the neutral control condition, both negative and positive stimuli produced strong and overlapping activations in several brain regions bilaterally, including medial orbitofrontal cortex, rostro-ventral ACC, dorsolateral prefrontal cortex, superior anterior temporal gyrus, posterior cingulate cortex, and temporo-parietal junction. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

3.3.3. Comparison of re-appraisal versus suppression

Of greater interest for the current study were the specific activations related to different ER strategies. Distinct clusters were identified in right prefrontal cortex (PFC) for the direct comparison REAP > ESUP (which activated the anterior part of the superior frontal gyrus [SFG] and posterior part of the middle frontal gyrus [MFG]; see Fig. 5a and Table 3), and for the comparison ESUP > REAP (which activated superior frontal sulcus and supplementary motor area [SMA]; see Fig. 5d and Table 3).

For both PFC clusters found to activate during REAP (Fig. 5a), we conducted further statistical tests using a full $3 \text{ (INST)} \times 2 \text{ (VAL)} \times 2 \text{ (SC)}$ repeated-measure ANOVA on beta values extracted from activated voxels (in SPSS, see Section 2). This analysis confirmed a main effect of INST [$F(1,18) > 6.09$, $p < .005$], which was due to significant increases during REAP relative to ESUP [$t(18) > 5.86$, $p < .001$], and to a lesser extent during NAT relative to ESUP [$t(18) \geq 2.24$, $p < .038$]. However, in both clusters, only the REAP condition produced significant increases as compared with the neutral baseline condition [BASE; $t(18) > 2.32$, $p < .032$] (Fig. 5b). Moreover, in the posterior right MFG cluster ($xyz = 39 \ 24 \ 54$), there was a significant $SC \times VAL$ interaction during REAP [$F(1,18) = 6.51$, $p = .02$], indicating that this activation was predominantly driven by the social negative (SN) image category, with a significant effect of picture content for negative [SN > NSN, $t(18) = 2.62$, $p = .017$], but not positive [Sp > NSP; $t(18) = .0443$, $p = .97$] images. In the SFG, there was also a marginally significant $SC \times VAL$ interaction [$p = .08$], but no main effects of SC [$p \geq .14$] in pairwise comparisons.

Conversely, for the right superior frontal sulcus cluster activated during ESUP (Fig. 5b and Table 3), a $3 \times 2 \times 2$ repeated measure ANOVA on beta values confirmed a significant main effect of INST [$F(1,18) = 9.42$, $p = .001$], reflecting a marked difference between ESUP and REAP [$t(18) = 5.07$, $p < .001$]. Moreover, only ESUP showed significant increases as compared with the neutral baseline [BASE; $t(18) = 3.16$, $p = .005$] (Fig. 5e). Finally, for the right supplementary motor area (SMA; Fig. 5c and Table 3), a similar

Table 1
Brain areas activated for the comparison between social and nonsocial emotional image categories.

Social content comparisons					
Region	BA	Voxel	T-value	xyz	ROI
<i>Social > Nonsocial</i>					
Amygdala left*		13	3.55	−21 −9 −18	x
Amygdala right*		26	4.21	21 −6 −18	x
mOFC	11	40	5.26	−3 54 −18	x
mPFC	10	28	4.36	3 57 15	x
PCC/PREC	7/23	393	7.32	0 −51 33	x
FG right	37	98	6.59	42 −42 −27	
dIPFC left	6	6	4.99	−39 3 60	
dmPFC left	9	9	4.77	−9 48 51	
dIPFC right	44	16	4.15	51 21 27	
ATP right	20	9	4.37	33 12 −36	
Temporal inferior left	20/21	109	6.85	−57 −3 −27	
Temporal inferior right	21	111	6.29	60 −6 −24	
pSTS left	19	458	7.82	−45 −84 0	
pSTS right	19	711	7.07	45 −48 18	
FG left	18	18	6.5	−15 −60 −6	
FG left	19/37	25	4.43	−42 −63 −21	
FG left	20	10	4.4	−42 −33 −24	
Occipital left	17	331	7.74	−6 −102 9	
<i>Nonsocial > Social</i>					
Insula middle right		151	6.42	57 3 −6	x
Insula middle right		39	4.78	33 18 −6	x
dIPFC left	6	32	4.71	−24 6 54	
dIPFC left	9	9	4.09	−21 54 24	
PFC right	11	17	5.38	12 39 −3	
dIPFC right	46	29	5.84	48 48 15	
dIPFC left	45	85	5.63	−42 33 18	
vOFC left	47	76	5.43	−36 36 −15	
vOFC right	47	22	4.78	24 24 −15	
Cingulate left	23	81	5.71	−3 −30 42	
Cingulate left	24	136	5.41	−3 3 30	
Cingulate right	23	9	5.39	9 −9 42	
ACC left	32	38	4.31	−6 36 18	
Insula medial left		94	7.28	−39 −6 6	
Insula posterior right		7	4.33	39 −18 15	
Insula anterior left		30	5.54	−39 15 −9	
Insula posterior right		18	5.79	39 3 9	
Temporal superior right	22	53	5.04	63 −18 9	
Supramarginal left	40	293	5.39	−54 −45 39	
Supramarginal right	40	301	7.41	51 −39 54	
Heschl's right	41	24	5.27	45 −30 15	
Calcarine left	17	25	5.47	−15 −60 15	
Calcarine right	17	62	6.3	18 −57 15	
FG right	37	923	9.51	30 −45 −12	
Occipital left	18	415	7.92	−33 −87 15	
Occipital left	37	43	7.22	−48 −63 −9	
Occipital left	17/18	5	4.12	−15 −99 −3	
Occipital right	18	265	7.61	30 −81 15	

Peak coordinates are given in MNI space and listed with best estimates of anatomical location. $p \leq .001$ for all clusters ($*p < .005$). BA = Brodmann's area, ACC = anterior cingulate cortex, ATP = anterior temporal pole, FG = Fusiform gyrus, mOFC = medial orbitofrontal cortex, vOFC = ventro-lateral orbitofrontal cortex, dIPFC = dorso-lateral prefrontal cortex, dmPFC = dorso-medial prefrontal cortex, mPFC = medial prefrontal cortex, PCC = posterior cingulate cortex, PREC = precuneus, ROI = region of interest, pSTS = posterior temporal sulcus.

ANOVA again indicated a main effect of INST [$F = 13.86$, $p < .001$], while pairwise comparisons revealed greater activity during both ESUP [$t(18) = 5.34$, $p < .001$] and NAT [$t(18) = 5.03$, $p < .001$] as compared with REAP. Moreover, both ESUP and NAT showed significant increases relative to BASE [$ts(18) > 2.38$, $ps \leq .028$] (Fig. 5f). No effect or interaction involving SC was found in these two clusters.

In all these regions, the repeated-measure ANOVAs showed no main effects of VAL [$Fs(1,18) \leq .09$, $ps \geq .76$] and no other interactions.

3.4. Selective regulation effects in different stimulus conditions

3.4.1. Regulation as a function of valence (INST \times VAL interactions)

No brain areas that responded to POS > NEG images were found to display different effects as a function of INST. By con-

trast, however, three brain regions that responded to NEG > POS images showed significant differences between regulation conditions (INST \times VAL interaction), as described below.

The dorso-medial prefrontal cortex (dmPFC, xyz = −3 33 51, Brodmann area 8, see Fig. 6a and Table 4) was significantly activated in the critical interaction test comparing the natural viewing condition NAT to REAP (i.e., $[NAT_{NEG} - NAT_{POS}] > [REAP_{NEG} - REAP_{POS}]$). A subsequent 3 (INST) \times 2 (VAL) \times 2 (SC) ANOVA on beta values from this cluster confirmed a significant INST \times VAL interaction [$F(1,18) = 4.89$, $p = .023$] (see Fig. 6d), and post hoc comparisons showed that it was due to a lack of increases to negative scenes during REAP [NEG > POS, $t = 1.95$, n.s.], unlike the increases seen in the other two conditions [$ts(18) \geq 3.33$, $ps \leq .004$]. Thus, the magnitude of the negative valence effect (activation difference between NEG vs. POS images) was significantly reduced during REAP relative to both NAT [$t(18) = 2.96$, $p = .008$] and to ESUP [$t(18) = 2.04$, $p = .057$];

Table 2

Brain areas activated for the comparison between positive and negative emotional image categories.

