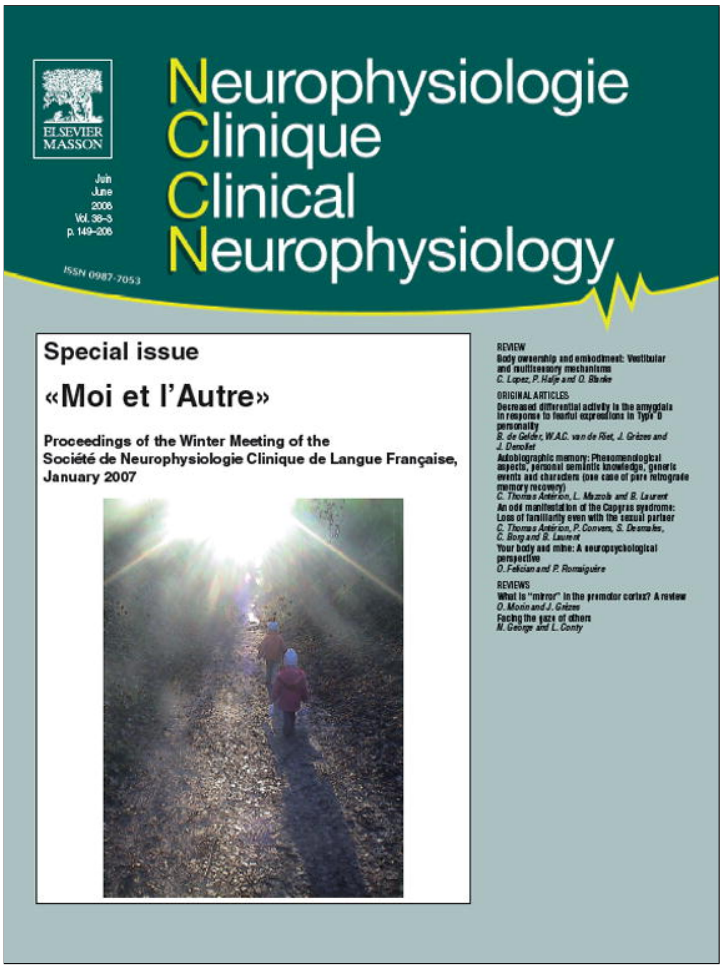

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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Decreased differential activity in the amygdala in response to fearful expressions in Type D personality

Diminution de l'activité au sein de l'amygdale en réponse à des expressions de peur dans les personnalités de Type D

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Summary Recent advances in functional brain imaging offer unique opportunities to explore the neurofunctional basis of tools used to assess personality differences which have proven their clinical usefulness. In this functional magnetic resonance imaging (fMRI) study, the focus was on the amygdala activation and we investigated whether individual differences in activity of the amygdala following presentation of emotional expressions in the face and the whole body may be systematically related to the presence of Type D (distressed) personality or to its constituting factors, Negative Affectivity (NA) and Social Inhibition (SI). Our results show that the observed difference in amygdala activity between fearful and neutral expressions was present in participants that did not meet the criteria for Type D personality, while this effect was absent in participants that could be classified as Type D personality. Our correlation analyses further showed that the activation in the left amygdala elicited by fearful versus neutral bodily

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expressions correlated negatively with the Negative Affectivity score. The same pattern was observed for the right amygdala for fearful facial and bodily expressions when contrasted with neutral facial and bodily expressions.

MOTS CLÉS
Émotion ;
IRMf ;
Amygdale ;
Personnalité de Type D

Résumé Les progrès récents en imagerie fonctionnelle cérébrale nous offrent un moyen privilégié d'étude des fondements neurofonctionnels d'outils utilisés pour évaluer les différences de personnalités et dont la valeur clinique est reconnue. Le but de cette étude en imagerie par résonance magnétique fonctionnelle (IRMf), qui portait sur l'amygdale, était de déterminer si les différences interindividuelles d'activité au sein de l'amygdale en réponse à l'observation d'expressions corporelles et faciales émotionnelles pouvait être expliquée par la présence d'une personnalité D (détresse) ou de l'un de ses facteurs constituants, mesurés par des scores d'affects négatifs ou d'inhibition sociale. Nos résultats montrent qu'une différence d'activité au sein de l'amygdale entre expressions de peur et expressions neutres est présente chez les individus qui ne répondent pas aux critères de personnalité D, cette différence disparaît chez les sujets répondant aux critères de personnalité D. Les analyses de corrélation montrent de plus que l'activation de l'amygdale gauche détectée dans la comparaison entre expressions corporelles de peur et expressions corporelles neutres est corrélée négativement avec les scores d'affects négatifs. Une corrélation négative entre les scores d'affects négatifs et l'activation de l'amygdale droite est également observée lorsque les expressions de peur sont contrastées aux expressions neutres, indépendamment du fait que ces expressions soient faciales ou corporelles.

