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Research report

## Activity in medial prefrontal cortex during cognitive evaluation of threatening stimuli as a function of personality style

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### Abstract

Cognitive evaluation of emotional stimuli involves a network of brain regions including the medial prefrontal cortex (mPFC). However, threatening stimuli may be perceived with differential salience in different individuals. The goal of our study was to evaluate how different personality styles are associated with differential modulation of brain activity during explicit recognition of fearful and angry facial expressions. Twenty-eight healthy subjects underwent fMRI. Based on a cognitivist model, subjects were categorized according to how they attribute salience to emotional stimuli and how they regulate their emotional activation. We compared 14 phobic prone (PP) subjects, whose identity is more centered on the inner experience ("inward") and around control of environmental threat, and 14 eating disorders prone (EDP) subjects, whose identity is more centered on external referential contexts ("outward") and much less around control of threatening stimuli. During fMRI subjects either matched the identity of one of two angry and fearful faces to that of a simultaneously presented target face or identified the expression of a target face by choosing one of two simultaneously presented linguistic labels. The fMRI results indicated that PP subjects had greater mPFC activation when compared with EDP subjects during cognitive labeling of threatening stimuli. Activity in the mPFC also correlated with personality style scores. These results demonstrate that PP subjects recruit greater neuronal resources in mPFC whose activity is associated with cognitive aspects that are closely intertwined with emotional processing. These findings are consistent with the contention that cognitive evaluation and salience of emotional stimuli are associated with different personality styles.

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**Keywords:** Emotion recognition; Fear; Prefrontal cortex; fMRI; Personality

### 1. Introduction

Emotion recognition in humans has been considered as an innate ability which is critical for social communication and survival [23,57]. Among others, facial expressions represent salient signals for emotion recognition, providing a means for dynamic nonverbal language and social interactions [23,28]. In particular,

facial expressions of fear and anger are universally recognized as signals of potential threat. Recognition of these signals in humans involves both perceptual processing of facial features and interpretation of the emotional meaning of the expression [1]. The latter process varies in the degree to which it is implicit (relatively automatic, reflexive and, perhaps, unconscious) or more explicit (deliberate and conscious) [31], therefore requiring additional cognitive processing.

Converging evidence from studies in animals and neuroimaging studies in humans shows that the amygdala is centrally involved in implicit processing of emotional stimuli. More specifically, amygdala activity is elicited by passive viewing

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of faces [30,38], especially with fearful expression [7,15,73], by implicit processing of fearful faces (e.g., gender discrimination or matching expressions) [34,50,62], and by masked fearful faces [51,65,75,76]. These findings suggest that the amygdala is implicated in automatic (even unconscious) processing of salient threatening stimuli and confirm its role in detecting danger [43].

On the other hand, cognitive evaluation of emotional stimuli, including explicit recognition of fearful facial expressions (e.g., cognitive labeling) has been associated with attenuated responses in the amygdala [35,42,53,54] and with greater activity in the prefrontal cortex (PFC) relative to implicit processing. Also, the medial part of the prefrontal cortex (mPFC) has been associated with cognitive evaluation of emotional stimuli [56] and with judgement of their emotional valence [36]. Furthermore, this prefrontal region is engaged to a greater degree when more complex, conscious appraisal is required by asking evaluation of the extent of personal relatedness of the stimuli [60].

The above-described studies may suggest a relative functional specialization within the neuronal network involved in emotion recognition, with medial prefrontal cortical nodes more involved in the conscious explicit evaluation on the one hand, and the amygdala, on the other, more associated with automatic implicit processing of emotional stimuli. Moreover, these brain regions seem to interact. Relative disengagement of the amygdala is simultaneous to greater engagement of the prefrontal cortex during cognitive labeling of emotional stimuli, possibly reflecting cognitive control of emotional responses through appraisal and evaluation of emotional stimuli [35].

