Neural Activity of the Anterior Insula in Emotional Processing Depends on the Individuals' Emotional Susceptibility

Giuseppe Iaria,[1*] Giorgia Committeri,[3,4] Concetta Pastorelli,[2] Luigi Pizzamiglio,[2,3] Kate E. Watkins,[5,6] and Antonio Carota[7]

[1]*Human Vision and Eye Movement Laboratory, Department of Medicine, University of British Columbia, Vancouver, Canada*
[2]*Dipartimento di Psicologia, Università di Roma "La Sapienza", Rome, Italy*
[3]*Sezione di Neuropsicologia e Laboratorio di Neuroimmagini, IRCCS Fondazione Santa Lucia, Rome, Italy*
[4]*Dipartimento di Scienze Cliniche e Bioimmagini, Università "Gabriele D'Annunzio", Chieti, Italy*
[5]*Department of Experimental Psychology, University of Oxford, Oxford, United Kingdom*
[6]*FMRIB, University of Oxford, Oxford, United Kingdom*
[7]*CHUV Neurology Department, Lausanne, Switzerland*

Abstract: Differences in personality factors between individuals may manifest themselves with different patterns of neural activity while individuals process stimuli with emotional content. We attempted to verify this hypothesis by investigating emotional susceptibility (ES), a specific emotional trait of the human personality defined as the tendency to "experience feelings of discomfort, helplessness, inadequacy and vulnerability" after exposure to stimuli with emotional valence. By administering a questionnaire evaluating the individuals' ES, we selected two groups of participants with high and low ES respectively. Then, we used functional magnetic resonance imaging to investigate differences between the groups in the neural activity involved while they were processing emotional stimuli in an explicit (focusing on the content of the stimuli) or an incidental (focusing on spatial features of the stimuli, irrespectively of their content) way. The results showed a selective difference in brain activity between groups only in the explicit processing of the emotional stimuli: bilateral activity of the anterior insula was present in subjects with high ES but not in subjects with low ES. This difference in neural activity within the anterior insula proved to be purely functional since no brain morphological differences were found between groups, as assessed by a voxel-based morphometry analysis. Although the role of the anterior insula in the processing of contexts perceived as emotionally salient is well established, the present study provides the first evidence of a modulation of the insular activity depending on the individuals' ES trait of personality. *Hum Brain Mapp 29:363–373, 2008.*

Key words: insula; emotions; fMRI; humans; personality; variability

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*Correspondence to: Giuseppe Iaria, Ph.D, Human Vision and Eye Movement Laboratory, VGH Eye Care Centre, 2550 Willow Street, Vancouver, BC, Canada V5Z 3N9. E-mail: giaria@eyecarecentre.org

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INTRODUCTION

In the domain of personality research there is a wide consensus on the Five Factor Model (FFM) of personality, which includes the traits of extraversion, neuroticism, conscientiousness, agreeableness, and openness to experience [Costa and McCrae, 1992]. The existence of a relationship between these personality dimensions and the brain functioning in emotional processing is a major topic in the neurosciences [Damasio, 1994]. Indeed, recent neuroimaging techniques have been adopted to investigate the relationships between the phenotypic variance of some personality dimensions of the FFM and the neural activity involved while individuals process stimuli with emotional valence (for a review, see Canli, 2004]. For instance, Canli and colleagues [Canli et al., 2002] showed that the personality trait of extraversion modulates the neural activity within the amygdala, a brain structure that has been long considered critical for the processing of emotional stimuli [Davis and Whalen, 2001]. More specifically, the authors reported a positive correlation between the individuals' degree of extraversion and the amygdala activity while viewing facial expression of happiness: the more extraverted the participants were, the more their amygdala responded to the visual stimuli. No extraversion modulation of the amygdala was found while processing facial expressions of anger, fear, or sadness, suggesting that different personality factors may affect brain responses depending on both the kind of stimuli processed and the personality trait examined.

Although there is no doubt that the five broad high-order traits of personality (FFM) may usefully represent the structure of an adult personality, specific lower-order traits of personality may be more suitable for testing the hypothesis of differences in neural mechanisms depending on individuals' personality [Caprara and Pastorelli, 1989; Caspi et al., 2005]. In the present study we investigated the personality trait of emotional susceptibility (ES), a facet of the neuroticism dimension [Caprara et al., 1994], defined as the tendency to experience feelings of discomfort, helplessness, inadequacy, and vulnerability after exposure to stimuli with salient emotional content [Caprara et al., 1985]. The individuals' ES has been found to positively relate to diverse indicators of proneness to emotional experience, responsivity, and control [for a review, see Bettencourt et al., 2006; Caprara et al., 1989]; thus, this specific trait of personality seems to be a suitable and congruent construct to investigate the variability within individuals in processing emotions. Individuals with high ES are generally more vulnerable to both negative and positive emotional events than are individuals with low ES. For instance, individuals with high ES may cry at the cinema, have difficulty in controlling tears in public, and feel easily overwhelmed by emotions. On the other hand, subjects with low ES generally appear clear-thinking, self-confident, efficient, and unselfish. In sum, ES affects the individuals' behaviors in social contexts, reflecting a great variability within individuals without ever reaching a pathological degree.