Introduction

The affective dimension occupies a prominent place in normal and disturbed information processing. Recent advances in functional brain imaging offer unique opportunities to explore the neurofunctional basis of many tools used to assess personality differences, which have proven their clinical usefulness. Investigations of the links between personality and recent findings in affective neuroscience look like a particularly promising area to build bridges between these two hitherto unconnected research areas.

Traditionally researchers in affective cognition and those exploring the neural basis of affective information processing have used facial expressions as stimuli. Many studies have now shown that human observers excel at recognizing facial expressions and that this ability is implemented in a network of brain areas including the amygdala as one of the core structures that compute the valence of the face for the observer [1] in concordance with the face-specific region in the fusiform gyrus [2,3], as shown in numerous neuroimaging studies [4—6].

In everyday life, bodies are just as common as faces and they typically carry much of the same information like that about personal identity and emotional expression as faces do. Social communication includes intuitive grasping signals of hostility and reacting with empathy to signals of distress, and communicative ability relies heavily on decoding messages provided by bodily signals. Failure to engage in body talk is associated with major social handicaps like for example in one of its extreme manifestations in autism. The neural basis of bodily perception is probably as complex and rich as that of face perception and investigations are just beginning. Recent findings confirm the notion that there exist similarities between the neural basis of processing of emotional facial and bodily expressions. The studies of Hadjikhani and de Gelder [7] and de Gelder et al. [8] show that the activity of the amygdala and of the fusiform gyrus is enhanced by the fearful expression of the presented body stimuli. In a previous study [9], we systematically compared the neural underpinnings of the perception of facial and bodily expressions. For an extensive overview of the brain regions common and different in the perception of facial and bodily expressions, the reader is therefore referred to that study.

Data from amygdala lesion studies tell a similar story. Among the emotions used in these experiments, affected patients are most profoundly impaired in the recognition of fear, whether tested with facial expressions [10—17] or with body stimuli [17].

In a previous study [9], we undertook a systematic comparison of common and category-specific neural underpinning of the processing of facial and bodily expressions. Our observations clearly yielded that the left and right amygdala were equally activated by fearful faces and bodies, compared to their neutral counterparts.

By including various conditions in a within-subject design, one can determine which factors are of influence on the observed activity levels. Underlying assumption is that the tested population is homogeneous considering the observed activation. Inspection of the individual activation patterns in the brain sometimes reveals large inter-subject differences. This can be deemed as unwanted noise, but in some case it can also be related to other between-subject factors, like temperament, personality, etc.

There are already numerous studies of blood oxygenation level dependent (BOLD) activation in the amygdala that point to the importance of individual differences. Some studies compare clinical with non-clinical samples with regard to the volume, the resting state, or the reactivity of the amygdala [18]. Interesting findings concern increased volume of the amygdala in, for example, bipolar disorder or in major depression when patients are compared to normal

controls [19] while other studies point to decreased amygdala volumes [20] or find no differences [21]. In addition, several studies that investigated resting state activity differences between patient groups and control participants, report increased metabolism of the amygdala during resting state in bipolar disorder and major depression [22] while other studies report a decrease in amygdala metabolism [23]. In the neuroimaging study of Fu et al. [24] larger increases in amygdala activity for sad facial expressions were found in participants with major depressive disorder compared to normal controls. Anand et al. [25] showed that the difference in amygdala activity triggered by pictures with negative versus neutral valence is larger in depressed than in normal participants. However, in the study of Davidson et al. [26] depressed and healthy controls did not differ considering their differential amygdala activity elicited by fearful and negative stimuli. A study of recovery from depression by Canli et al. [27] indicated that amygdala activity for sad, happy, and fearful facial expressions was positively associated with improved scores on the Beck Depression Inventory administered eight months after the fMRI experiment. Thomas et al. [28] showed that depressed versus anxious children showed contrasting abnormal patterns of amygdala activity in relation to normal control participants. Anxious children showed increased amygdala response to fearful faces while depressed children showed a blunted amygdala response to fearful faces.