Valence comparisons					
Region	BA	Voxel	T-value	xyz	ROI
<i>Positive > Negative</i>					
ACC subcallosal right	25	69	6.07	3 9 -9	
Hippocampus left	37	7	4.58	-36 -39 -3	
Postcentral left	3	129	6.26	-42 -30 63	
Occipital left	18	17	5.54	-30 -99 -9	
Occipital right	17	6	4.31	15 -90 12	
<i>Negative > Positive</i>					
Insula anterior right		874	8.05	30 24 -12	x
dmPFC	8	309	6.83	0 42 48	x
FG/LG left	17	1581	9.13	-3 -84 6	x
dmPFC left	6	7	4.41	-15 12 63	
dIPFC right	8/9	8	4.38	27 30 42	
Cingulate medial right	32	37	5.06	9 18 36	
Caudate left		62	5.46	-9 6 3	
Caudate right		202	5.88	15 3 15	
Insula lateral left		662	7.86	-42 21 3	
Lingual/Precuneus right	17/18	796	7.53	21 -57 6	
Heschls' right	42	5	3.94	57 -39 24	
Postcentral left	3	12	4.61	-51 -18 51	
Precentral left	6	55	5.7	-45 -6 45	
aSTS right	20	17	4.91	51 -24 -15	
aSTS right	21	7	3.8	54 -39 -3	
Parietal superior right	7	136	5.35	12 -57 69	
Parietal superior left	40	53	4.54	-60 -39 39	
Temporal inferior left	20	10	4.46	-51 -3 -24	
FG right	19	15	3.97	24 -66 -9	
FG right	37	13	3.92	30 -51 -12	
FG left	37	17	4.56	-42 -42 -21	
Occipital right	18	54	5.68	21 -93 -6	
Brainstem		6	3.93	9 -21 -36	

Peak coordinates are given in MNI space and listed with best estimates of anatomical location. $p \leq .001$ for all clusters. BA = Brodmann's area, ACC = anterior cingulate cortex, FG = fusiform gyrus, LG = lingual gyrus, dIPFC = dorso-lateral prefrontal cortex, dmPFC = dorso-medial prefrontal cortex, ROI = region of interest, aSTS = anterior superior temporal sulcus.

but there was no significant reduction of this valence effect during ESUP compared to NAT [$t(18) = 1.45$, $p = .16$]. An ANOVA for each VAL condition separately confirmed that this pattern was produced by a selective modulation of responses to NEG scenes, as indicated by a main effect of INST for NEG [$F(1,18) = 3.96$, $p = .029$] but not POS pictures [$F(1,18) = .22$, $p = .80$]. In addition, the full $3 \times 2 \times 2$ ANOVA also indicated a clear main effect of VAL [NEG > POS; $F(1,18) = 24.35$, $p < .001$], but no effect of SC [SOC > NSOC; $F(1,18) = .365$, $p = .553$] and no other interaction [VCON \times SC; $F(1,18) = 3.02$, $p = .10$].

A second cluster in the *medial fusiform/lingual gyrus* (mFG/LG, $xyz = -24 -66 -9$) showed a similar interaction effect between VAL and INST (see Fig. 6b and Table 4). The full $3 \times 2 \times 2$ ANOVA on beta values also confirmed an interaction of INST \times VAL [$F(1,18) > 5.16$, $p < .011$] (see Fig. 6e), while post hoc comparisons indicated that it was due to a reduced VAL effect (difference between NEG vs. POS images) during REAP as compared with NAT [all $t(18) > 3.21$, $ps < .005$], but also during ESUP as compared with NAT [Fig. 6c,

yellow peak; $t(18) = 3.25$, $p = .004$]. Moreover, an ANOVA for each VAL condition again indicated that these changes were selective for the NEG images (main effect of INST: [$F(1,18) > 6.76$, $p < .003$]). There were no such effects for POS images (main effect of INST: $F(1,18) = .587$). In addition, the $3 \times 2 \times 2$ ANOVA showed main effects of both the VAL [NEG > POS; $F(1,18) > 33.52$, $p < .001$] and SC [NSOC > SOC; $F(1,18) > 27.06$, $p < .001$] of pictures, but no other interactions [VCON \times SC: $F(1,18) < 1.43$, $ps > .25$].

The third activation was found in the right *anterior insula* (aINS; $xyz = 36 27 -3$; see Fig. 6c [yellow cluster] and Table 4). A significant INST \times VAL interaction was confirmed by the full $3 \times 2 \times 2$ ANOVA on beta values [$F(1,18) > 4.76$, $p < .015$], reflecting a decrease of the VAL effect (difference between NEG vs. POS images) during both REAP [$t(18) > 2$, $p < .05$] and ESUP [$t(18) > 2.1$, $p < .05$; paired t -tests], relative to NAT (see Fig. 6f). Additional ANOVAs and pairwise comparisons again showed that these effects were specific to NEG scenes [main effect of INST: $F(1,18) > 5.47$, $p < .008$]; whereas

Table 3

Brain areas activated for the direct comparison between the two different Emotion Regulation Strategies.

Emotion regulation strategy comparisons					
Region	BA	Voxel	T-Value	xyz	ROI
<i>Reappraisal > Suppression</i>					
dIPFC right	9	12	5.13	18 51 45	x
dIPFC right	9	5	4.42	39 24 54	x
Parietal superior right	7	6	3.87	18 -57 69	
<i>Suppression > Reappraisal</i>					
IPFC right	46	6	4.1	27 42 24	x
SMA right	6	10	4.3	9 -6 63	x

Peak coordinates are given in MNI space and listed with best estimates of anatomical location. $p \leq .001$ for all clusters. BA = Brodmann's area, dIPFC = dorso-lateral prefrontal cortex, IPFC = lateral prefrontal cortex, ROI = region of interest, SMA = supplementary motor area.

Table 4
Brain areas displaying significant INST \times SC or INST \times VAL interactions.

Region	Contrast	BA	Voxel	T-Value	xyz
INST \times SC interactions					
<i>Social > Nonsocial</i>					
Insula middle right	NAT > ESUP		30	3.92	39 12 –9
Insula middle right	REAP > ESUP		20	5.06	51 –3 –3
<i>Social > Nonsocial</i>					
Amygdala left*	NAT > REAP		22	3.55	–21 –9 –18
Amygdala right*	NAT > ESUP		11	3.77	24 –9 –27
mOFC	NAT > ESUP	11	14	4.19	6 54 –15
mPFC	NAT > REAP	10	11	3.94	3 54 21
PCC/PREC	NAT > REAP	23	332	7.32	0 –51 33
PCC/PREC	ESUP > REAP	23	381	7.32	0 –51 33
INST \times SC Interactions					
<i>Negative > Positive</i>					
Insula anterior right	NAT > REAP		65	7.49	39 30 –3
Insula anterior right	NAT > ESUP		81	6.29	36 27 –3
dmPFC	NAT > REAP	8	25	5.28	–3 33 51
FG/LG left	NAT > REAP	18	251	8.12	–24 –66 –9
FG/LG left	NAT > ESUP	18	40	8.12	–24 –66 –9
<i>Positive > Negative</i>					
n.s.					

Peak coordinates are given in MNI space and listed with best estimates of anatomical location. $p \leq .001$ for all clusters (T-value for maximal voxel > 3.61 , $*T = 3.55$). BA = Brodmann's area, FG = fusiform gyrus, LG = lingual gyrus, mOFC = medial orbitofrontal cortex, PCC = posterior cingulate cortex, mPFC = medial prefrontal cortex, PREC = precuneus, ROI = region of interest.

there was no such modulation for POS scenes [main effect of INST: $F_s(1,18) \leq .739$, $p_s \geq .485$]. An additional main effect of VAL [NEG > POS; $F_s(1,18) > 46.6$, $p_s < .001$] was also present, with only a marginal main effect of SC [NSOC > SOC; $F_s(1,18) < 3.42$, $p_s > .081$], but no other interactions [INST \times SC: $F_s(1,18) < 1.92$, $p_s > .16$].

Taken together, these results indicate that both REAP and ESUP had an impact on responses to negative scenes in the insula and medial fusiform/lingual gyrus, whereas in addition REAP produced a selective reduction of responses to negative scenes in the dorso-medial PFC. No difference in the impact of ER strategies was observed for positive scenes. Only the medial fusiform/lingual gyrus was differentially sensitive to nonsocial content (presumably reflecting the predominance of objects (Pourtois, Schwartz, Spiridon, Martuzzi, & Vuilleumier, 2009) and places (Haxby et al., 2001) in these images (see above), but this factor did not interact with the valence condition.