Here, we investigated the relationship between the individuals' ES and the brain mechanisms involved in emotional processing. First, we adopted a standardized scale [Caprara et al., 1985] to select two groups of healthy young individuals who were at the opposite extremes of the ES trait (i.e. high and low ES). Then, we used functional magnetic resonance imaging (fMRI) to verify the hypothesis that individuals with high and low ES show different neural activity within the brain regions known to be involved in the processing of visual stimuli with emotional valence. In addition, we aimed to assess whether differences in neural activity between individuals with high and low ES depend on the explicit (focusing on the emotional content of the stimuli) or the incidental (focusing on the spatial features of the stimuli, irrespectively of the emotional content) processing of the emotional stimuli. Finally, we used voxel-based morphometry (VBM) to investigate differences in brain morphology between individuals with high and low ES.

MATERIALS AND METHODS

Subjects and Psychological Testing

Two hundred and fifty-eight students from the University of Rome "La Sapienza" were administered a questionnaire evaluating their ES [Caprara et al., 1985]. The questionnaire consists of a six-point Likert scale (1, false; 6, true) including 40 self-description items (30 effective, 10 control). Examples of the effective items are as follows: "I easily get involved when someone tells me their troubles," "When I am afraid I completely lose control," "More than once I have been moved to tears at movies." Twenty subjects (10 males; mean age ± SD: 22.8 ± 4.07) were selected to participate in the fMRI study: 10 subjects (five males) scoring under the 25th percentile constituted the group with low emotional susceptibility (LES); 10 subjects (five males) scoring over the 75th percentile formed the group with high emotional susceptibility (HES). To further assess different personality traits, participants were administered the Big Five Questionnaire [Caprara et al., 1993a], including the personality traits of energy, consciousness, friendliness, openness and emotional stability, which correspond to the five dimensions described in the FFM [Costa and McCrae, 1992] (extraversion, conscientiousness, agreeableness, openness, and neuroticism respectively). In addition, participants completed the Center for Epidemiologic Studies Depression Scale (CES-D) [Radloff, 1977] evaluating individuals' states of depression, the scores of which resulted in the normal range (CES-D, mean ± SD score: 1.71 ± 0.4). None of the subjects ever had a history of neurological or neuropsychiatric disorders. Written informed consent was obtained from each subject in a manner approved by the local ethics committee of the "Fondazione Santa Lucia". The study conforms with The Code of Ethics of the World Medical Association (Declaration of Helsinki) as printed in the *British Medical Journal* (18 July, 1964).

Stimuli and Tasks

Stimuli were 180 colored photographs with positive ($N = 60$), negative ($N = 60$) and neutral ($N = 60$) emotional contents taken from the International Affective

Picture System (IAPS) [Lang and Greenwald, 1993]. Although a matching of content is not available by the IAPS itself, we nevertheless tried to match the photographs as much as possible for orientation, content, and scenes. In other words, for each emotional category of stimuli (positive, negative, neutral), we selected a similar number of pictures including people, animals, and natural scenery. A texture filter with different orientation (vertical or horizontal) was added to all the 180 photographs (see Fig. 1). The number of vertical and horizontal texture orientations was balanced in each category of stimuli (positive, negative, neutral). Participants were administered two tasks: in the "emotional" task they were presented photographs with positive and negative emotional contents and they were required to judge the emotional content (positive or negative) of each stimulus; in the "orientation" task participants were presented photographs with positive, negative, and neutral emotional content and asked to identify the texture orientation (horizontal or vertical) of each stimulus. The texture orientation did not include the central part of the photographs, where instead a fixation cross was present (see Fig. 1). This specific feature of the stimuli did not allow the subjects to solve the orientation task by simply focusing on the central part of the photographs, thus forcing the incidental processing of the photograph's content as driven by the entire photograph.

Experimental Paradigm and Procedure

By manipulating the tasks (emotional, orientation) and the content of the stimuli (positive, negative, neutral), we obtained three different conditions: (1) "explicit emotional processing," in which participants judged the emotional valence of photographs with positive (30 stimuli) or negative (30 stimuli) emotional content; (2) "incidental emotional processing," in which participants judged the texture orientation of photographs with positive (30 stimuli) or negative (30 stimuli) emotional content (in this case, the emotional content of the photographs was processed in an incidental way while subjects focused on spatial features of the images); and (3) "neutral condition," in which the orientation task was performed on photographs with neutral emotional content (60 stimuli). Photographs with both positive and negative emotional content presented in the explicit and incidental conditions were matched for emotional valence as reported by the IAPS data scores. We have deliberately chosen not to request an explicit emotional judgement of photographs with neutral emotional content in order to avoid ambiguous processing and delayed responses. This led to a hierarchical design, unbalanced from the point of view of task per conditions number, which however allowed us to clearly evaluate the processing of interest. By subtracting the explicit condition from the incidental one, we were able to highlight the neural mechanisms subserving the explicit processing of the photographs' emotional content. In this case, for both explicit and incidental conditions, the emotional contents