However, in many clinical studies the samples are selected and drawn from a clinical and non-clinical population with the purpose to maximize effects. It is, however, of importance when testing a normal population, like for example college students that participate in an experiment for money or study credits, to account for possible between-subject variance observed in the data. The studies mentioned clearly show that the amygdala activity reflects some important aspects of mood and personality in clinical populations. It is therefore of interest to investigate whether small differences in these personality factors can also account for the observed difference in brain activity found in the sampled normal population.

For this purpose we concentrated on the amygdala activation as observed in our previous study [9] and investigated whether individual differences in BOLD signal in the amygdala may be systematically related to Negative Affectivity (NA) or to Social Inhibition (SI) as measured by assessment of Type D personality. The distressed personality type (Type D) denotes the combined effect of Negative Affectivity (tendency to experience negative emotions) and Social Inhibition (tendency to inhibit self-expression towards others). The first subscale, Negative Affectivity, is associated with increased vulnerability to anxiety and depression [29] and the second subscale, Social Inhibition, with increased vulnerability to interpersonal stress and failure to adapt [30]. Type D patients experience more feelings of dysphoria, anxiety, and irritability but tend to inhibit the expression of these emotions in order to avoid disapproval by others. Type D is relatively common in the general population, with 21% that scores as Type D personality [31]. More importantly, Type D is associated with various indices in health and disease. Previous research shows that Type D in cardiac patient predicts poor prognosis [32,33] and poor outcome of invasive treatments such as coronary artery stent implantation [34], bypass surgery [35] and heart transplantation [36]. Hyper-reactivity of the hypothalamic-pituitary-adrenal axis and greater cortisol reactivity to stress [37—39], as well as increased pro-inflammatory cytokine levels [40,41] have been suggested as biological pathways that may explain this increased risk for adverse health outcomes in Type D patients.

Such findings clearly indicate that Type D is associated with a range of somatic effects. The Type D questionnaire is thus a useful instrument to make distinctions at the personality level and incorporates similar dimensions as the studies mentioned on depression and amygdala volume, metabolism and reactivity, it may be a factor in explaining the observed between-subject variance in amygdala reactivity in the normal population.

Methods

Participants

The group consisted of the same 17 right-handed healthy male volunteers (mean $\pm$ standard deviation: 23.0 ± 2.4 years) described more extensively in van de Riet et al. [9].

Materials

Stimuli of fMRI experiment

We used black-and-white pictures of faces and of bodies with the faces covered by a gray mask. For each category fearful, happy, and neutral expressions were used. Face pictures were selected from the karolinska directed emotional face (KDEF) database [42]. Body pictures were taken from our own database. See for a full description of the stimuli construction and validation van de Riet et al. [9]. Stimuli consisted of 18 face and 18 body images including three expression categories, that is, fearful, happy, and neutral and of different identities, that is, three males and three females. For the neutral bodily expression, we used pictures of bodies performing an instrumental action, that is, pouring water into a glass. Faces were fitted inside a gray oval shape and body images were cut out, removing all background and the faces of the body pictures were covered by a gray mask. Additionally, a scrambled version of each neutral image was created using a phase scrambling procedure [43,44]. All stimuli were resized to 300 pixels in height and presented on a gray background. For the current analysis as described in the fMRI data analysis section only the conditions containing fearful and neutral facial and bodily expressions were used (See Fig. 1 for stimulus examples).

Task

Type D assessment

All subjects completed the DS14 scale as a standard measure of Type D personality [31] within a few minutes and after the fMRI session. The questionnaire was taken after the experiment to prevent possible mood-inducing influences of the questions on the fMRI experiment and to keep the participants naively. The 14 items of this scale are answered on a five-point response scale ranging from zero (false) to four

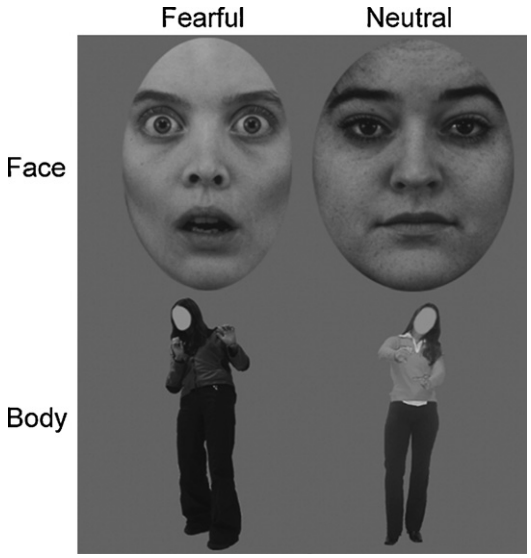

Figure 1 Examples of the stimuli used in the fMRI experiment.