3.4.2. Regulation as a function of social content (INST \times SC interactions)

For brain regions showing responses to NSOC > SOC images, a differential effect of each regulation task (INST \times SC interaction) was found in the right middle insula (see Fig. 7a and Table 4). An interaction effect was also observed in the mid-dorsal cingulate and left prefrontal cortex, but primarily driven by relative changes in the response to SOC images (data not shown), rather than to NSOC images. Therefore, only data from the right middle insula (mINS) were further analyzed.

This right mINS cluster (Fig. 7a) showed a selective activation to nonsocial emotional scenes that was significantly reduced during ESUP relative to the other INST (i.e., $[NAT_{NSOC} - NAT_{SOC}] > [ESUP_{NSOC} - ESUP_{SOC}]$, yellow cluster in Fig. 5). This INST \times SC interaction was confirmed by a full $3 \times 2 \times 2$ repeated-measures ANOVAs on extracted beta values [$F(1,18) = 7.40$, $p = .002$], and observed because the relative activation difference between NSOC versus SOC images was selectively abolished during ESUP as compared to both NAT [peak xyz = 39 12 –3; $t(18) = 3.99$, $p = .001$; Fig. 7b, red cluster] and REAP conditions [peak xyz = 51 –3 –3; $t(18) = 2.45$, $p = .025$; Fig. 7b, yellow cluster]. Additional ANOVAs and pairwise comparisons revealed that only responses to NSOC images were significantly modulated by INST [red cluster:

main effect of INST: $F(1,18) = 7.57$, $p = .002$]. There was no significant modulation for SOC images [main effect of INST: $F_s(1,18) < 2.0$, $p_s > .15$].

Finally, in addition to a main effect of SC [NSOC > SOC: $F_s(1,18) > 17.55$, $p_s < .001$], the full repeated-measure ANOVA on betas from the right mINS revealed main effects of VAL [NEG > POS; $F_s(1,18) > 19.78$, $p_s < .001$] and INST [$F_s(1,18) > 5.11$, $p_s < .01$], but there was no INST \times VAL interaction [$F_s(1,18) < .38$, $p_s > .69$].

For the opposite contrast SOC > NSOC, we observed different effects between each of the regulation conditions (INST \times SC interaction) in several cortical brain areas as well as in the amygdala.

First, two distinct clusters were found in the medial PFC (xyz = 3 54 21) and medial OFC (xyz = 6 54 –14) when comparing REAP to NAT or to ESUP (Fig. 8a, red and yellow voxels, respectively; see Table 4). The repeated-measure ANOVAs on extracted betas confirmed a significant INST \times SC interaction [$F_s(1,18) > 6.65$, $p_s \leq .004$] for both clusters, which was driven by the fact that the relative activation to SOC vs. NSOC images was significantly reduced during REAP [$t_s(18) > 3.42$, $p_s < .003$] and to a lesser extent during ESUP [$t_s(18) > 2.11$, $p_s \leq .049$] as compared to NAT. There was no effect when comparing REAP with ESUP [$t_s(18) < 1.81$, $p_s \geq .10$] (Fig. 8c). Additional ANOVAs and pairwise comparisons confirmed that INST modulated the neural response to SOC images only [main effect of INST: $F_s(1,18) > 5.29$, $p_s < .01$]; but no reliable modulation was found for NSOC images [main effect of INST: $F_s(1,18) < 3.24$, $p_s > .06$]. For both the mPFC and mOFC, there was also a clear main effect of SC [SOC > NSOC, $F_s(1,18) > 36.12$, $p_s < .001$], but no other interaction [INST \times VAL, $F_s(1,18) < 1.74$, $p_s > .19$].

A second effect was found in the posterior cingulate cortex (xyz = 0 –51 33, Fig. 8b and Table 4): The ANOVA on extracted beta values also revealed a highly significant INST \times SC interaction [$F(1,18) = 10.71$, $p < .001$, and $F(1,18) = 8.18$, $p = .001$, respectively for red and yellow voxels in Fig. 8b]. This interaction reflected a reduced activation to SOC versus NSOC images during REAP as compared with both NAT [red: $t(18) = 5.54$, $p < .001$; yellow: $t(18) = 3.76$, $p = .001$] and ESUP [red: $t(18) = 3.22$, $p = .005$; yellow: $t(18) = 4.44$, $p < .001$], but not for ESUP as compared to NAT [all $t(18) \leq 1.22$, $p_s \geq .38$] (Fig. 8d). Additional ANOVAs and pairwise comparisons confirmed the specificity of this modulation for SOC images [main effect of INST: $F_s(1,18) > 6.54$, $p_s < .004$]. Except

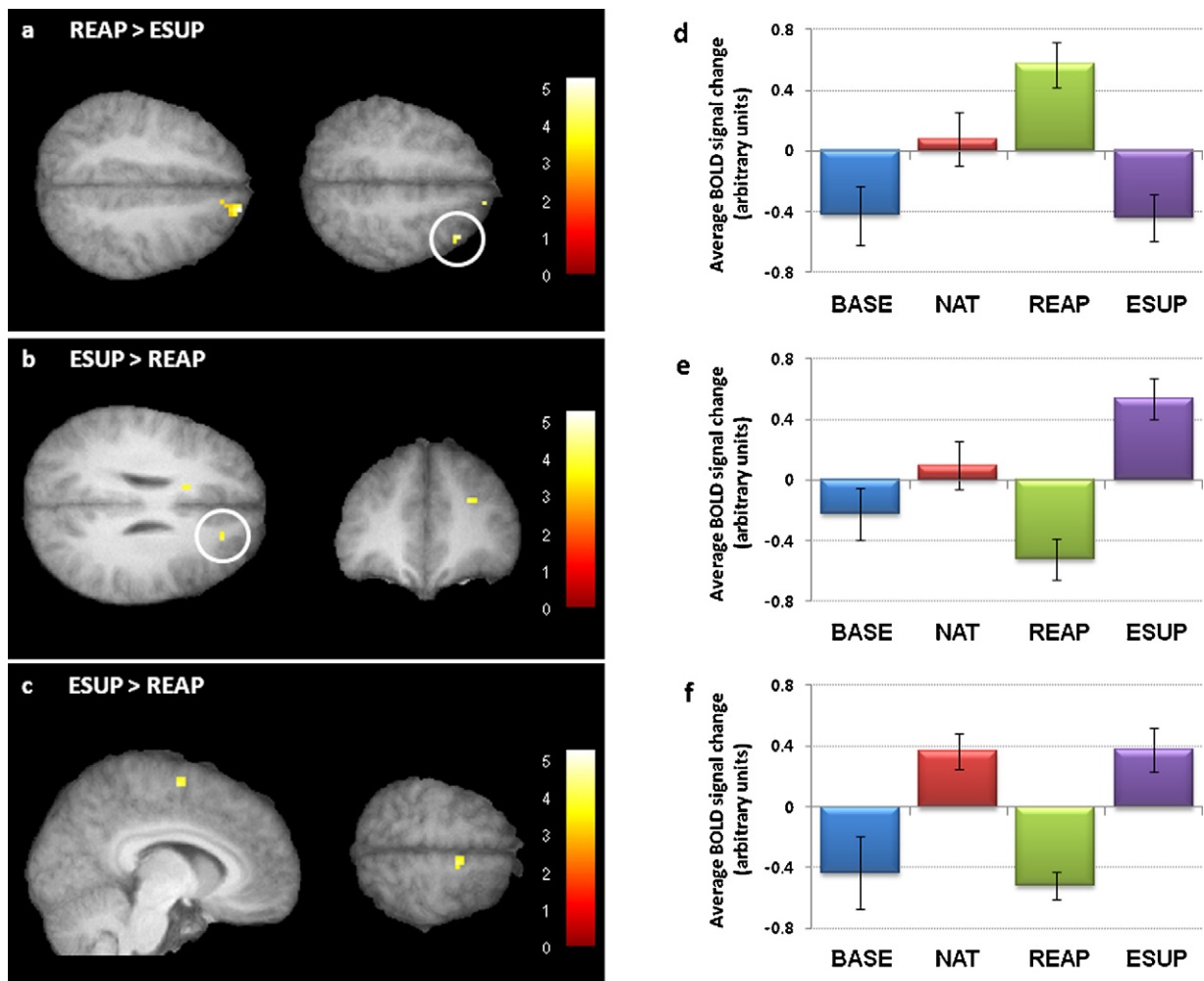


Fig. 5. Distinct PFC and SMA activations for the two Emotion Regulation Strategies. (a) Statistical parametric map for the contrast REAP > ESUP (at $p < .001$), showing activation in two areas of the right dorsal PFC (superior and middle frontal gyri [SFG and MFG]). (b) Statistical parametric map (at $p < .001$) for the contrast ESUP > REAP, showing activation in right superior frontal sulcus (SFS). (c) Statistical parametric map (at $p < .001$) for the contrast ESUP > REAP, showing activation in right supplementary motor area (SMA). (d) Parameter estimates (beta values) extracted from the MFG cluster in (a), averaged across voxels and participants, showing increases during REAP relative to ESUP, but also decreases during ESUP relative to NAT. A similar pattern of activity was also found for the right SFG cluster (see text). (e) Parameter estimates from the SFS cluster in (b), displaying significant increases during SUP relative to both REAP and NAT. (f) Parameter estimates from the SMA in (c), revealing decreases during REAP as compared to both NAT and ESUP. BASE = neutral condition with neutral pictures (see text). All values are displayed with ± 1 S.E.M.). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

for the additional main effect of SC [SOC > NSOC; $F(1,18) > 68.94$, $p < .001$], the repeated-measure ANOVA showed no other effect or interaction [$F(1,18) < .338$, $p > .72$].