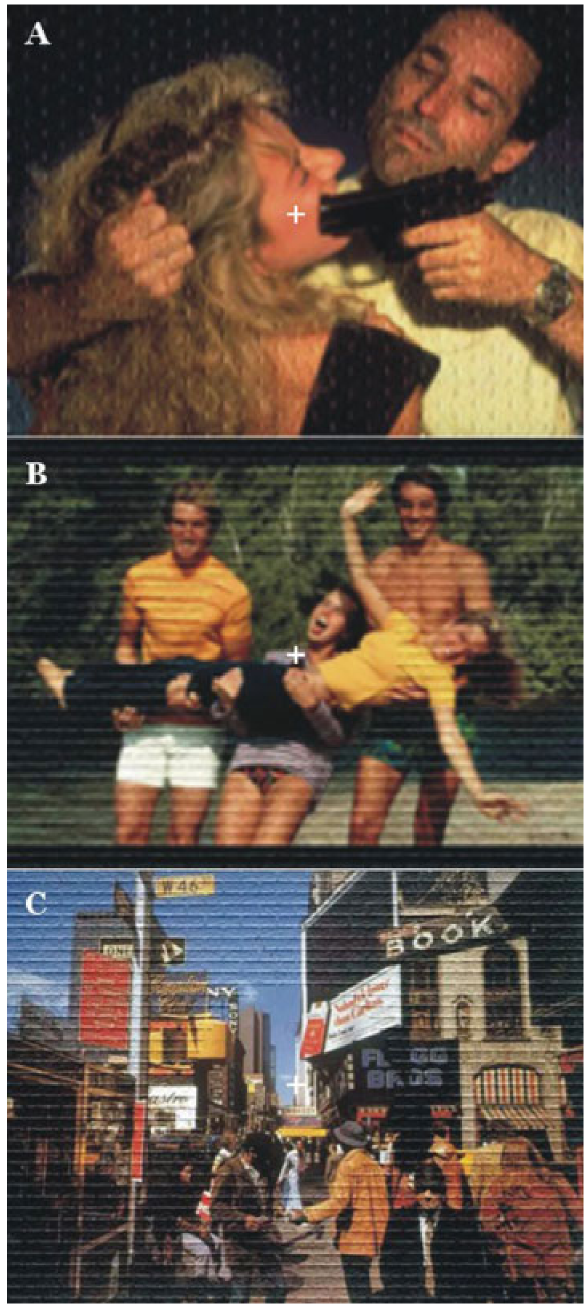

Figure 1.
Examples of the three stimulus types. Photographs with negative (**A**), positive (**B**), and neutral (**C**) emotional content were used with a superimposed-texture of different orientation (in these examples, vertical orientation for the negative stimulus and horizontal orientation for the positive and neutral stimuli). Stimuli with negative and positive emotional content were used for both emotional and orientation tasks; stimuli with neutral content were used only for the orientation task. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

of the stimuli were the same (positive and negative) whereas the tasks were different (emotional content versus orientation). On the other hand, by subtracting the neutral condition from the incidental one, we were able to investigate the brain activities involved in the incidental processing of the photographs' emotional content. Here, the participants performed the same orientation task on photographs with or without emotional content. Before scanning, the subjects participated in a training session of 10 min to practice the motor aspects of the tasks and to be familiar with the experimental procedure. During this session, the participants viewed photographs different from the ones used during the scanning sessions. Participants were administered two scans, each including fifteen 24-s epochs. In each scan (184 volumes), the 15 epochs included five blocks of trials for each condition (explicit, incidental, neutral) administered in a randomized order. For each condition, six different photographs were shown in each epoch (three negative and three positive for explicit and incidental conditions; six neutral for the neutral condition). Each epoch started with an instruction slide (1,000 ms) stating whether the task would had been the emotional or the orientation one ("emotions" or "lines," respectively), followed by a 500-ms fixation point; then, the photograph was presented for 400 ms, followed by a central fixation cross on a dark background for six different durations (ranging from 2,100 to 4,600 ms in steps of 500 ms) randomized within the epoch. The order of the two scanning sessions was counterbalanced between subjects. At the end of the scanning sessions, the subjects were moved to a different testing room and administered an emotional-valence judgement task by using SuperLab Pro Software (Cedrus Corporation, USA). This task consisted of a random presentation, on a computer screen, of all the photographs (positive, negative, neutral) administered during scanning: participants were required to judge the emotional valence of each photograph by using a 11-point Likert Scale ranging from -5 (very negative) to $+5$ (very positive). In this task, each photograph was present on the screen until the subject gave his/her emotional-valence judgement.

Apparatus and Imaging Parameters

Whole-brain fMRI data were acquired on a 3 T Siemens Allegra MR system (Siemens Medical Systems, Erlangen, Germany) equipped with a quadrature head volume coil. Stimuli were generated by a control computer located outside the MR room, running in-house software, implemented in MATLAB (The MathWorks Inc., Natick, MA) using Cogent 2000 (developed at FIL and ICN, UCL, London, UK). An LCD video projector was used to project visual stimuli to a back projection screen, visible through a mirror mounted above the head coil. Responses were given by using a two-buttons MRI compatible keypad connected to the control computer, which recorded both RT and error rates. Functional images were obtained with echo-planar sequences using blood-oxygenation-level-dependent (BOLD) contrast, each comprising a brain volume of 30 axial slices covering the entire brain, including most of the cerebellum. Standard imaging procedures were applied (TR = 2 s; TE = 30 ms; flip angle = 70°; image matrix = 64 × 64; FOV = 192 × 100; voxel size = 3 × 3 × 2.5). The 2.5-mm-thick slices were oriented parallel to the orbito-frontal cortex. A three-dimensional high resolution anatomical image in the sagittal orientation was acquired for each subject using a 3-D Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence (number of slices = 276; TR = 2 s; TE = 4.38 ms; inversion time = 910 ms; flip angle = 8°; image matrix = 224 × 256; FOV = 256 × 87.5%; voxel size = 1 × 1 × 1).