(true). Seven of these items refer to ''Negative Affectivity'' or the tendency to experience negative emotions in general (for example, ''*I am often down in the dumps*, *I often find myself worrying about something*''). The remaining seven items refer to the patient's level of ''Social Inhibition'' or the tendency to inhibit the expression of emotion/behaviour in social relationships (for example, ''*I am a closed kind of person*, *I often feel inhibited in social interactions*''). These personality scales are reliable (Cronbach's $\alpha = 0.88/0.86$) and stable over time.

fMRI experiment

Participants were instructed to categorize the emotion irrespective of whether the stimulus was a face or a body. A trial consisted of a fixation cross (200 ms), followed by a stimulus (500 ms), by a gray screen (1750 ms) and an answer screen (1400 ms) which prompted the participants to respond by pressing one of the three buttons corresponding to the different emotions. Button-emotion pairings varied randomly per trial. To prevent differences in eye-movements between the face and body conditions, a fixation cross was presented throughout the trial in the same position, and the presentation duration of the stimulus was kept to a minimum. The scrambled pictures were presented with strictly the same temporal parameters as the other experimental trials. However, subjects had no judgment to perform during those trials; they just had to select one of the three buttons according to the instruction given on the answer screen. The stimulus set of 48 different images (six faces $\times$ three expressions, six bodies $\times$ three expressions, six neutral scrambled faces, six neutral scrambled bodies) was presented six times resulting in 288 trials. Null-events were included in our design to establish a better implicit baseline [45] improving statistical power to detect effects of interest. Additionally, 96 null-events consisting of a gray screen lasting the whole trial were included. During the null-event trials participants had to fixate the screen without performing any task. All trials, including the null-event trials, were pseudo-randomly presented during one run. The pseudo-randomization ordering for the conditions and the button-emotion pairing ordering was different for each subject. The experiment was preceded by a short practice session using different face [46] and body stimuli.

fMRI procedure

Participants lay supine in the scanner with head movements minimized by an adjustable padded head holder. The stimuli were projected onto a mirror above the participant's heads. Responses were recorded via an MR-compatible keypad (MRI Devices, Waukesha, WI), positioned on the right side of the participant's abdomen. A PC running Presentation 9.70 (Neurobehavioral Systems, San Francisco, CA) controlled stimulus presentation and response collection.

fMRI data acquisition

Images were acquired using a 1.5T Sonata scanner (Siemens, Erlangen, Germany). Blood oxygenation level dependent (BOLD) sensitive functional images were acquired using a single shot gradient echo-planar imaging (EPI) sequence (repetition time (TR) = 3790 ms, echo time (TE) = 40 ms, 43 transversal slices, ascending acquisition, 2.5 mm slice thickness, with 0.25 mm gap, FP = 90°, field of view (FOV) = 32 cm, matrix size 96×64 mm). An automatic shimming procedure was performed before each scanning session. A total of 624 functional volumes were collected for each participant. Following the experimental session, structural images were acquired using an MP-RAGE sequence (TR = 2250 ms, TE = 3.93 ms, Inversion Time (TI) = 850 ms, voxel size $1 \times 1 \times 1$ mm).

Analysis

Type D questionnaire

Each subject was scored on three levels, first on the negative affectivity scale, with scores ranging from zero to 28, second on the Social Inhibition scale, with scores also ranging from zero to 28 and third on Type D personality, which was scored if a subject had a score of 10 or more on both the negative affectivity and the Social Inhibition scale.

fMRI data analysis

Imaging data were analyzed using SPM2 (Statistical Parametric Mapping, www.fil.ion.ucl.ac.uk/spm). The first five volumes of each functional run were discarded to allow for T1 equilibration. The remaining 398 functional images were reoriented, slice-time corrected to the middle slice and spatially realigned to the first volume. The images were normalized to the standard Montreal Neurological Institute (MNI) template and subsampled at an isotropic voxel size of 2 mm. The normalized images were smoothed with an isotropic six-mm full-width-half-maximum (FWHM) Gaussian kernel.

