Central control of heart rate changes during visual affective processing as revealed by fMRI

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Abstract. In the present study we addressed the question of central control of heart rate (HR) in emotions. Parallel measurement of HR changes and changes of local intensity of blood flow as indexed by fMRI in a procedure eliciting emotions allowed us to pinpoint areas of the brain responsible for HR variations during emotional arousal. In condition eliciting positive emotions we detected activation of occipito-temporal regions, anterior insula, and hypothalamus. In condition eliciting negative emotions we also detected activation of occipito-temporal regions and additionally activation of bilateral anterior insulae, right amygdala and right superior temporal gyrus. The results show that structures constituting neural network involved in HR control during emotional arousal are affect specific. Particularly the central circuit controlling HR in negative affect includes the amygdala, while central circuit controlling HR in positive affect includes the hypothalamus. Additionally activation of bilateral occipito-temporal cortex proves enhancement of visual processing of emotional material as compared to neutral material in both positive and negative affect. This might be attributed to top-down processes originating in the frontal lobe and related to shifting attention to the emotionally relevant stimuli. Activation of insular cortex is probably related to autonomic arousal accompanying watching emotional content (e.g. sweating, heart-rate changes etc.). Activation of the amygdala in the negative condition supports the well documented engagement of this structure in processing of fear and disgust.

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INTRODUCTION

The concept of emotion traditionally includes changes in autonomic responses. There is an ongoing debate whether the autonomic changes in particular emotions form specific patterns unique to the emotion or whether those changes are common to wide range of emotional states (Ekman and Davidson 1994). Despite this controversy it is agreed that the autonomic changes accompanying emotion must result from the activity of higher brain centres, which are responsible for analysing emotionally relevant stimuli. The structure widely described as being involved in emotional processing is the amygdala (Calder et al. 2001, Davis and Whallen 2001, LeDoux et al. 1995). LeDoux and his colleagues (LeDoux et al. 1995) have shown that the intact pathway from thalamus or cortex to the lateral nucleus of amygdala is necessary for fear conditioning. Moreover, evidence exists for the statement that amygdala is involved in the association of environmental stimuli with reward (Everit et al. 1991) (see also: Baxter and Murray 2002, Han et al. 1997, Malkova et al. 1997, Muramoto et al. 1993).

The typical reaction of an animal to conditioned fear stimuli involve several autonomic and behavioural components that are known as the "freezing reaction" (Świergiel 2003). It encompasses immobility, except for movement related to breathing, and several autonomic changes involving HR, blood pressure and respiration. In examining the role of the amygdala in autonomic changes associated with freezing, Kapp et al. (1992) have shown in rabbits that the central nucleus of amygdala is responsible for HR deceleration during fear conditioning. These authors also showed that direct electrical stimulation of the central nucleus of the amygdala produces immediate bradycardia.

Experiments on rats which tested the relation between fear conditioning and HR yielded mixed results. Some laboratories reported a HR deceleration while others a HR acceleration following presentation of stimulus paired with an electric shock. Researchers suggest that those discrepancies might stem from minute differences in methodology (Fendt and Fanselow 1999, Iwata and LeDoux 1988, Jeleń and Zagrodzka 2001). In spite of these discrepancies, our group has managed to describe a correlation between the activity of the central nucleus of the amygdala and HR deceleration in response to an aversively conditioned stimulus (CS+) in rats (Kuniecki at al. 2002). Moreover, this correlation

between the activity of the amygdala and HR changes was absent when the stimulus signaled safety (CS-). This suggests that different central structures govern autonomic reactions to the threatening and neutral stimuli.

In studies on human subjects it was shown that there are specific changes in HR following presentation of negative stimuli, differing from the HR changes following presentation of neutral and pleasant stimuli (Bradley and Lang 2000, Coles 1984, Hare at al. 1971, Libby at al. 1973). These changes involve a prolonged deceleration as a result of exposition to negative stimulus, typically a visual slide. Such a prolonged HR deceleration has been termed the "late deceleratory component", and it is hypothesised that this component indicates some kind of mental processing associated with the analysis of the negative valence of the stimulus (Kuniecki, unpublished).

Findings in animals concerning the role of the amygdala in processing of emotional stimuli encouraged human research using brain imaging techniques. The results obtained so far show that the amygdala is engaged in a wide range of experimental procedures all eliciting emotions (for review see Davis and Whallen 2001). Despite the steady progress in research towards the central correlates of an emotional processing *per se*, there are only a few studies directly examining role of central structures engaged in autonomic control of emotional processing. Most of them rely on the "skin conductance response" and do not address directly the question of HR regulation in emotion (Bechara et al. 1995, Büchel et al. 1998, Critchley et al. 2000a, LaBar et al. 1998). All these authors identified structures common to emotional arousal, namely: the amygdala, the anterior insula, and the anterior cingulate gyrus.