Functional Data Analysis

Statistical parametric mapping (SPM2, Wellcome Department of Imaging Neuroscience, London, UK) was used for image spatial preprocessing and statistical analysis. Functional time series from each subject were spatially corrected for head movement, temporally corrected for slice timing (using the middle slice acquired in time as a reference), spatially normalized to MNI (Montreal Neurological Institute) coordinates and spatially smoothed with a three-dimensional Gaussian filter (8 mm FWHM). First-level single-subject analyses were performed by using an event-related model, with five trial types deriving from task by emotional content combinations: emotional-positive (EmP), emotional-negative (EmN), orientation-positive (OrP), orientation-negative (OrN), and orientation-neutral (OrNeu). The onset of each trial constituted a neural event, which was modeled through a canonical hemodynamic response function, chosen to represent the relationship between neuronal activation and blood flow changes [Friston et al., 1998]. Separate regressors were included for each trial type, yielding parameter estimates for the average hemodynamic response evoked by each. Additionally modeled explanatory variables included a set of cosine basis functions working as a high-pass filter (to remove low-frequency confounds, with a period greater than 144 s), and overall differences across scans. These subject-specific models were used to compute a set of contrast images per subject, each representing the estimated amplitude of the hemodynamic response for each effect of interest. The effect of explicit emotional processing was assessed through a 2 × 2 factorial model, with task (emotional/orientation) and emotional content (positive/negative) as within-subjects factors. We tested for the main effect of emotional task independently from the emotional content [(EmP + EmN) > (OrP + OrN)], and for the possible interaction, that is for the effect of the photograph's emotional content on the explicit emotional (vs. orientation) judgement [positive content: (EmP − OrP) > (EmN − OrN); negative content: (EmN − OrN) > (EmP − OrP)]. The effect of incidental emotional processing was assessed through an analysis on the orientation task, with the emotional content as a 3-level factor (positive, negative, neutral). We tested for the main effect of incidental emotional processing [(OrP + OrN) > OrNeu)] and for possible differences between positive and negative emotional content (OrP > OrN, and vice versa). Contrast images from all subjects were entered into one-sample *t*-tests in order to perform second-level random-effect group analyses in the entire pool of subjects. For each effect of interest, we obtained a statistical parametric map of the *t* statistic, whose significance was judged at the voxel level and by cluster size. Correction for multiple comparisons was performed using distribution approximations from the theory of Gaussian fields [Worsley et al., 2002] at the cluster level ($P < 0.05$ corrected), after forming clusters of adjacent voxels surviving a threshold of $P < 0.001$ corrected for false discovery rate (as implemented in SPM2). The same subject-specific contrast images were entered into two-sample *t*-tests in order to perform between groups random-effect analysis (HES group > LES group) (voxelwise thresholding at $P < 0.001$ uncorrected; cluster-level thresholding at $P < 0.05$ corrected for multiple comparisons) for both emotional and incidental tasks. Nonsphericity correction (as implemented in SPM2) was applied for all the group analyses. To assess the possible role played by other personality traits on the between-groups differences, we operated in two ways: (1) for each subject, we extracted the percent signal change from each region significant at the group level, by using the MarsBar region of interest toolbox for SPM (http://marsbar.sourceforge.net), and submitted these data to a multiple regression analysis with the extracted signal as dependent variable and the personality scores as independent ones; (2) for the personality measures showing a significant behavioral correlation with the ES scores, we repeated the fMRI analysis which eventually had shown significant differences between the two groups, by treating the personality measures as nuisance variables (ANCOVA model). Anatomical labels were assigned with reference to standard brain atlases [Duvernoy, 1991; Talairach and Tournoux, 1988] and a macroscopic anatomical parcellation of the MNI single-subject brain [Tzourio-Mazoyer et al., 2002].

Morphology

The 3-D anatomical datasets were preprocessed using methods implemented in SPM2 using MATLAB scripts available via Christian Gasers' website (http://dbm.neuro.uni-jena.de/vbm.html). Each dataset was segmented to produce grey, white, and CSF images and these were then spatially normalized to a customized template image derived from the group data. The grey matter normalized partitions were then smoothed using a 12-mm Gaussian smoothing kernel. We also produced images modulated by the Jacobian determinants derived from the deformation field of the spatially normalized data. This modulation produces voxel values more representative of the original volume of tissue than the unmodulated data, which represents relative amounts of tissue locally, known as tissue "concentration" or "density." Both modulated and unmodulated smoothed grey matter partitions were entered into statistical analyses where the two groups were contrasted.

RESULTS

Behavioral Data

Separate statistics were performed to analyze the reaction time (RT) and the number of errors that the participants made while performing the tasks. To investigate differences in RT between groups while perceiving the content of the photographs in an explicit or incidental way, we performed an ANOVA Group (HES, LES; independent variable) by Task (Emotional, Orientation) by Emotional Content (positive, negative) with RT (ms) as a repeated measure. This analysis revealed a statistically significant main effect of the Task ($F_{1,1} = 4.62$; $P = 0.045$): post hoc comparisons (Duncan test) revealed that the participants showed longer RTs while performing the Emotional Task than while performing the Orientation one (emotional task, mean ± SD: 829.73 ± 163.34 ms; orientation task, mean ± SD: 778.28 ± 133.89 ms). No statistically significant main effects of Group and Emotional Content, nor interaction effects were found.