A random effects analysis was performed. The BOLD response to the stimulus onset for each event-type was convolved with the canonical hemodynamic response func-

tion of 3.65 s (0.96 TR). For each subject's session, six covariates were included in order to capture residual movement-related artefacts (the three rigid-body translations and the three rotations determined from initial registration) and a single covariate representing the mean (constant) over scans. The data were high-pass filtered with a frequency cut-off at 128 s.

At the first level, eight separate *t*-test contrasts, representing each a separate condition, that is, fearful, happy, neutral, and scrambled face conditions and fearful, happy, neutral and scrambled body conditions, were modelled. The null-events were modelled implicitly.

Definition of the region of interest

In our previous study [9], we found a significant main effect for the emotion as expressed by face and the body, with higher activity for fearful than for neutral expressions in the left and right amygdala. Using the anatomy toolbox [47] we created a region of interest (ROI) for the amygdala as described by Amunts et al. [48]. With the aid of MarsBar (http://marsbar.sourceforge.net; see [49]), the parameter estimates of activation (beta weights, an index of blood oxygen level dependent (BOLD) signal change) were extracted for each ROI on a individual subject basis for each condition of the model.

As we found an effect for fearful versus neutral expression, we included in the repeated measures analyses of variance (ANOVA) for the extracted beta weights the factor Emotion, with two levels, that is, fearful and neutral and the factor Category with two levels, that is, face and body for both the left and the right amygdala. To determine the relation between Type D personality and the effect of emotional modulation of the activity of the amygdala we included Type D in the 2×2 ANOVAs as a between-subject factor. This allows us to determine whether there is difference between participants that can be scored as Type D personality and those who do not have a Type D personality concerning the observed effect of Emotion on the amygdala activity. For the respective scores on NA and SI, we included NA and SI each as covariant in the aforementioned 2×2 ANOVA. Additionally, in case one of the subscales covariated significantly with the factor Emotion, correlations were calculated.

Results

Type D personality

Of the 17 participants, four participants scored as Type D personality, while 13 participants did not meet the criteria for Type D personality. The 2×2 ANOVA (factors Emotion, that is, fearful and neutral and Category, that is, face and body) with the between-subject factor, Type D, did not yield any significant interactions with the factor Type D in the left amygdala. For the right amygdala, however, there was a significant interaction between Type D and Emotion ($F(1,15) = 7.251$, $p = 0.017$). As the factor Category did not show an effect, we collapsed the two levels (that is, face and body) of this factor. *T*-tests for fearful versus neutral expression showed a significant difference in amygdala activation for non Type D participants with higher activation for fearful compared to neutral expressions ($t(12) = 3.528$, $p = 0.004$), while there was no difference between the fearful and the neutral condition for Type D participants ($t(3) = 2.254$, $p = 0.110$). Note that the observed non-significant difference is reversed, that is, neutral non-significantly larger than the fearful expression, in the latter case.

Negative affectivity

A three-way interaction between the factors Category, Emotion and NA was observed for the left amygdala ($F(1,15) = 7.667$, $p = 0.014$). A further correlation analysis showed a negative correlation between the score on NA and