Individual variability in implicit processing of emotional stimuli has been highlighted by previous studies [55]. For example, fMRI studies have indicated association between amygdala activity during implicit processing of emotions and personality traits such as extraversion, neuroticism [18,19], or inhibited temperament [68]. More recently, Bertolino et al. [8] have also demonstrated that amygdala activity during perceptual processing of fearful and angry faces varies as a function of personality style.

The most widely accepted theories of personality focus upon the necessity of integrating biological determinants with the environment. A model that can take into account both aspects of personality is the post-rationalist approach developed from within the cognitive school of thought [32]. One of the most important theories on which this model is developed is the attachment theory [2,9–14,17]. Recognizing an ontological value to the attachment relationships, the concept of personality style [3,4,32] has been elaborated based on the style with which individuals organize their emotional and cognitive domains in relationship to their attachment patterns. Based on this framework, two general categories of constructing identity are identified which differ in regulation of emotional and cognitive processes: the “inward”, more focused on the inner experience; and the “outward” more focused on external referential contexts or figures to control and regulate their emotional experiences [4]. Within these two categories, four personality styles are identified among which “phobic prone” (PP, inward)

and “eating disorders prone” (EDP, outward) individuals. The “phobic prone” personality style is more focused on inner bodily references; that is, they primarily focus on emotions using bodily reactions to evaluate events in the world, especially emotions. For instance, PP subjects tend to use their bodily reactions to automatically evaluate how dangerous may be stimuli that are implicitly threatening. Therefore, these subjects preferentially show automatic appraisal [27], rapid and intense responses to emotional signals. Basic emotions (especially fear) play a central role in the development of personality and they are usually perceived with immediacy [4,32]. Emotions are generated through automatic appraisal [27] so that they begin without the individuals being necessarily aware of the processes involved which also induce emotional activation (arousal). For these individuals it is also important to keep intensity of internal reactions within a manageable range because it allows a clearer demarcation of one’s own experience from the experience of others. Moreover, when the stimuli are explicitly dangerous, PP subjects tend to use cognitive resources to match the saliency of the stimulus with bodily reactions to control their intensity. Accordingly, control of bodily reactions becomes an important constituent of the phobic prone identity when the stimuli are implicitly and/or explicitly dangerous. Therefore, the only difference between evaluation of implicit and explicit stimuli is the more or less automatic appraisal afforded by the stimuli. In sum, the emotion of fear and its control are centrally salient to PP individuals to regulate their emotional life.

On the other hand, the “Eating disorders prone” personality style is more focused on an external frame of reference, such as contexts or persons, to discriminate among its own internal emotional states. Since these persons are constantly centered on the external environment, they have a limited ability to discriminate among internal emotional states and reactions. Therefore, an undifferentiated arousal prevails, which can only be interpreted with the aid of specific circumstances and external contexts. On the other side, these persons tend to be more apt in the discrimination of “cognitive” and “self-conscious” emotions [3,4,32,46,67]. In other words, these individuals will build inner stability by continuously referring to the outside world, attempting to match their own feelings and emotions with it. In sum, EDP individuals tend to be more consciously aware of the evaluative processes generating an emotion, while their emotional life is much less centered around fear. In conclusion, PP and EDP subjects seem to differ prominently in terms of the immediacy with which they process basic emotions such as fear. Of note, it is necessary to underline that the terms “phobic prone” and “eating disorders prone” do not necessarily implicate that these subjects are at higher risk of pathological phobias or of eating disorders.

The goal of this fMRI study was to explore how different personality styles may be associated with differential modulation of brain activity during explicit recognition (cognitive labeling) of threatening emotional facial expressions. Since threatening stimuli may have greater salience in healthy PP subjects [8], we hypothesized that these individuals would engage greater neuronal resources in brain regions associated with explicit cognitive labeling of angry and fearful faces.