Differences in error rates between groups in the explicit and incidental emotional processing were assessed by performing a similar ANOVA Group (HES, LES; independent variable) by Task (Emotional, Orientation) by Emotional Content (positive, negative) with number of errors as a repeated measure. The results showed a statistically significant main effect of Emotional Content ($F_{1,1} = 15.95$; $P = 0.0009$): Post hoc comparisons (Duncan test) revealed that the participants made less errors while processing stimuli with positive emotional content than stimuli with negative one (positive content, mean ± SD, %: 2.1 ± 2, 5.3%; negative content, mean ± SD, %: 3.3 ± 2.4, 8.3%). No statistically significant main effects of Group and Task, nor interaction effects, were found.

Similar analyses on RT and errors were performed to assess any difference between groups while perceiving the content of the photographs in an incidental way (i.e. the orientation task including the neutral condition). An ANOVA Group (HES, LES; independent variable) by Emotional Content (positive, negative, neutral) with RT (ms) as a repeated measure revealed no statistically significant effects. Identical results were found with respect to the error rates.

Differences between groups (HES, LES) on the emotional-valence judgements (−5, very negative; +5, very positive) given after the fMRI scanning sessions were assessed with a Mann–Whitney nonparametric analysis. The analysis did not reveal a statistically significant effect of the Group ($U = 424$, Z-Value $= 476$, $P = 0.701$), confirming that participants with high and low emotional sus-

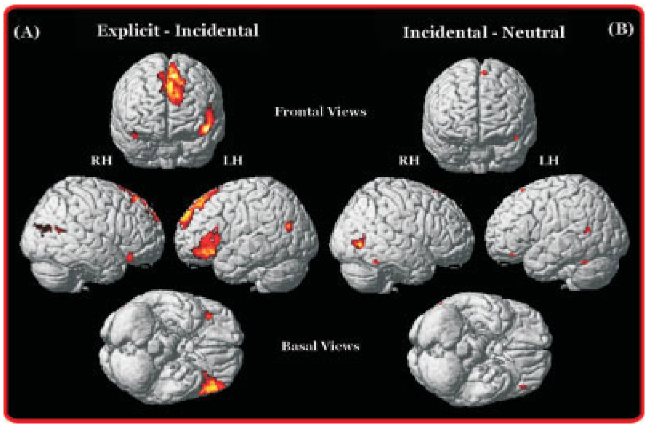

Figure 2.
Functional data in the entire pool of participants. (**A**) Main effect of explicit emotional processing (Emotional task *minus* Orientation task, both performed on photographs with emotional valence). Brain activity in the left amygdala is not shown in the figure. (**B**) Main effect of incidental emotional processing (Orientation task performed on pictures with emotional valence *minus* the same task performed on neutral pictures). Neural activities are superimposed on frontal, lateral, and basal views of the rendered single-subject MNI brain. See Table I for coordinates and peak of neural activities. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

ceptibility judged the positive and negative emotional content of the photographs in a similar way.

Finally, multiple regression analysis between degrees of ES and scores of the five personality traits (energy, consciousness, friendliness, openness, and emotional stability) measured by the Big Five Questionnaire [Caprara et al., 1993a] revealed a statistically significant negative correlation ($\beta = -0.89$; $P < 0.001$) between ES and emotional stability (the opposite facet of neuroticism).

Functional Data

In the entire pool of subjects, the main effect of explicit emotional processing (i.e., Emotional task *minus* Orientation task on photographs with emotional valence) revealed bilateral neural activity of the medial superior frontal cortex, the inferior frontal cortex, the temporo-parietal-occipital junction, and the middle occipital cortex (Fig. 2A and Table I). Both medial superior and inferior frontal neural activities were more extensive on the left hemisphere. Further clusters of activation were detected in the left fusiform gyrus, in the left orbito-frontal cortex, in the left amygdala, and in the right cerebellum (Fig. 2A and Table I). Neither the main effect of emotional valence nor the interactions between emotional valence and task showed significant activation, suggesting no differences in brain activity depending specifically on positive or negative emotional valence for both emotional and orientation tasks.

The main effect of incidental emotional processing (i.e., photographs with emotional content *minus* neutral photographs during the execution of the Orientation task) showed neural activity within the middle and inferior temporal cortex bilaterally, and within the medial superior and inferior frontal cortex, in the left hemisphere (Fig. 2B and Table I). While the left frontal activity overlapped the same anatomical location as that observed during the explicit emotional processing, the bilateral middle temporal activity was located more ventrally with respect to the one previously described in the temporo-parietal-occipital junction. We did not detect any significant differences between positive and negative emotional content during the orientation task.

Direct comparisons between groups of subjects with HES and LES revealed a significant difference only for the main effect of explicit emotional processing, independently from the positive or negative emotional content of the stimuli. This difference consisted in a significantly greater activity in the anterior insula of both hemispheres in the

TABLE I. Brain activity observed during the explicit and incidental emotional processing

		Coordinates		
Anatomical region (BA)	*t*-value	*x*	*y*	*z*
Explicit emotional processing				
Left superior frontal gyrus (8)	12.10	−6	34	56
Right superior frontal gyrus (8)	8.18	8	36	56
Left superior frontal gyrus (9)	10.19	−12	56	34
Left superior frontal gyrus (10)	7.96	−14	58	18
Left inferior frontal gyrus (47)	9.80	−48	46	−12
Left inferior frontal gyrus (45)	8.71	−40	34	2
Right inferior frontal gyrus (47)	9.50	40	28	−22
Right Inferior frontal gyrus (45)	8.71	−40	34	2
Left orbitofrontal cortex (11)	6.78	−4	50	−20
Right middle temporal gyrus (39)	7.08	56	−70	18
Left fusiform gyrus	7.47	−24	−34	−22
Right middle occipital gyrus (19)	6.34	38	−74	24
Left middle occipital gyrus (19)	6.80	−36	−84	26
Left amygdale	6.43	−26	−10	−14
Right cerebellum	7.08	10	−86	−26
Incidental emotional processing				
Left superior frontal gyrus (8)	8.71	−6	24	64
Left inferior frontal gyrus (47)	7.67	−44	34	−20
Left inferior temporal gyrus (37)	8.00	−46	−52	26
Right inferior temporal gyrus (37)	8.10	46	−48	−22
Left middle temporal gyrus (21)	7.71	−60	−56	14
Right middle temporal gyrus (37)	10.25	54	−70	−2