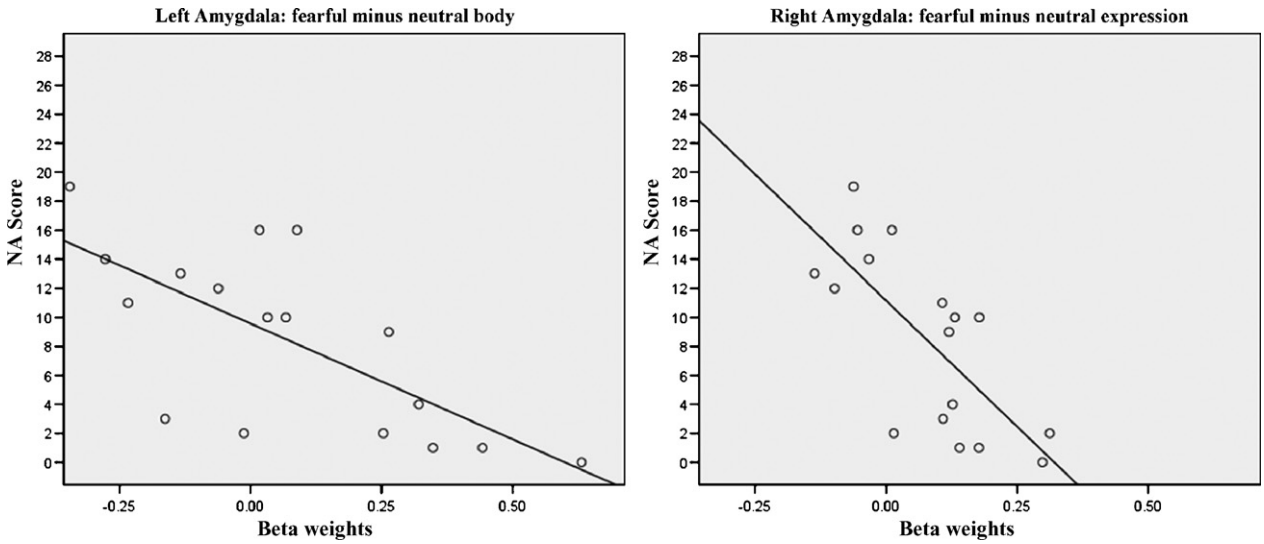

Figure 2 Left panel: scatter plot of the observed correlation between the score on Negative Affectivity (NA) with the differential activity of the left amygdala (expressed in beta weights) elicited by the fearful and neutral bodily expressions. Right panel: scatter plot of the observed correlation between the score on Negative Affectivity with the differential activity of the right amygdala (expressed in beta weights) elicited by the fearful and neutral expressions.

the difference in amygdala activity between the fearful and neutral bodily expression ($r = -0.698$, $p = 0.02$). For the right amygdala, a two-way interaction existed between the factors Emotion and NA ($F(1,15) = 17.011$, $p = 0.001$). As there was no effect for the factor Category, the two levels, that is, face and body, were collapsed. A further correlation analysis showed a significant negative correlation between the score on NA and the difference in amygdala activity between the fearful and neutral expression, ($r = -0.729$, $p = 0.01$), indicating that the higher the score on NA, the less the distinction between the fearful and neutral expression is perceptible concerning the amygdala activity. Scatter plots of the observed correlations for the left and right amygdala are shown in Fig. 2.

Social Inhibition

No interactions between SI and Emotion were observed.

Discussion

Our goal was to investigate whether personality variables as measured in a normal college age population are systematically associated with differences in level of amygdala activity. We contrasted images of fearful and neutral expressions and used both facial expressions and bodily fear signals. For the left amygdala a negative correlation obtained between the Negative Affectivity score and the differential activation of the amygdala and this for the contrast fearful versus neutral bodily expressions. For the activation level of the right amygdala a negative correlation obtained between Negative Affectivity and differential activation of the amygdala when contrasting fearful with neutral expressions, and additionally a group difference between Type D and non Type D participants, with the latter not showing the emotional modulation effect.

A serious caveat in this the study could be the limited number of Type D participants, that is, four, while the group of participants that did not meet the criteria for Type D personality consisted of 13 subjects. However, we took this into account by conducting additional analyses in which we looked at the relationship between the subscales Negative Affectivity and Social Inhibition with amygdala reactivity. This enabled us to compare two relative, continuous measures.

As the subscale Negative Affectivity is associated with vulnerability to depression [29], it is interesting to compare our results to studies in which amygdala activity was compared between clinical samples with depression and healthy controls. Contrary to our findings some of these studies find increased differences in amygdala activity between emotional and neutral images [25,50]. Two other studies, however, report less differential activity in the amygdala in depressed adults compared to control subjects when fearful faces are compared to neutral faces [51] and in depressed children compared to healthy controls when fearful faces are compared to a fixation cross [28].

There is, however, a large difference between these clinical studies and the current one. In the clinical studies, clinical populations are compared to healthy control subjects. In our study we look at the normal variance in negativity affectivity scores in healthy participants and relate the between-subject differences to between-subject differences in amygdala reactivity. This makes clear that differences in Negative Affectivity, characterized by the tendency to worry, to often feel unhappy, etc., is related to difference in amygdala reactivity within the normal population. In contrast, the multitude of functional imaging studies assumed that the sampled population is homogeneous.

Acknowledgements

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