## 2. Subjects and methods

### 2.1. Subjects

Twenty-eight healthy subjects were enrolled in the study (18 females, mean age  $\pm$  S.D.  $33.5 \pm 8.5$ ). Exclusion criteria included any psychiatric diagnosis (assessed with SCID for DSM-IV), history of significant drug or alcohol abuse (no active drug use in the past year), head trauma with loss of consciousness, and any significant medical condition. The semi-structured interview for personality style [8] was administered independently by two investigators (GPA and VM). Briefly, the interview was structured in three consecutive steps: (1) a detailed account of two episodes (involving fear and/or anger), (2) a description of the emotional experience of anger and fear to assess the style of emotional activation and regulation, (3) an analysis of onset, manifestations and extinction of the emotional experience [8]. Based on this interview, 14 subjects were categorized as PP (nine females, mean age  $\pm$  S.D.  $32.7 \pm 9.6$ ) and 14 EDP (nine females, age  $34.3 \pm 7.6$ ). The two groups were matched for a series of variables, including age, gender, intelligence quotient (IQ, as assessed by the WAIS-R), parental social–economical status [37], level of education and handedness [58].

Subjects also completed the personality meaning questionnaire (PMQ), [63] evaluating key cognitive themes characterizing different personality styles. The questions in which PP subjects tend to score higher identify greater need for emotional over-control in situations that may be felt as potentially dangerous (PP score [63]). The questions in which EDP subjects score higher identify increasing need for consent and approval, sensitivity to judgment, and vulnerability to criticism (EDP score, [63]). Subjects also completed a series of questionnaires identifying different personality characteristics such as the NEO five factors inventory [22], the temperament and character inventory (TCI) [21], the positive and negative attitude scale (PANAS) [74], the eyseck personality inventory (EPI) [29], and the big five questionnaire (BFQ) [20].

The present study was approved by the local IRB. Moreover, after complete description of the study to the subjects, written informed consent was obtained.

### 2.2. Experimental paradigm

Subjects were required to perform a facial affect discrimination task [34] during fMRI. The paradigm consisted of two experimental and one control condition. Both experimental conditions involved presentation of unfamiliar faces with either angry or afraid expressions [28]. In the “match” condition, subjects were required to match one of two either angry or fearful faces simultaneously presented at the bottom of the screen with an identical target face at the top. The data relative to this condition were reported in an earlier study [8]. During the “label” (cognitive labeling of threatening stimuli) condition, subjects were asked to label the target face at the top of the screen by selecting one of two words (angry and afraid) simultaneously presented at the bottom of the screen. This condition required subjects to judge the displayed emotions based on acquired knowledge of social standards and definitions for specific emotions. During the “control” condition, subjects were asked to select one of two simple geometric shapes (circles, vertical and horizontal ellipses) simultaneously presented at the bottom of the screen matching a target shape presented at the top.

A total of nine blocks (two blocks of “match” and two of “label” conditions, interleaved with five control blocks), each lasting 32 s, were acquired. Total scan duration was of 4 min and 48 s. Each experimental block consisted of six stimuli sequentially presented for 5 s, three for each gender and target affect (angry or afraid). Each control block consisted of six different stimuli sequentially presented for 5 s. The order of the stimuli was counterbalanced across subjects.

Subjects responded by pressing one of two buttons on a response button box with their right hand, allowing measurement of accuracy and reaction time while performing the task.

### 2.3. Physiology

We measured skin conductance load (SCL) [24] during the acquisition of functional scans in 18 of the 28 subjects. Skin conductance load was recorded with fMRI-compatible equipment (Contact Precision Instruments, Inc., Cambridge, MA) as in Hariri et al. [35]. Briefly, mean changes in SCL in the experimental and the adjacent blocks of the sensorimotor control task were

determined and then standardized ( $[(\text{mean of the label task} - \text{total mean}) / \text{total standard deviation}]$ ).

### 2.4. fMRI

Blood oxygenation-level dependent (BOLD) functional images were acquired with a GE Signa 3T scanner (Milwaukee, WI) from each subject while performing the emotion task. A gradient echo EPI sequence was used, with 24 axial contiguous slices (5 mm thick, no gap) encompassing the entire cerebrum and the majority of the cerebellum (TR/TE = 3000/30 msec, FOV = 24 cm, matrix =  $64 \times 64$ ) [34]. The first four scans were discarded to allow for signal saturation. All scanning parameters were selected to optimize the quality of the BOLD signal while maintaining a sufficient number of slices to acquire whole-brain data.