Lastly, an interaction was found in *bilateral Amygdala* (see Fig. 9a and Table 4), but with a different pattern of effects for each regulation condition on each side.

In the left amygdala, a significant INST \times SC interaction emerged [$F(1,18) = 6.19$, $p = .005$, red] because the relative activation for SOC > NSOC scenes was abolished during REAP [SOC > NSOC, $t(18) = 1.76$, n.s.] and thus significantly differed from the activation for SOC > NSOC during NAT [$t(18) = 3.46$, $p = .003$]. This preferential amygdala response to SOC scenes still persisted in the ESUP condition [SOC > NSOC, $t = 2.81$, $p = .012$], even though activity was globally reduced and also slightly lower in this condition as compared to NAT [$t(18) = 2.27$, $p = .04$] (see Fig. 9c). Importantly, these modulations were specific for SOC images, as demonstrated by separate ANOVAs showing a significant main effect of INST for SOC [$F(1,18) = 4.68$, $p = .016$], but not for NSOC stimuli [$F(1,18) = .675$, $p = .456$].

In the right amygdala (Fig. 9b), however, a significant INST \times SC interaction [$F(1,18) = 6.41$, $p = .004$, yellow] was found because the

activation for SOC > NSOC scenes was selectively abolished during ESUP [$t(18) = .61$, n.s.]. This differed from the significant increase to SOC stimuli seen during both NAT [$t(18) = 3.32$, $p = .004$] and REAP [$t(18) = 2.64$, $p = .017$]. Additional ANOVAs also revealed a selective effect of INST on responses to SOC images [$F(1,18) = 3.38$, $p = .05$], but no effect for NSOC images [$F(1,18) = .50$, $p = .61$], and no other interactions (see Fig. 9d).

To verify this hemispheric asymmetry between left and right amygdala, we computed an additional 2 (SIDE) \times 3 (INST) \times 2 (VAL) \times 2 (SC) repeated-measure ANOVA, which revealed a significant triple interaction between SIDE \times INST \times SC [$F(1,18) = 5.05$, $p = .012$]. This triple interaction was driven by two factors: Firstly, the activation difference between SOC versus NSOC images showed a significant decrease during REAP as compared with NAT in the *left* amygdala only [left: $t(18) = 3.46$, $p = .003$; right: $t(18) = 1.16$, $p = .26$], leading to a marginally significant 2 (SIDE) \times 2 (INST) interaction [$F(1,18) = 3.60$, $p = .072$]. Secondly, the activation difference between SOC versus NSOC images showed a significant decrease during ESUP as compared to REAP in the *right* amygdala only [right: $t(18) = 2.64$, $p = .017$; left: $t(18) = 1.35$, $p = .193$], leading to a significant 2 (SIDE) \times 2 (INST) interaction [$F(1,18) = 9.85$, $p = .006$].

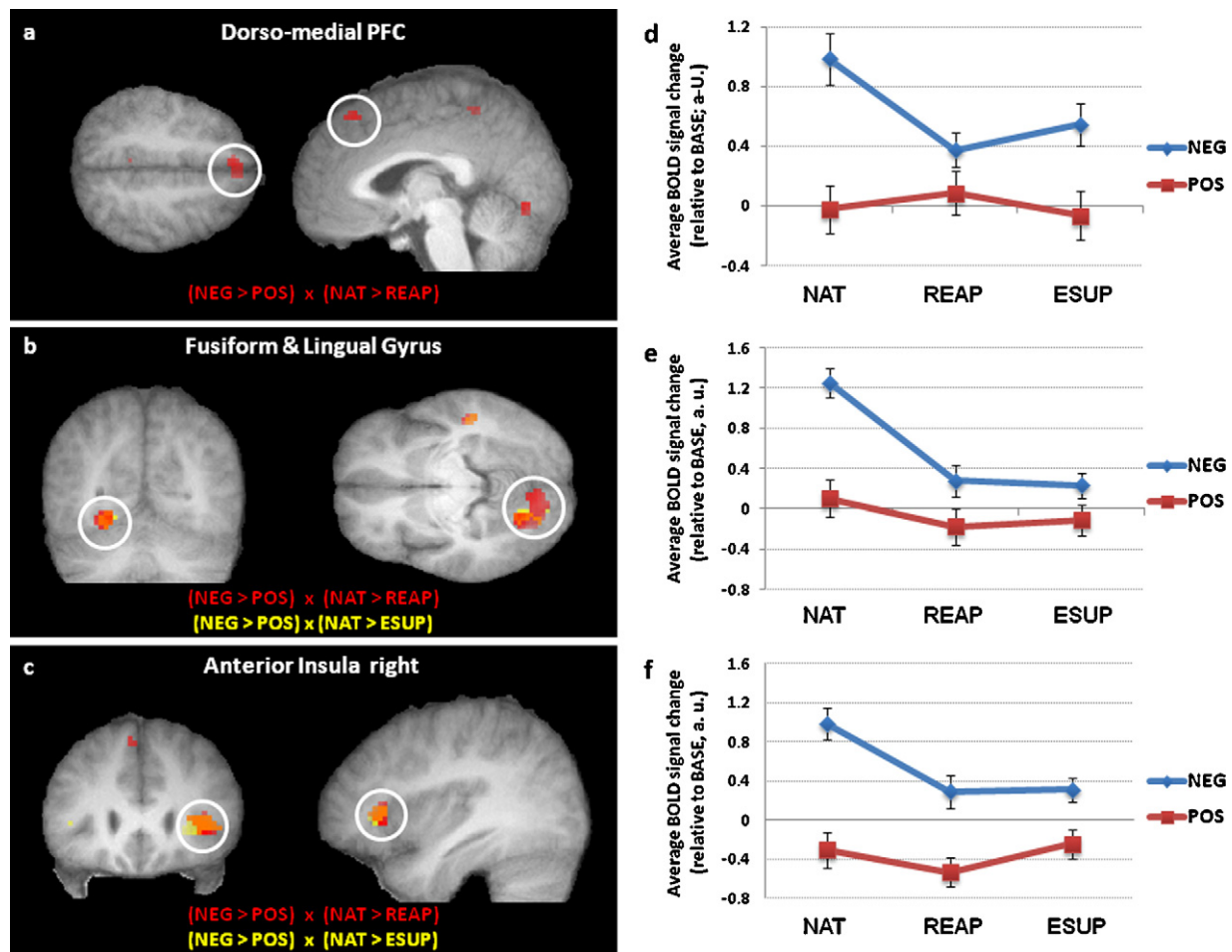


Fig. 6. Interactions of emotion regulation strategy with differential responses to negative > positive scenes (INST \times VAL). Statistical parametric maps are illustrated for the masked paired *t*-test model (threshold $p = .025$) comparing valence-specific responses between different instruction conditions [NEG > POS \times NAT > REAP (red); and/or NEG > POS \times NAT > ESUP (yellow)]. Significant effects were found in (a) left dmPFC ($xyz = -3\ 33\ 51$), (b) left medial fusiform ($xyz = -24\ -66\ -9$), and (c) right anterior insula ($xyz = 39\ 30\ -3$). Parameter estimates (beta values) extracted from the clusters in (d) dmPFC, (e) fusiform, and (f) insula, averaged across voxels and participants, are plotted for the different stimulus and viewing conditions, showing greater activation to NEG > POS pictures during NAT relative to REAP and ESUP in all cases, but a total lack of valence effect in the dmPFC during REAP, and a significant reduction of responses to NEG valence in other areas and other conditions. All values are displayed relative to the neutral baseline condition (BASE), with ± 1 S.E.M. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