The Table shows brain region activities, in the entire pool of subjects, for the main effect of explicit emotional processing (Emotional task *minus* Orientation task, both performed on pictures with emotional valence) and for the main effect of incidental emotional processing (Orientation task performed on pictures with emotional valence *minus* the same task performed on neutral pictures). Brodmann areas (BA) [Talairach and Tournoux, 1988], *t*-values, and coordinates in MNI space are given for voxels representing main local maxima of activation [Duvernoy, 1991; Tzourio-Mazoyer et al., 2002].

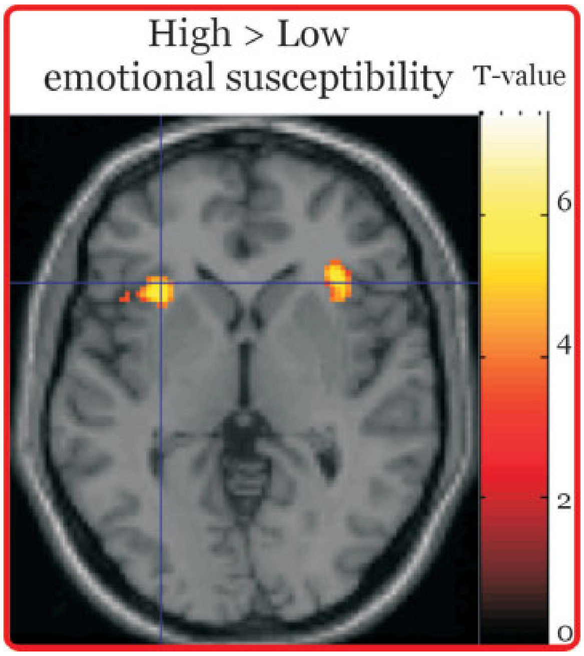

Figure 3.
Difference in neural activity depending on the emotional susceptibility. The transverse slice shows the significantly greater activity in the left ($x = -30$, $y = 24$, $z = 4$; $t = 7.45$; 191 voxels) and right ($x = 36$, $y = 28$, $z = -2$; $t = 6.96$; 180 voxels) anterior insula in the group of subjects with HES while performing the explicit emotional task. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

HES group (Fig. 3). This result was confirmed by further analyses performed separately for each group of subjects: during the explicit emotional processing, the anterior insula was activated in the HES group but not in the LES group. The plot of extracted percent signal change for explicit processing of positive (EmP − OrP) and negative (EmN − OrN) photographs in the two groups of subjects clearly shows that subjects with HES activated both the left and the right anterior insula independently from the emotional content (see Fig. 4).

With respect to the role played by other personality traits, such as the five traits measured by the Big Five Questionnaire [Caprara et al., 1993a], the multiple regression analysis conducted on the signal extracted from the left and right insula during explicit emotional processing revealed a significant negative correlation with the emotional stability trait (that is a positive correlation with the neuroticism trait, since this is the opposite facet of the emotional stability) (left insula: $\beta = -0.57$, $P < 0.05$; right insula: $\beta = -0.64$, $P < 0.05$). Accordingly, the fMRI analysis repeated by introducing the emotional stability measure as nuisance variable (ANCOVA model) did not reveal any significant difference in the insular activity (nor in other regions) between the two groups of subjects. These findings were confirmed by a mediation analysis in which we carried out two regression analyses: in the first analysis, we regressed the activity within the anterior insula on the personality traits, including the ES and the Big Five factors (energy, conscientiousness, emotional stability, agreeableness, openness); in the second analysis, we regressed the ES on the Big Five factors. The standardized partial regression coefficients revealed that only the ES had a direct effect on the insular activity ($\beta = 0.65$, $P < 0.001$) and that, among the Big Five factors, only the emotional stability had a direct effect on the ES ($\beta = -0.89$; $P < 0.001$).

Morphological Data

Direct comparisons of the processed anatomical data between groups of subjects with high and low emotional susceptibility revealed no significant differences in grey matter concentration or volume (unmodulated and modulated data, respectively). Also we examined the data specifically for differences in the anterior insula that might be related to the functional difference described earlier: there were no statistically significant differences in these regions even at relaxed statistical thresholds ($P < 0.05$, uncorrected).