Stimuli were presented via a back-projection system, and responses were recorded through a fiberoptic response box, which allowed measurement of accuracy and reaction time for each trial.

### 2.5. Data analysis

#### 2.5.1. Demographic, behavioral and physiologic data

ANOVAs with demographic data, questionnaire scores, performance during the tasks and SCL as dependent variables and personality styles as the independent factor were performed to explore potential differences between the two groups. A  $\chi^2$  was used to assess potential differences in gender distribution. Spearman's correlation analyses were also performed between activity (percent signal change) in medial prefrontal cortex during cognitive labeling and both PP and EDP scores as measured by the PMQ.

#### 2.5.2. fMRI analysis

Analysis of the fMRI data was completed using statistical parametric mapping (SPM99; <http://www.fil.ion.ucl.ac.uk/spm>). Images for each subject were realigned to the first volume in the time series to correct for head motion and spatially normalized into a standard stereotaxic space (Montreal Neurologic Institute template) using a 12-parameter affine model. Finally, the normalized images were smoothed to minimize noise and residual differences in gyral anatomy with a Gaussian filter, set at 10 mm full-width at half-maximum. For each experimental condition, a box car model convolved with the hemodynamic response function (HRF, SPM99) at each voxel was modeled.

For each subject and scan, predetermined condition effects at each voxel were calculated using a *t* statistic, producing statistical maps for the contrasts: (1) “label” > “control”, to evaluate the main effect of labeling threatening facial expressions and (2) “label” > “match”, as a further analysis to subtract out from cognitive labeling more emotional components associated with implicit processing. The “label” condition requires subjects to judge the displayed emotions based on acquired knowledge of social standards and definitions for specific emotions. Differently, during the “match” condition subjects have to match faces based on perceptual characteristics and do not judge or interpret the displayed emotion. Both individual contrast images were then entered in a second-level random effects models analysis to determine condition-specific regional responses at group level. With this purpose, one-sample *t*-tests and ANOVA were used. In particular, one-sample *t*-tests were used to explore the effect of “label” > “control” and “label” > “match” ( $p < .005$ ,  $k = 4$ , uncorrected). As we were not interested in differences in anatomical areas that were not activated during cognitive labeling of threatening facial expressions, we restricted the second level random effects analysis to only areas that were activated during “label” > “match” contrast images. To facilitate this, a functional mask was created by using the combined group activation maps of “label” > “match” ( $p < 0.005$ ,  $k = 4$ ). This procedure controls for the possibility that potential differences between the groups arise from areas that are engaged by only one of the groups. Direct comparisons between the PP and EDP were then performed with ANOVA on “label” > “match”, with brain activity associated with this contrast as the dependent variable and personality style as the independent variable. Because of our strong *a priori* hypothesis regarding the differential response of the medial prefrontal cortex and our use of a rigorous random effects statistical model, a statistical threshold of  $p < .005$ ,  $k = 4$ , with a further family wise error (FWE) small volume correction for multiple comparisons (using a 12 mm

radius sphere centered around the coordinates in the medial prefrontal cortex published in Heinzel et al. [36] ( $x = 12$ ;  $y = 48$ ;  $z = 24$ ),  $p = 0.05$ , was used to identify significant responses for all comparisons. In this study, the authors found an association between activity in a medial prefrontal region with this center of mass and judgement of emotional valence of stimuli. Furthermore, because we did not have *a priori* hypotheses regarding the activity of brain regions outside of the mPFC, we used a statistical threshold of  $p = 0.05$ , family wise error corrected for multiple comparison across all voxels, for these whole-brain comparisons.

Anatomical localization of the local maxima was obtained after converting the Montreal Neurological Institute to Talairach coordinates [71] by mni2tal (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>). Signal change was extracted using MarsBar (<http://marsbar.sourceforge.net/>).