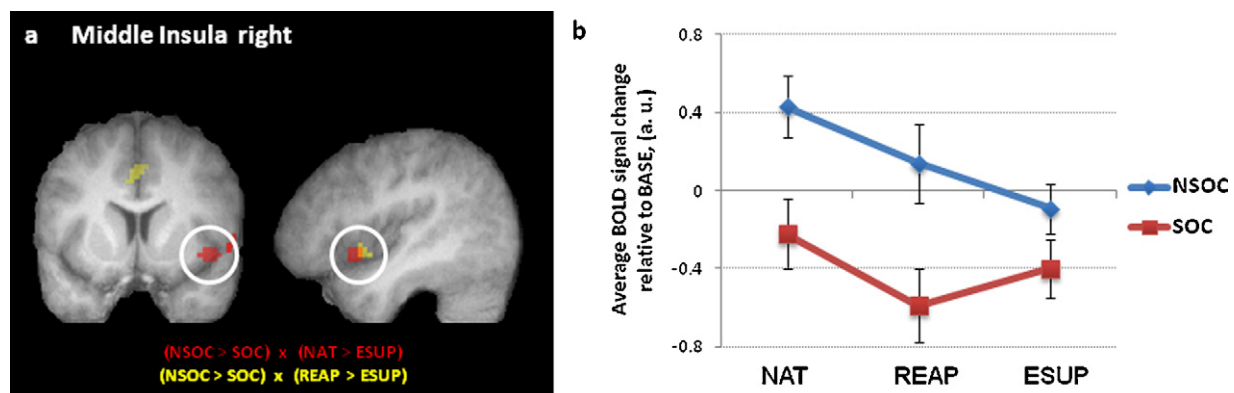


Fig. 7. Interactions of emotion regulation strategy with differential responses to nonsocial > social scenes (INST \times SC). (a) Statistical parametric map for the masked paired *t*-test model (threshold $p = .025$) comparing selective responses to nonsocial scenes between the different viewing conditions [NSOC > SOC \times NAT > ESUP (red); and NSOC > SOC \times REAP > ESUP (yellow)], showing a significant effect in the right mid insula. (b) Parameter estimates (beta values) for this region (as defined by the second cluster above, in yellow), averaged across voxels and participants, show a selective decrease of the NSOC > SOC activation difference during SUP. All values are displayed relative to neutral baseline (BASE), with ± 1 S.E.M. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

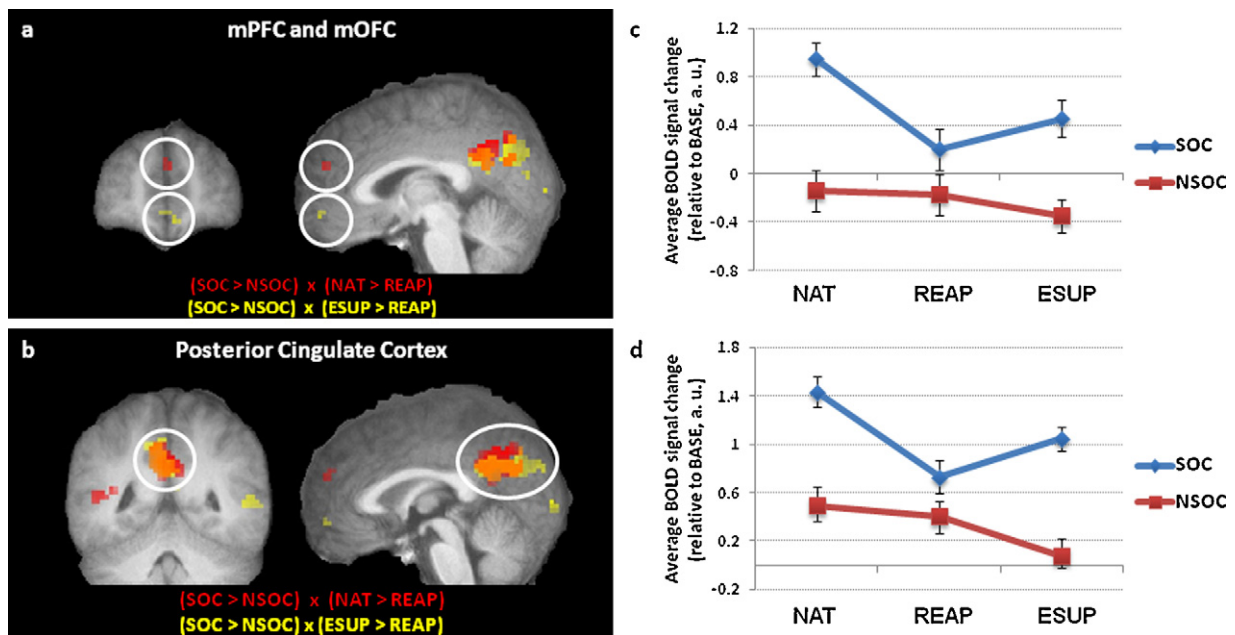


Fig. 8. Interactions of emotion regulation strategy with differential responses to social > nonsocial scenes (INST \times SC). Statistical parametric maps are illustrated for the masked paired t -test model (threshold $p = .025$) comparing activations to social stimuli between different viewing conditions, showing interaction effects (a) in mPFC ($xyz = 3\ 54\ 21$) for the contrast $[SOC > NSOC \times NAT > REAP]$ (red) and in mOFC ($xyz = 6\ 54\ -15$) for the contrast $[SOC > NSOC \times ESUP > REAP]$ (yellow); and (b) in PCC ($xyz = 0\ -51\ 33$) for the contrasts $[SOC > NSOC \times EXP > REAP]$ (red) and $[SOC > NSOC \times EXP > ESUP]$ (yellow). Parameter estimates (beta values) extracted from (c) the mPFC, (d) PCC, averaged across voxels and participants, showed consistent modulations for SOC images during REAP in all three regions. All values are displayed relative to neutral baseline (BASE), with ± 1 S.E.M. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

The repeated-measure ANOVA indicated additional main effects of SC bilaterally $[SOC > NSOC]$; left: $F(1,18) = 19.13$, $p < .001$; right: $F(1,18) = 10.11$, $p = .005$, but no main effects of VAL and no other interactions $[INST \times VAL: F_s(1,18) < 1.63]$, $ps > .21$.

4. Discussion

The current fMRI study aimed at differentiating the impact of emotion regulation strategies on activity in limbic and cortical brain areas as a function of the nature of affective cues, i.e., when