Recently Critchley's group (Critchley et al. 2000b) conducted research concerning central mechanisms of HR regulation in different arousal states. They extend results of their work to emotional arousal. They did not, however, use an emotional factor to elicit autonomic change. Instead, they used mental arithmetic and isometric exercise. Therefore, the experiment of Critchley et al. (2000) cannot be treated as directly addressing the question of autonomic regulation in emotional reactions. This is specially true, when is taken into account that there are reliable reasons to hypothesise that autonomic reactions are specific to particular emotions and central structures engaged in these changes might also be specific (Calder et al. 2001). Considering this, we designed an experiment that would tackle more directly

the question of structures responsible for HR changes in negative and positive emotions. We expected to find an activation in the amygdala in negative emotions and an activation in the cingulate gyrus in both positive and negative emotions. In addition, we expected to observe activation in structures commonly reported to be involved in autonomic changes such as the anterior insula and the hypothalamus. The experiment was carried out with fMRI measures as well as with HR measures.

METHOD

Subjects

Healthy male students ($n = 16$) aged between 19 and 25 years recruited by means of community advertisements from various faculties (excluding psychology) served as subjects. All signed an informed consent before the start of the experiment. Participants were paid 20 PLN (Euro 5) for their effort. To raise the incentive value all participants were given a structural image (MRI) of their own brain.

Experimental design

The stimuli which were used were prepared from three sets of pictures, namely: negative and positive sets, each consisting of six pictures selected from International Affective Picture System (Lang et al. 1999)[1], and a neutral set consisting of three coloured checkerboards.

The experiment comprised of three individual sessions separated by a time period randomly varying from two weeks to four months. The first two sessions involved the fMRI measurement, while the last session was conducted outside the fMRI facility recording autonomic activity. A single experimental run was divided into five consecutive blocs, every block lasting 30 s. During each block there were three successive picture presentations each lasting 10 s. The first, third and fifth block belonged to a baseline condition and included the presentation of checkerboards. The second and fourth block belonged to the experimental condition during which the IAPS pictures were presented. In the first session the experimental blocs were composed of negative IAPS pictures, while during the second session experimental blocs were composed of positive IAPS pictures.

[1]The IAPS slide numbers were as follows: positive, 4180, 4210, 4220, 4250, 4652, 4664; negative, 3000, 3053, 3064, 3080, 3102, 3170

For the presentation of visual material we used back projection method with a screen placed in front of the MRI device. The subject watched the experimental material by means of the mirror placed inside the head coil.

The third session was conducted in order to measure heart rate changes throughout the course of picture (slide) presentation. Subjects were seated in a comfortable armchair in an air-conditioned, electrically shielded, sound-isolated chamber which was separated from the recording equipment. A slide projector was located behind a double-pane window. Slides filled a 50 x 30 cm area on a screen positioned 2 m in front of the subject. During this last session subjects first went through an experimental run with negative IAPS pictures and then, after a 10 min break, through an experimental run with positive IAPS pictures. In all three sessions subject's task was to give attention to the pictures presented to him.

HR acquisition

Heart rate was recorded from S&W standard electrodes connected to an S&W/BIAZET ECG device. The output from an R-wave peak detector was used to compute R-R intervals in ms.

Imaging procedure

Images were acquired with a 1.5 T Signa Horizon MR scanner (GEMS). Functional images were acquired using a spin-echo echoplanar sequence sensitive to blood oxygenation level dependent (BOLD) contrast, with following parameters: TR = 3,000 ms, TE = 60 ms, FOV = 28 x 21 cm, matrix 96 x 96, 1 NEX. During each functional scanning run 50 sets of 10 contiguous, 7-mm-thick axial images were acquired parallel to the anterior-posterior commissure plane. High-resolution anatomical images were acquired in the same locations as the functional images, using SPoiled GRadient-echo (SPGR) sequence with following parameters: TR = 50 ms, TE = 6 ms, flip angle 60°, FOV 28 x 21 cm, matrix 256 x 256, 2 NEX.