### 3. Results

#### 3.1. Demographics and questionnaires

ANOVAs and  $\chi^2$  indicated that the two groups of subjects were well matched for age, gender, IQ, parental education, years of education, handedness (all  $p > 0.2$ ). Consistent with the diagnosis based on the semi-structured interview, an ANOVA with personality style as a between subjects factor and with PP and EDP scores (as measured by PMQ) as within subjects factor showed no effect of personality style ( $F_{1,26} = 0.4$ ,  $p > 0.5$ ), a significant effect of scores ( $F_{1,26} = 6.4$ ,  $p < 0.02$ ), and a significant interaction between personality style and scores ( $F_{1,26} > 15$ ,  $p < 0.001$ ). *Post hoc* analysis with Tukey HSD test indicated that PP subjects have higher PP scores ( $p < 0.001$ ) and that EDP subjects have higher EDP scores ( $p < 0.001$ ). Similar ANOVAs were performed with personality style as a between subjects factor and the various sub-scores (those identifying different aspects of personality) of the different questionnaires (NEO, TCI, PANAS, EPI, and the BFQ) as within subjects factor. These ANOVAs did not indicate any significant effect of personality style (all  $F_{1,26} < 1.3$ , all  $p > 0.3$ ) or any interaction between personality style and sub-scores (all  $F_{1,26} < 1.4$ , all  $p > 0.2$ ), suggesting that the two groups of subjects did not significantly differ on other aspects of personality identified by these questionnaires.

#### 3.2. Behavioral and physiological data

All subjects performed well on the sensory motor control, match and label task (mean  $\pm$  SD match accuracy =  $94.6 \pm 5.5\%$ , reaction time =  $1967.4 \pm 348.3$  ms; sensory motor control task accuracy =  $94.3 \pm 8.01\%$ , reaction time =  $1204.2 \pm 205.8$  ms; label accuracy =  $94.6 \pm 8.7\%$ , reaction time =  $1737.3 \pm 502.3$  ms). ANOVA on accuracy during the three task conditions showed no effect of condition ( $F_{2,52} = 0.02$ ,  $p = 0.98$ ), of personality style ( $F_{1,26} = 2.53$ ,  $p = 0.12$ ) and no interaction ( $F_{2,52} = 0.99$ ,  $p = 0.37$ ). A similar ANOVA on reaction time showed an effect of condition ( $F_{2,52} = 17.85$ ,  $p < 0.0001$ ), no effect of personality style ( $F_{1,26} = 0.27$ ,  $p = 0.61$ ) and no interaction ( $F_{2,52} = 0.44$ ,  $p = 0.65$ ). *Post hoc* analysis with Tukey HSD indicated faster reaction time during sensorimotor control relative to both the 'match' and the 'label' tasks ( $F_{2,54} = 18.2$  (all  $p < 0.001$ )).

ANOVA on SCL data indicated task condition as the only statistical significant effect ( $F_{1,32} = 28.33$ ,  $p < 0.001$ ), with lower

Table 1a

One sample *t*-test: coordinates of the voxel with the highest *t* value relative to standard stereotactic space (Talairach and Tournoux, Tal) during the "label" > "control" condition in all subjects

Tal x	Tal y	Tal z	<i>t</i> -Value	<i>k</i>	BA
-38	-59	-12	10.45	200	BA 37 left fusiform gyrus
-8	17	60	9.59	327	BA 8/9 left superior frontal gyrus
-44	26	15	9.29	307	BA 48 left inferior frontal gyrus
44	19	21	7.16	176	BA 46 right middle frontal gyrus
26	-77	-6	5.29	32	BA 18 right lingual gyrus
-22	-15	-9	4.73	27	Left globus pallidus/amygdala

SCL during the sensorimotor control relative to both the match and the label tasks (both  $p < 0.001$ ).

#### 3.3. Imaging data

##### 3.3.1. Effect of label > control

Consistent with prior reports [34] analysis of label > control revealed significant BOLD responses in regions including: left fusiform gyrus, left superior, inferior and right middle frontal gyrus, right lingual gyrus, left globus pallidus and amygdala. (Table 1a).