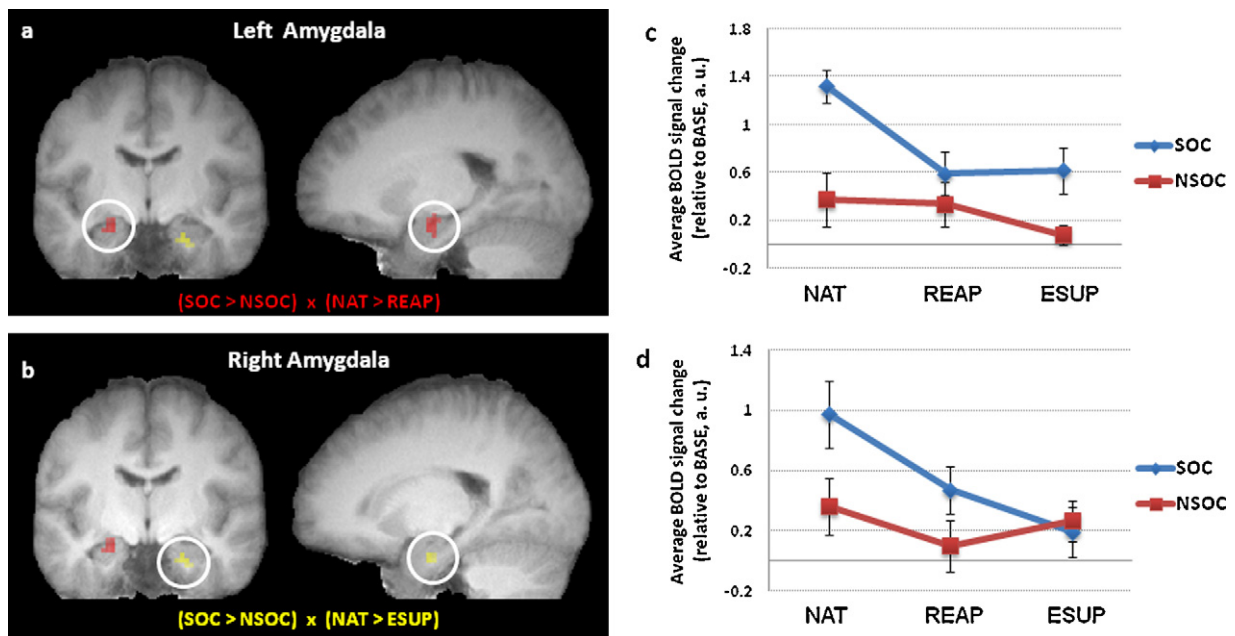


Fig. 9. Amygdala lateralization during emotion regulation. Statistical parametric maps for the masked paired t -test model (threshold $p = .025$) comparing activations to social stimuli between different viewing conditions, showing a significant interaction effects in (a) the left amygdala ($xyz = -21\ -9\ -18$) for the contrast $[SOC > NSOC \times NAT > REAP]$ (red); and (b) the right amygdala ($xyz = 24\ -9\ -27$) for the contrast $[NSOC > SOC \times NAT > ESUP]$ (yellow). Parameter estimates (beta values) extracted from the (c) left and (d) right amygdala clusters, averaged across voxels and participants, show different regulation effects in each hemisphere. The left amygdala displayed a selective elimination of differential responses to social (vs. non-social) images during REAP only. Conversely, the right amygdala exhibited a selective elimination of the social content effect during SUP only. This pattern led to a significant three-way interaction of hemisphere \times scene content \times regulation condition (see text). All values are displayed relative to neutral baseline (BASE), with ± 1 S.E.M. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

related to social (SOC) *versus* nonsocial (NSOC) information and when associated with negative (NEG) *versus* positive (POS) valence. To this aim, ER using either reappraisal (REAP) or expressive suppression (ESUP) strategies were systematically compared with a natural viewing condition (NAT) across different stimulus content conditions.

4.1. Behavioral results

Subjective ratings of visual scenes during fMRI scanning indicated that REAP was more efficient than ESUP in modulating emotion experience intensity, for all types of scenes (see Fig. 2). This pattern is consistent with previous data on the volitional control of emotions, particularly in response to negative stimuli (Goldin et al., 2008; Gross, 2002; Ochsner, Ray et al., 2004). By contrast, ESUP produced a significant reduction of emotion intensity ratings for POS scenes only (not NEG scenes). However, the social content (SC) of stimuli had no significant influence on subjective emotion experience, as evidenced by similar effects of REAP and ESUP on the rating scores for both social and nonsocial emotional scenes. This different impact of the two ER conditions accords with the notion that the ESUP strategy primarily regulates the behavioral expression of emotions but not the experienced feelings (Gross, 1998). It is also possible that the lack of effect of ESUP on the ratings of negative stimuli reflected their higher arousal values relative to the positive stimuli (see Section 2), although this difference had no such effect in the REAP condition. Because social stimuli typically tend to be judged as more arousing than nonsocial stimuli (Ewbank et al., 2009), we could not totally match emotion intensity between positive and negative scenes in order to obtain similar valence values for the more crucial comparisons of social and nonsocial content. Thus, social and nonsocial images were well matched on arousal (and control) judgments, and showed similar changes in subjective ratings across the different ER conditions. Nevertheless, despite this similarity in ratings, our fMRI results revealed specific effects of ER on the response of several brain areas as a function of the different content of emotional scenes. These results therefore point to specific neural sites where emotional processing can be modified by ER (e.g., in limbic and sensory areas), in addition to the possible neural sources where modulatory influences are presumably generated (e.g., in prefrontal cortices).

4.2. Prefrontal cortical regions as a putative source of emotion regulation

By directly contrasting brain activation in the two ER conditions with each other (REAP > ESUP and ESUP > REAP), irrespective of stimulus type, we identified a set of regions in the right prefrontal cortex (PFC) whose activity was differentially increased either during REAP (superior and middle frontal gyrus; SFG and MFG, respectively) or during ESUP (superior frontal sulcus and supplementary motor area; SFS and SMA, respectively; see Fig. 5). These regions showed no main effects or interactions due to the VAL or SC of scenes. Thus, activity in these regions depended on the nature of the ER strategy but not on the nature of emotional information to be regulated (except for MFG that was more activated by negative social scenes than other pictures). This pattern suggests a general role of the right PFC in processes subserving ER, rather than in the representation of emotional information per se.

Anatomically, these activations accord with previous studies describing increased activity in dorsolateral PFC during cognitive up- and down-regulation of both positive and negative emotions (Goldin et al., 2008; Kim & Hamann, 2007; Ochsner et al., 2002; Ochsner, Ray et al., 2004), as well as during behavioral suppression of negative affect (Goldin et al., 2008; Levesque et al., 2003). Such activations are thought to subserve the maintenance of appraisal

instructions or scripts used to re-interpret stimuli, as well as the resistance to interference by emotionally salient inputs, implicating in particular the SFG (Kim & Hamann, 2007; Ochsner et al., 2002), in addition to behavioral inhibition and voluntary suppression of bodily expressions, implicating more inferior frontal areas in SFS and lateral OFC (Levesque et al., 2003). Several regions in right dorsolateral PFC have also been involved in controlling task-set or stimulus–response mapping in various conditions, suggesting that this region is generally involved in the regulation and control of behavior (Brass, Derrfuss, Forstmann, & von Cramon, 2005). On the other hand, activation in the SMA was similarly increased during ESUP and natural viewing (NAT), relative to both the neutral baseline condition and REAP. This is consistent with a role of medial prefrontal areas in the planning and monitoring of affective motor behavior (Morecraft, Stilwell-Morecraft, & Rossing, 2004), which might operate during both ESUP and NAT but not when emotion experience was diminished by REAP (as indicated by subjective ratings).

Thus, our data provide new evidence for a functional anatomical segregation within PFC, including regions more specifically implicated in REAP (SFG and MFG) and others implicated in ESUP (SFS and SMA). These functions could be distinguished independently of any difference in their temporal dynamics as postulated in a previous study comparing REAP and ESUP (Goldin et al., 2008). In the latter study, brain regions associated with different ER strategies were primarily determined by imputing early responses after stimulus onset to REAP, while later responses after stimulus onset were ascribed to ESUP. Here, because ER was applied in a block-design, we could not reliably compare the time-course of stimulus-evoked responses in the different viewing conditions.

Even though there were no main effects of VAL or SC in right PFC, the MFG was the only area that displayed some degree of stimulus-related specificity during REAP. Signal changes in right MFG during REAP showed a selective social *versus* nonsocial effect for negative but not positive images, implying that its activity was the highest for SN information. These findings suggest that the down-regulation of negative emotion during REAP may require more cognitive processing or more effort for social as opposed to nonsocial stimuli, presumably because negative social information has a stronger intrinsic relevance for affect and behavior than nonsocial features (Hariri et al., 2002).

It should be noted that overall, the differences in activity representing the neural sources of regulation were less widespread in the present study, as compared with previous studies on ER. One possible reason for this could be the blocked presentation of ER instructions in our study, which ensured a stable task-set and allowed us to assess event-related responses to brief emotional stimuli, contrary to many prior studies where participants had to deploy a different ER strategy on each trial and stimuli were therefore presented for longer duration (e.g., Kim & Hamann, 2007; Ochsner et al., 2002; Ochsner, Ray et al., 2004). Such a design is likely to induce greater modulations of prefrontal regions with sustained activity related to top-down control, as opposed to sensory-driven regions involved in bottom-up perceptual processing. Another possibility is that in many other studies, instructions for the “natural” condition required participants to simply “look” at the pictures (Kim & Hamann, 2007; Koenigsberg et al., 2010; Mak et al., 2009; Ochsner et al., 2002; Ochsner, Ray et al., 2004), whereas we also asked participants to imagine that the situation could be experienced in reality, which may imply a first person perspective with personal involvement. Thus, our NAT conditions could actually have led to up-regulation attempts, which were treated as a different ER condition in some studies (e.g., “increase” strategy, see Ochsner, Ray et al., 2004). Because emotion up- and down-regulation may engage partly similar prefrontal areas, some effects could therefore cancel each other out when comparing regula-

tion conditions. However, note that we used a similar instruction to “imagine real situations” during ESUP (but with the additional suppression task), and nevertheless found reliable differences in brain responses between these conditions. More importantly, these task parameters did not affect our findings concerning the different impact of each ER strategy on emotional stimulus processing in other cortical and limbic brain areas, such as the amygdala, insula, and ventro-medial prefrontal areas (see below).