DISCUSSION

The goal of the present study was to investigate the relationship between individuals' personality traits and the neural mechanisms involved in processing the positive and negative emotional content of photographs. More specifically, we used fMRI to examine the relationship between the individuals' ES and the neural activity involved in

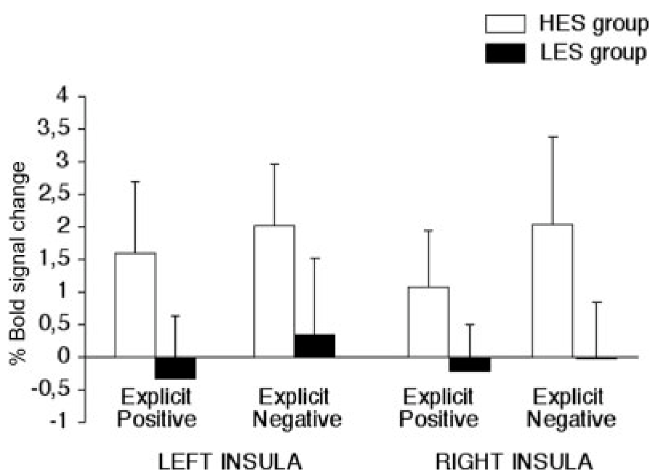

Figure 4.
Plot of percent signal change in the left and right anterior insula. Explicit processing of positive (ExpP = EmP − OrP) and negative (ExpN = EmN − OrN) emotional content in the group of subjects with high (HES) and low (LES) emotional susceptibility.

processing the content of the photographs in an explicit and incidental way.

In the entire pool of subjects (irrespective of personality traits), we found increased brain activity mainly involving the frontal and temporal cortex (see Table I). These findings are in accordance with previous neuroimaging studies [i.e., Beauregard et al., 2001; Northoff et al., 2000; Paradiso et al., 1997; Sergerie et al., 2005], suggesting the critical role of such a fronto-temporal neural network subserving the processing of visual stimuli with positive and negative emotional contents. Interestingly, however, our findings suggest that the activity within the fronto-temporal neural pattern may be modulated by the way the emotional content is processed: the frontal cortex (mainly in the left hemisphere) seems to be strongly involved when the stimulus content is processed in an explicit way, i.e. when subjects focus their attention on the emotional content of the photographs, whereas the temporal cortex (mainly in the right hemisphere) appears to be mostly involved in processing the emotional content of the photographs in an incidental way, i.e. when individuals focus their attention on a different spatial feature of the photographs irrespective of their emotional valence. In addition, increased activity within the left amygdala, known to be involved in processing stimuli with emotional valence [i.e. Morris et al., 1998], was revealed only while individuals processed the emotional content of the photographs in an explicit way.

The novel finding in the present study comes from the direct comparisons between groups of individuals with high and low ES, which revealed a significant difference in brain activity only while subjects process the emotional content of the photographs in an explicit way. More specifically, increased activity of the anterior insula, bilaterally, was engaged in subjects with high ES but not in subjects with low ES. This difference in brain activity is unlikely to be due to differences in behavioral effort, since the two groups of subjects did not differ in RTs or errors made while performing the tasks. Moreover, no differences between groups were observed when, out of the scanner, individuals explicitly judged the emotional content of the photographs: both groups with high and low emotional susceptibility gave similar judgements to the photographs with either positive or negative emotional content. Although one may expect such a difference in neural activity while processing the emotional content of the photographs both in explicit and incidental ways, we found that the activity within the anterior insula was present in individuals with high ES only when they were required to process the emotional content of the photographs in an explicit way. The most parsimonious explanation for these results may be due to the short duration (400 ms) the stimuli were presented to the participants; it is possible that while performing a task that is not related to the emotional content of the photographs (i.e. the texture orientation task) a longer delay of exposition is needed to reveal differences in brain activity related to emotional traits of personality. Hereafter, we discuss the findings reported in the present study in the context of both the healthy and the clinical population in order to shed more light on the relationship between the neural mechanisms and the regulation of the emotions in normal and pathological states.

The anterior insula has long been considered part of the emotional and viscerosensory brain [Janig and Habler, 2002] and its role seems to regulate both physiological and psychological homeostasis [Flynn et al., 1999]. The anterior insula contains primary cortical representation of smell and taste [Francis et al., 1999; Rolls, 1996], viscerosensation [Craig, 2002], and pain perception [Coghill et al., 1999; Davis et al., 1998]. For this reason, the insula has been associated with the subjective feeling of emotional states [Craig, 2002, 2003; Critchley et al., 2004]. Recent evidence from neuroimaging studies corroborates this view showing anterior insular activity while subjects physically experience a painful [Singer et al., 2004] or disgusting [Wicker et al., 2003] stimulation, or imitate facial expressions of different emotions (happiness, sadness, anger, surprise, disgust, and fear) [Carr et al., 2003]. Altogether, these findings have been discussed in the context of the biological basis of social cognition with reference to the understanding of the actions and the emotions of others [Miller, 2005; Rizzolatti and Craighero, 2004]. Our data are in accordance with this interpretation, showing that bilateral activity of the anterior insula is present during the explicit rating of stimuli as having positive or negative emotional content. More important, however, here we demonstrated that the anterior insula is involved in emotional processing only in subjects with high ES. In our opinion, this result advances our understanding regarding the function of the anterior insula in emotional processing, showing that the activity of this brain region in emotional processing is modulated by a specific personality trait such as the ES. In other words, our data suggest that although the anterior insula is involved in processing the contents of emotional stimuli, its activity is triggered by the individuals' ES. This finding points out two important issues: first, differences in ES may contribute to individual differences in triggering somatic markers of emotions in humans [Damasio, 1994]; second, differences in the involvement of the anterior insula in processing emotional stimuli may play an important role in explaining why individuals may respond differently to the same emotional event.