##### 3.3.2. Effect of label > match

Brain activity related to this contrast showed increased bilateral activity in several brain regions, including left superior, middle, and inferior frontal gyri, right middle frontal gyrus, left middle and right temporal gyrus, right lentiform nucleus, right pulvinar and left cingulate gyrus. (Table 1b).

##### 3.3.3. Effect of personality style

During label > match, one-sample *t*-tests revealed similar patterns of brain activation in both PP and EDP groups, including the regions previously found examining the effect of label > match (Table 1b). Direct comparisons between the two

Table 1b

One sample *t*-test: coordinates of the voxel with the highest *t* value relative to standard stereotactic space (Talairach and Tournoux, Tal) during the "label" > "match" condition in all subjects

Tal x	Tal y	Tal z	<i>t</i> -Value	<i>k</i>	BA
-8	18	60	6.48	202	BA 6/BA9/45/46/47 left superior, middle, and inferior frontal gyri
-48	-58	8	3.95	19	BA 39 left middle temporal gyrus
40	-29	-3	3.75	12	BA 41 right superior temporal gyrus
19	5	16	3.64	6	Right lentiform nucleus/putamen
44	19	21	3.57	32	BA 46 right middle frontal gyrus
22	-29	18	3.45	30	Right pulvinar/thalamus
-11	12	27	3.10	5	BA 24 left cingulate gyrus

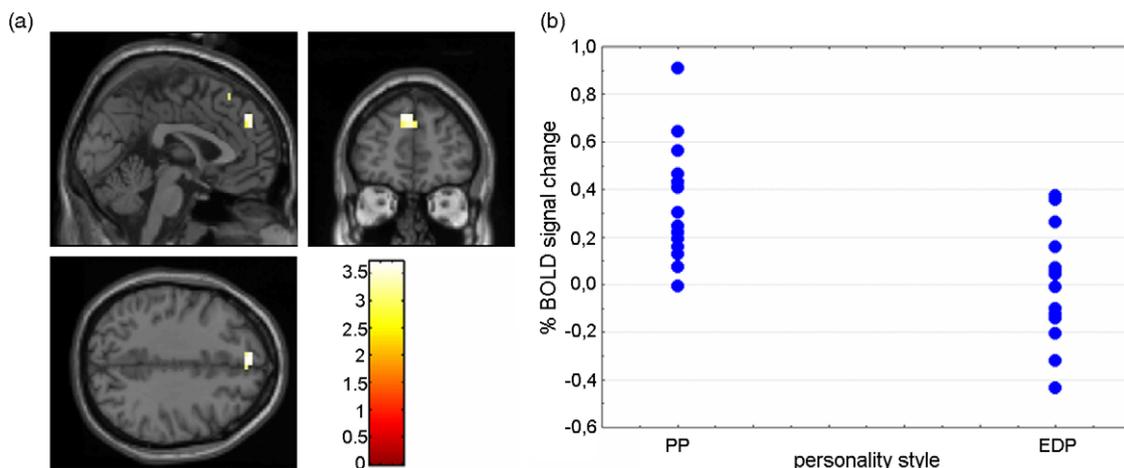


Fig. 1. (A) ANOVA within SPM99 ( $p < 0.005, k = 4$ ) of the “label” > “match” condition for the comparison phobic prone (PP) > eating disorders prone (EDP), overlaid onto an average structural MRI in all three planes. In the mPFC (maximal voxel, Talairach coordinates:  $x = 0, y = 45, z = 31$ ), PP subjects had a greater fMRI response compared with EDP subjects; (B) Effect of personality style on mPFC activity – individual circles represent the activity for each subject in the maximal voxel (PP mean  $\pm$  S.D. =  $0.338 \pm 0.25$ ; EDP mean  $\pm$  S.D. =  $0.001 \pm 0.24$ ; ANOVA:  $df = 1,26, F = 13.4, p = .001$ ).