4.3. Emotion regulation as a function of valence

We were able to identify three brain areas where different ER conditions selectively influenced the processing of negative valence information (NEG vs. POS emotional images), including the dorso-medial PFC (dmPFC), anterior insula (aINS), and medial fusiform/lingual gyrus (mFG/LG; see Fig. 6). By contrast, no specific effects were found for the processing of positive valence (POS vs. NEG emotional pictures). Because NEG images were generally perceived as more arousing than POS images (see above), these effects of valence might also be partly attributed to the arousing value of visual scenes. However, both arousal and valence represent the most salient affective dimensions that can influence perception and attention towards emotional stimuli (Sabatinelli, Bradley, Fitzsimmons, & Lang, 2005; Vuilleumier & Huang, 2009). Importantly, these differences in arousal did not confound our critical comparisons between SOC and NSOC stimuli (see below).

In the dmPFC (see Fig. 6a), the relative increase to NEG *versus* POS scenes was selectively abolished during REAP (as compared to NAT as well as ESUP). Activation of this pre-frontal brain area in the context of ER has previously been described during up- and down-regulation of either negative (Ochsner, Ray et al., 2004) or positive (Kim & Hamann, 2007) emotions. In addition, the dmPFC has previously been reported to mediate self-monitoring and self-evaluation processes by computing internal representations of one's own and others' mind (Harris, Todorov, & Fiske, 2005; Mitchell et al., 2006), and is thought to contribute to the continuous updating of the value of actions (or errors) in order to regulate behavior (Amodio & Frith, 2006; Botvinick, 2007). Previous work on dmPFC responses to emotional stimuli also suggests that this brain region is involved in explicit affective judgments (Lane, Fink, Chau, & Dolan, 1997; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Lane, Reiman, Bradley et al., 1997), and preferentially activates to emotionally arousing conditions (Dolcos, LaBar, & Cabeza, 2004; Kensinger & Schacter, 2006). Accordingly, our new data suggests that REAP might reduce the cognitive aspects of emotion processing in dmPFC, related to self-monitoring and evaluation of behavioral actions, when emotional significance of visual scenes is lessened by the “pretend unreal” instruction (REAP). This reduction in activity nicely dovetails with our behavioral data showing a significant decrease of subjective emotion ratings during REAP (but not ESUP).

By contrast, the anterior insula (aINS) activation to NEG stimuli was attenuated during both REAP and ESUP (see Fig. 6c). Previous imaging work has consistently demonstrated that the aINS is involved in the representation of aversive stimuli, particularly disgust (Mataix-Cols et al., 2008; Phillips et al., 2004) and pain (Singer et al., 2004). Insula responses are specifically linked to the affective, but not sensory, components of pain (Singer et al., 2004). Moreover, its activation reflects the degree of bodily arousal evoked by NEG stimulus content, which might interface cognitive control with changes in autonomic responses during ER (Critchley et al., 2002). Because NEG scenes in our study often displayed people experiencing pain or distressing conditions (SOC category), as well as situations representing harmful or disgust conditions (NSOC category), the decreases in aINS activation might be interpreted as a reduction of the affective component of empathic responses and/or disgust. However, inspection of aINS responses across conditions

showed a relative preference for nonsocial over social stimuli (see result section 3.4.1), and a selective effect of REAP and ESUP on the processing of nonsocial (but not social) stimuli was also found in a partly overlapping region (see result section 3.4.2 and Fig. 7). Taken together, these data indicate that insula responses were mainly driven by negative nonsocial scenes, hence presumably related to disgust more than to pain or empathy. This interpretation is corroborated by the main effects of NEG > POS and NSOC > SOC that both revealed significant activations in the insula (Tables 1 and 2). Thus, our results demonstrate that both REAP and ESUP strategies produced a convergent modulatory effect on emotional processing of nonsocial aversive information in the insula, a brain area known to play a central role in the autonomic and subjective dimensions of affective responses (Critchley et al., 2002).

We also found that the processing of negative stimuli was selectively reduced by both REAP and ESUP in the medial fusiform/lingual cortex (see Fig. 6b). These regions showed preferential responses to nonsocial stimuli, consistent with their role in the visual processing of complex objects and scenes (Haxby et al., 2001; Pourtois et al., 2009). This modulation by ER accords with top-down influences on sensory processing in extrastriate visual areas for emotionally arousing and threat-related (e.g., fear conditioned) stimuli (Pourtois, Schwartz, Seghier, Lazeyras, & Vuilleumier, 2006; Sabatinelli et al., 2005; Vuilleumier & Driver, 2007), which may be driven by greater attention allocation and/or direct influences from amygdala (Vuilleumier & Huang, 2009; Vuilleumier et al., 2004). Accordingly, the reduction of differential responses to negative *versus* positive scenes during REAP as well as ESUP in visual cortex suggests a decrease in attention allocation to the sensory content of emotional scenes as a consequence of ER. During REAP, participants had to look at the scenes while imagining an artificial setting (“pretend unreal” as in TV or movie clips); whereas during ESUP, they had to concentrate on the inhibition of behavioral manifestations of emotion, thereby altering emotional responses and limiting attentional resources.

In sum, we found distinct effects of ER on the representation of negative emotional information, partly reflecting a modulation of the high arousal value of these stimuli, and involving several processing stages in distinct brain areas. Whereas the cognitive processes mediated by dmPFC were more specifically affected during REAP, visual processing in extrastriate cortex and affective responses in insula were modulated during both REAP and ESUP.

4.4. Emotion regulation as a function of social content

Differential responses to social (vs. nonsocial) emotional images were attenuated by ER in medial prefrontal (mPFC) and medial orbitofrontal (mOFC) cortex, and posterior cingulate cortex (see Fig. 8). All these regions are implicated in distinct aspects of social cognition. In addition, their activity was selectively modulated by REAP (not ESUP), except for the mPFC that was equally influenced by both ER conditions.

Abundant evidence points to a major role of mPFC in mentalizing about self and others (Gilbert et al., 2007; Mitchell et al., 2006), including the representation of personal emotional experiences and dispositions (called reflective awareness; Lane & McRae, 2004). Likewise, increased activity in PCC has been observed during tasks involving the attribution of emotion to self and/or other (Johnson et al., 2006; Ochsner, Knierim et al., 2004) and during theory of mind (Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2007), besides an activation to social stimuli and affective information about familiar persons in general (Britton et al., 2006; Pourtois, Schwartz, Seghier, Lazeyras, & Vuilleumier, 2005; Vrtička, Andersson, Sander, & Vuilleumier, 2009). Therefore, the response of mPFC and PCC to social *versus* nonsocial images in our study was most likely related to mentalizing processes and the attribution of emotional experi-

ences to humans seen in social images, as opposed to the inanimate displays seen in nonsocial images. Importantly, our results suggest that these attributional processes were attenuated by both REAP and ESUP strategies. These data further demonstrate that medial prefrontal activity during emotion regulation might be specifically related to the social meaning of emotional events.

In contrast, mOFC activation was significantly reduced during REAP only, and is generally considered to play a major role in reinforcement-guided decision making, especially in terms of the context-sensitive evaluation of outcomes (Rushworth, Behrens, Rudebeck, & Walton, 2007). This reduced activation of mOFC to social images during REAP might correspond to a decrease in cognitive operations required to compute the possible outcomes of social scenarios displayed in these scenes, involving for example intentionality—unlike the representation of more basic emotional cues such as appetitive food and disgusting material, typically depicted in nonsocial scenes (Hariri et al., 2002).

It should be noted here that both PCC and mPFC activation are also activated during resting, representing important components of the so-called default network (Buckner, Andrews-Hanna, & Schacter, 2008). Such overlap may agree with the notion that, when resting, subjects often tend to engage in internally focused mental activity that includes autobiographical memory retrieval and thinking about others (Buckner et al., 2008). Accordingly, changes in resting state activity have been observed following transient emotional events (Eryilmaz et al., 2011) and may reflect a role for these regions in social emotion regulation. Future studies should address more directly the possible associations between default mode and emotion regulation processes.

4.5. Amygdala lateralization during emotion regulation

Finally, and importantly, our results unveil a significant hemispheric lateralization in amygdala responses as a function of both the stimulus content and the ER strategy used (see Fig. 9). While bilateral amygdalae were generally more responsive to social than nonsocial scenes, this activation showed a distinct impact of REAP and ESUP in the left and right hemispheres. Firstly, REAP (but not ESUP) led to a complete elimination of the relative increase to social versus nonsocial images only in left amygdala. Conversely, in the right amygdala, this relative increase to social versus nonsocial images was selectively abolished during ESUP (but not REAP). In other words, cognitive re-evaluation (REAP) of social emotional information predominantly influenced neural activity in the left amygdala, whereas the right amygdala activation to the same scenes was more influenced by behavioral inhibition of emotional expression (ESUP).