The most common model of personality adopted in the literature refers to the FFM [Costa and McCrae, 1992], which includes the trait of neuroticism, extraversion, openness, agreeableness, and conscientiousness. Individuals' differences in personality factors may manifest with different behavioral responses to daily life events. The understanding of the relationship between personality dimensions and the pattern of behavioral and neural mechanisms in response to selective stimuli may give further insight into the clinical expression and the pathogenesis of personality disorders such as neuroticism. Neuroticism is conceived as a series of symptoms that affect the individual's emotional status: neurotic individuals usually show a decreased feeling of subjective well-being, expressive laughter and smiling, and increased negative emotionality [Costa and McCrae, 1980; DeNeve and Cooper, 1998; Procyk et al., 2000]. Although, some studies showed that neuroticism affects emotional processing, [i.e. Canli et al., 2002; Mobbs et al., 2005], very little is known about the neural underpinnings of regulation of emotion and emotional expression. The data we have reported in this study allowed us to make some considerations. The opposite facet of neuroticism is the emotional stability [Caprara et al., 1993b], which refers to the individuals' ability to react properly to emotional events. Here, we found that individuals' emotional stability, as assessed by the Big Five Questionnaire [Caprara et al., 1993a], was highly correlated with both the individuals' ES trait and the BOLD signal change extracted from the left and right anterior insula. Both statistical analyses resulted in a significant negative correlation: the higher the emotional stability scores that were assessed in the participants, the lower their ES scores were and the BOLD signal change within the anterior insula. Thus, since the emotional stability is the opposite facet of neuroticism, our findings suggest a strong relationship between ES and the personality dimension of neuroticism. Therefore, due to the varied involvement of the anterior insula depending on individuals' ES, our findings seem to suggest that the personality trait of neuroticism in some aspect may be related to differences in the insular activity while individuals process emotional stimuli. Such a relationship is in agreement with previous neuroimaging studies showing activity of the insular cortex being related to the personality trait of neuroticism [i.e., Johnson et al., 1999; Paulus et al., 2003; Sugiura et al., 2000]. For example, in a very recent study, Deckersbach and colleagues [2006] investigated the relationship between the personality dimensions of neuroticism and extraversion, as assessed by the NEO Five Factor Inventory [NEO-FFI; Costa and McCrae, 1992], and the regional cerebral glucose metabolism (rCMRglu) in healthy control subjects. The authors found a significant correlation between the neuroticism and the rCMRglu in the insular cortex, and a significant correlation between the extraversion and the rCMRglu in the orbitofrontal cortex. In this context of regional cerebral metabolism, our data may provide further information regarding the functional activity of the insular cortex related to neuroticism in response to emotional stimuli. However, this observation needs to be considered with precaution since we cannot exclude the possibility that other traits of personality may have affected the anterior insula activity while processing emotional stimuli.

The findings reported in our study may also shed more light on the understanding of the "emotionalism" syndromes, which are often observed in patients with stroke, multiple sclerosis or amyotrophic lateral sclerosis, and other neurological disorders (supranuclear progressive palsy, vascular dementia, pontocerebellar tumors) [i.e. Carota et al., 2002]. These patients report an increase in frequency of crying and laughing behaviors in comparison to their usual behavioral attitude before the disease. With little or no warning, they cry and laugh in any social context, demonstrating that their emotional expressions are out of control. Although there is some evidence that patients with lesions in the anterior insula manifest emotional disorders [for a review, see Critchley, 2005], the neural correlates of emotionalism in patients with brain lesions remain unclear. Emotionalism in neurological disorders may be assimilated to a pathological degree of ES in subjects without brain damage. If this is the case, our data clearly suggest that further functional neuroimaging studies investigating the neural activity involved while explicitly processing the emotional contents of stimuli may be helpful in understanding the mechanism of emotional regulation in such a specific pathological state.

The biological basis of human personality has been the focus of recent structural neuroimaging studies, which were directed at investigating the relationship between extraversion and neuroticism traits with structural brain features. In some cases, extraversion has been associated with gray matter volume of the right posterior fusiform gyrus in patients with chronic schizophrenia, but not in healthy individuals [Onitsuka et al., 2005], whereas neuroticism has been related to whole-brain relative volume [Knutson et al., 2001]. In other cases, the personality traits of extraversion and neuroticism have been related oppositely with the gray matter volume of the left and right amygdalae respectively [Omura et al., 2005]. Although the findings reported in the literature are not consistent, they clearly suggest the existence of a relationship between personality traits and morphology of the neural structures involved in emotional processing. Here, we raise the question whether the difference in neural activity revealed between groups with high and low ES reflects structural differences within the anterior insula. In our study, the VBM analysis did not reveal any difference in brain morphology related to the individuals' ES, suggesting that the difference in neural activity observed between individuals with high and low ES may be related only to functional differences in emotional processing rather than to morphological ones. In our opinion, future studies need to account for the interaction between functional, structural, and genetic factors, in both clinical and healthy samples, before the relationship between personality and brain morphology is understood.

In summary, the findings we have reported in the present study show that a specific trait of personality such as ES modulates the neural activity within the anterior insula while individuals process photographs with emotional contents. We also found that the ES trait is strongly related to the individuals' emotional stability, which suggests a clear relationship between neuroticism and functional activity of the insular cortex. The implications of this study directly relate to the understanding of the regulation and expression of emotions in healthy individuals, showing that the activity within the insular cortex, which has been shown to regulate the physiological aspects of emotions in humans, may vary depending on different personality traits. From a clinical perspective, these results may also have implications for understanding how brain functioning and the presence of certain personality factors make individuals vulnerable to developing psychiatric disorders.

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