groups (ANOVA) revealed greater BOLD response in PP relative to EDP subjects only in the mPFC (BA 9, local maxima in  $x = 0, y = 45, z = 31, k = 12, p = 0.04$  after FWE small volume correction; Fig. 1A and B). To further confirm that differences between the groups in this cluster were not because of differences in the match task, signal change was extracted during both label > control and match > control from this cluster. A repeated measures ANOVA performed on signal change values showed an effect of task ( $F_{1,26} = 12.4, p = 0.002$ ), of personality style, ( $F_{1,26} = 19.7, p = 0.0002$ ), and a strong trend towards an interaction between task and personality style ( $F_{1,26} = 3.6, p = 0.07$ ). *Post hoc* analysis with Tukey HSD test showed significant greater mPFC activity in PP than EDP subjects in the label > control condition ( $p = 0.0002$ ), while no statistically significant differences between groups were found in this brain region during the match > control condition. Another cluster in mPFC (BA6, local maxima in  $x = -11, y = 32, z = 54, k = 6$ ), did not survive correction for multiple comparisons. No other brain region in this analysis or any brain region in the inverse analysis (EDP > PP) crossed the statistical threshold.

### 3.3.4. Correlation analysis

Correlation analyses indicated a positive correlation between mPFC activity and phobic proneness scores ( $\rho = 0.44, p = 0.02$ ; Fig. 2) across both groups.

## 4. Discussion

Consistent with earlier experiments, the results of whole brain comparisons in the present study indicate that explicit recognition of fearful and angry faces (cognitive labeling) elicited activity in regions of the medial and lateral prefrontal cortex, as well as and in amygdala. In addition, subtraction of emotional components associated with implicit processing from cognitive labeling revealed a cortical network of brain regions including lateral and medial regions of the prefrontal cortex, as well as portions of the cingulate cortex. Moreover, our results sug-

gest that personality style, categorized according to a cognitivist model, is associated with differential brain activity during cognitive labeling of threatening facial expressions. More specifically, PP subjects engage the medial PFC (BA 9) to a greater extent when compared with EDP subjects. Furthermore, activity in this area linearly predicted phobic proneness scores across both groups. Importantly, the two groups were matched for a series of demographic variables, for scores assessing different aspects of personality, for SCL data and for performance (accuracy and reaction time).

Lesion and electrophysiological studies in animals have shown that the mPFC is involved in emotional processing [5] and extinction of conditioned fear [44,47,49,64]. Other functional imaging studies in human healthy subjects have also suggested mPFC engagement during extinction of fear [61]. Consistently, other studies in posttraumatic stress disorder (a compelling model of extreme fear exposure) have demonstrated altered mPFC activity during trauma recall or exposure to fear-

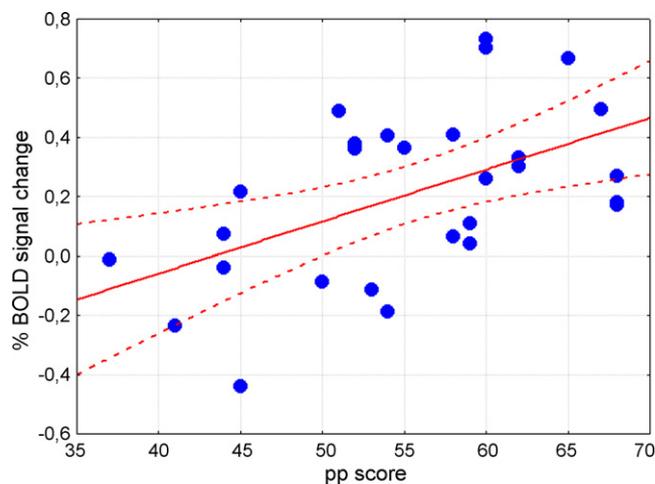


Fig. 2. Scatterplot of the correlation between phobic proneness score across both groups and fMRI percent signal change in mPFC (for statistics see text).