This lateralization appears consistent with asymmetries found in a few other fMRI studies. On the one hand, two studies reported that up- and down-regulation of negative emotions by REAP affected activity in the left amygdala more significantly than in the right amygdala (Kim & Hamann, 2007; Ochsner, Ray et al., 2004). On the other hand, another study found that down-regulation of sexual arousal influenced right amygdala activation selectively (Beauregard et al., 2001). Taken together, these data suggest that up- and down-regulation of emotion in left amygdala may reflect the use of more “cognitive”, perhaps verbally mediated strategies, whereas regulation in the right amygdala may be more related to “bodily” or nonverbal strategies specific to the non-dominant hemisphere (Kim & Hamann, 2007; Ochsner, Ray et al., 2004). Accordingly, a recent meta-analysis on lateralized amygdala activations linked to emotional memory (Sergerie, Lepage, & Armony, 2006) proposed that: (1) the right amygdala may be involved in the fast, relatively automatic detection of emotional stimuli; and (2) the left amygdala may be involved in a more sustained and detailed cognitive processing stage. These previous accounts accord

with our new data indicating that the left amygdala responses to social (negative) emotional stimuli might be more strongly influenced by cognitive re-evaluation (REAP), possibly using verbal scripts, whereas emotion processing in the right amygdala might more readily be modulated by behavioral inhibition (ESUP) with less explicit cognitive evaluative components. In the future, it will be important to further refine such lateralization effects in terms of associated peripheral arousal measures (apart from subjective emotional ratings).

Importantly, it should be emphasized that these bilateral amygdala activations were driven by differential responses to SOC versus NSOC stimuli, but we did not find significant amygdala activation for the contrasts between NEG versus POS scenes. This pattern is consistent with data from several previous experiments describing preferential amygdala activation to SOC stimuli including faces, pictures, or film-clips (e.g., Britton et al., 2006; Goossens et al., 2009; Hariri et al., 2002; Norris et al., 2004). These results also accord with recent proposals that the amygdala might be particularly tuned to the intrinsic salience or biological importance of SOC stimuli (Sander, Grafman, & Zalla, 2003), rather than to threat or other specific emotion categories.

Lastly, our findings do not entirely corroborate a previous fMRI study that also compared REAP and ESUP, but found a sustained insula and amygdala activation during the suppression of negative emotions (Goldin et al., 2008). However, this study identified the effects of ESUP at a late latency (10.5 – 15 s) after exposure to film-clips, based on the assumption that ESUP should operate only after emotions have been generated, and therefore arise later than REAP effects (Gross, 1998). Because we applied a different methodology with a brief image exposure of 2 s, the results of these two studies are difficult to compare. In addition, Goldin et al. (2008) did not distinguish between responses to social and nonsocial emotional stimuli, a dimension that clearly determined the magnitude of amygdala and insula responses in our study. More research is needed to further elucidate the distinct time-courses of ESUP and REAP on activity in subcortical and cortical brain regions during emotional processing.

4.6. Limitations

One potential limitation of the present investigation was that we studied women only and did not control for any possible menstrual cycle effects. Because females may show distinct patterns of brain responses to emotional stimuli and exhibit variations due to hormonal fluctuations (see e.g., Andreano & Cahill, 2010), it remains to be seen in future studies whether the current effects can be extended to males and whether they may vary according to hormonal levels. However, our results are comparable with other studies on emotion perception and regulation that also scanned female participants only and did not record the cycle parameters (e.g., Ochsner, Knierim et al., 2004; Ochsner, Ray et al., 2004; Kim & Hamann, 2007). Moreover, it is unlikely that any emotion or regulation effect contingent on a specific time-point in the menstrual cycle would survive our statistical threshold at the group level, and none of the emotional condition used here involved material associated with attractiveness or erotism which could be particularly sensitive to menstrual fluctuations (see e.g., Gizewski et al., 2006).

Another possible limitation might stem from the relatively short exposure time of 2 s used for emotional and neutral images (see Section 2). Although exposure times of 2 s or even less are standard in fMRI research involving emotional stimuli and effective to activate relevant brain structures (e.g., Britton et al., 2006; Goossens et al., 2009; Hariri et al., 2002; Norris et al., 2004), many paradigms in the field of emotion regulation have employed longer picture viewing times (e.g., Beauregard et al., 2001; Kim & Hamann, 2007; Koenigsberg et al., 2010; Levesque et al., 2003; Mak et al., 2009;

Ochsner et al., 2002; Ochsner, Ray et al., 2004). However, in contrast to these investigations where regulation strategies alternate on a trial-by-trial basis and hence require the search for image-specific adjustments (e.g., re-interpretations during REAP), here we applied a blocked design where regulation could be implemented in a more sustained manner (as already used elsewhere, e.g., Harenski & Hamann, 2006; Phan et al., 2005) and was guided by controlled instructions (e.g., “pretend unreal” for the REAP strategy) for all stimulus conditions and all participants. Therefore, although precluding a modulation of longer emotional “states” (see Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011), our study nonetheless could focus on the selective effects of REAP and/or ESUP on stimulus-driven emotional responses and was actually capable of delineating pronounced modulations in several subcortical and limbic brain areas.

5. Conclusion

By directly comparing cognitive reappraisal (REAP) and behavioral inhibition (ESUP) as two major strategies for emotion regulation, and differentiating their effect on distinct dimensions of emotional stimuli (including social *versus* nonsocial significance besides positive *versus* negative valence factors), the present study yields several new insights into the neural mechanisms of emotion regulation in humans.

On the one hand, we found that a number of regions in right dorsolateral PFC were differentially recruited by emotional scenes during REAP or ESUP, but regardless of content, suggesting a general role in regulatory processes. Only the right MFG showed greater increases for negative social scenes compared to other image categories, presumably reflecting the greater emotional saliency of these stimuli, and hence the greater demands for successful regulation.

On the other hand, we identified several sites where ER had a differential impact on specific aspects of stimulus processing. Some regions were selectively modulated by REAP. These included the right dmPFC, which was preferentially engaged by negative valence information, as well as the left amygdala, PCC, and medial OFC, which all were involved in processing social information. Altogether, these modulations are likely to reflect changes in self-monitoring, evaluation of personal relevance, and anticipation of potential outcomes, under the influence of REAP strategies. Because emotional responses to the negative or social conditions in these areas were selectively attenuated during REAP but not ESUP, our findings suggest that the “pretend unreal” strategy implied a predominant modulation of high-level cognitive representations related to social judgment, mental imagery, and/or self-relevant association processes. Conversely, the right amygdala was the only region to be more strongly modulated by ESUP than REAP, possibly reflecting a specific impact of ESUP on autonomic and physiological components of emotions mediated by the right amygdala. This predominant right-sided effect of ESUP contrasted with the stronger left-sided effect of REAP, although both amygdalae were equally responsive to social information overall. This result reveals a significant lateralization in ER effects on the human amygdalae, possibly reflecting a differential impact of verbal, cognitive strategies (REAP) and non-verbal, arousal-related strategies (ESUP) on the left and right side, respectively.

Finally, several brain regions were modulated by both REAP and ESUP. These included the right insula and extrastriate visual areas (medial fusiform/lingual gyrus), which were most sensitive to negative nonsocial scenes involving disgust and other harmful situations, but also the right mPFC which preferentially responded to social stimuli. These activation patterns may reflect common influences of the two ER strategies on attention and perception,

changes in affective processes underlying arousal and pain-related representations, as well as higher cognitive effects related to mentalizing about self and others. More generally, we surmise that the more widespread effects of REAP relative to ESUP may reflect the more efficient and greater benefits of the former over the latter strategy (Gross, 2002; Jackson et al., 2000).

Taken together, our findings therefore do not only highlight the distributed nature of neural changes induced by emotion regulation, but also reveal the selectivity of impact for different strategies (re-appraisal or expressive suppression) and for different dimensions of emotional information (social content or valence). This underscores the importance of comparing different strategies and different stimulus categories when investigating emotion regulation, in order to better understand the specificity and underlying mechanisms of these effects. Only by carefully taking into account these different factors, we will be able to better apprehend the effective impact of emotion regulation and eventually develop more efficient intervention therapies in clinical disorders related to emotion regulation dysfunctions.

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