ful stimuli [16,70,77]. All these findings might suggest that the mPFC serves as modulator of emotional responses involving threatening stimuli [48,69]. Other studies may provide a more specific explanation for the involvement of mPFC (mostly BA9 and 10) in processing of threatening stimuli. Studies with functional imaging have specifically implicated the mPFC in explicit cognitive aspects of emotional processing, such as attention to emotion, appraisal and awareness of emotion [26]. Other recent studies show increased mPFC activity during cognitive appraisal of aversive visual stimuli [72] and during cognitive reappraisal and volitional inhibition of emotionally evocative stimuli [6,60]. Activity in mPFC is increased during self-referential processing or when subjects make introspective judgments about their emotional experience while viewing salient pictures [26,33,39,40]. Furthermore, activity in medial PFC is elicited by the arousing valence of emotional stimuli [25,41,66] and it is predicted by individual ratings of emotional arousal [59]. It is important to note that appraisal of an emotional stimulus may involve both interpretation of the intrinsic characteristics of a stimulus as well as relevance of the stimulus for the individual [60]. The latter form of appraisal encompasses a self-referential evaluation and promotes the recall of personal history (e.g., events or emotional memories). Taken together, these earlier studies suggest that the mPFC is centrally involved in appraising, and giving relevance to emotion processing associated with a threatening stimulus. In the present fMRI study, phobic prone subjects engaged the medial PFC to a greater extent than eating disorders prone subjects during cognitive evaluation of threatening stimuli. Since control of emotion associated with threatening stimuli is central to the identity of PP subjects, these findings might be interpreted as an attempt of PP subjects to control or maintain emotional activation within a specific threshold of intensity during cognitive labeling of a salient stimulus through its conscious evaluation, in order to regulate their emotional and cognitive life [3,4,32]. This interpretation is consistent with the linear relationship between mPFC activity and phobic proneness scores across both groups, further suggesting an association between the increasing need for emotional over-control associated with phobic proneness and the greater mPFC activity.

Finally, we did not find differential activity between groups in amygdala during cognitive labeling. This brain region has been associated with fear conditioning [52], automatic appraisal of threatening stimuli and danger detection [43], less so with cognitive evaluation of affective stimuli, when its brain activity is possibly dampened by a negative relationship with mPFC [45]. Therefore, lack of difference between EDP and PP subjects within amygdala during cognitive labeling may further suggest that amygdala engagement with our task is not robust enough to elicit differences between the two groups. This interpretation would be consistent with the results of our earlier paper in which we did demonstrate that amygdala activity differentiates PP and EDP during implicit processing of threatening stimuli [8].

#### 4.1. Limitations

In the present study, we have not evaluated the full spectrum of basic emotions and we did not have a neutral face as

a baseline. Thus, we cannot address the specificity of differences in mPFC response to threatening stimuli. Therefore, it is theoretically possible that phobic prone subjects might engage to a greater degree this cortical brain region simply because of a higher level of arousal. Another limitation of our study is that we used the label > match contrast in which the number of emotional stimuli is not matched. It may be argued that the difference we report in the response of mPFC simply reflected a greater sensitivity of PP subjects to the number of emotional stimuli presented in our two experimental conditions. However, we believe that differential activity in other brain regions would have been manifest if the statistics of the imaging data were simply driven by arousal or by greater sensitivity to the number of emotional stimuli. Rather, the selectivity of the difference may suggest that it is in the way the subjects differently appraise the stimuli that the differential engagement of mPFC becomes more manifest. Finally, another interpretation of our data may be that greater prefrontal activity might simply reflect greater bottom-up amygdala drive in PP, as demonstrated in our earlier study. However, no between group difference in amygdala has been found during the 'label' condition, making this interpretation less likely.

#### 4.2. Conclusions

The results of this study suggest that personality style is associated with differential modulation of prefrontal cortex activity during cognitive evaluation of emotional stimuli. In recent years converging evidence has tried to elucidate the functional architecture underlying cognitive control of emotion. Our findings might provide a potential interpretation to explain some of the individual differences in neural networks mediating cognitive modulation of emotions.

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