Data analysis

HR

Measures of cardiac activity were calculated in terms of mean values of HR for 3 s intervals (time needed to

acquire one scan), relative to beginning of the experimental run. Heart rate data were analyzed using one-way repeated measures ANOVA over condition (baseline vs. experimental). Heart rate regressors were obtained by smoothing individual HR responses using T4253H method (SPSS 10.0).

fMRI

The first five volumes were discarded due to unsteady magnetization, the remaining 45 images were submitted to further analysis. Images were coregistered, realigned and corrected for head movements using SPM99b. Subsequently, the images were normalized to the standard space of Talairach and Tournoux (1988) using parameters obtained from normalization of a coregistered anatomical image to the MNI T2-weighted template. Lastly, the images were smoothed using 8 mm Gaussian kernel.

For the statistical analysis, besides the box-car function, representing the course of an experimental run, HR changes were entered as a regressor for each subject. Statistical inference was based on the conjunction analysis with box-car function and individual HR changes as an orthogonal contrast (Friston at al. 1997). This approach allowed us to locate regions that were activated both due to the experimental manipulation and to changes in HR. It must be pointed out, however, that not only was activity of certain brain regions "driven" by the experimental manipulation but also changes in HR (see Fig. 2). Therefore, the box car function and HR changes showed a significant correlation ($r = -0.52$, $P<0.001$ for session with negative slides and $r = -0.68$, $P<0.001$ for session with positive slides). Consequently, despite contrast orthogonalization, there was still considerable overlap between variance explained by box-car function and HR changes. The analysis was conducted with the threshold $P=0.001$ what in case of conjunction analysis actually produces $P^n=0.000001$ (where n is number of contrasts in the conjunction – see Veltman and Hutton 2001). The minimal cluster size was set to more than 10 voxels.

RESULTS

HR

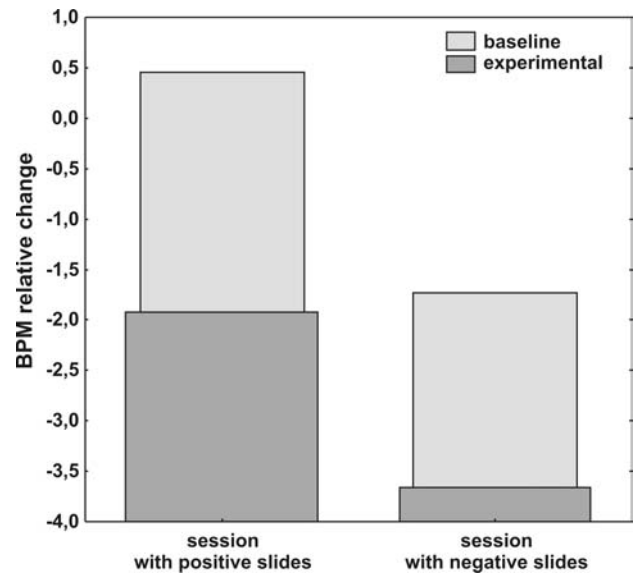Compared to the baseline condition, HR in the experimental condition was significantly lower in both sessions

Fig. 1. HR changes averaged for experimental conditions

(for session with negative slides $F_{1,15}=29.7$, $P<0.05$; for session with positive slides $F_{1,15}=44.8$, $P<0.001$) (Fig. 1). The HR change between baseline and experimental conditions had a clearly phasic deceleratory character as can be noticed in Fig. 2.

fMRI

In the negative vs. neutral session we detected significant ($P<0.001$, uncorrected) massive activations in bilateral occipito-temporal regions (fusiform gyri, middle
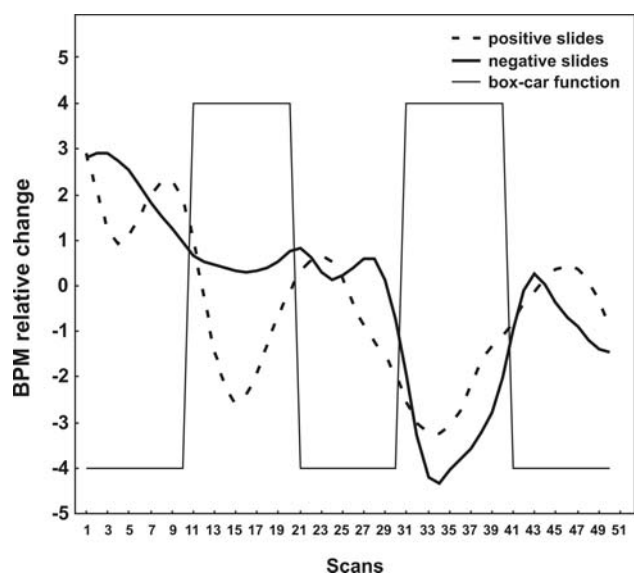

Fig. 2. HR changes averaged across all subjects (after smoothing)

Bilateral occipito-temporal regions including
fusiform gyri and middle temporal gyri

Right amygdala (A)

Bilateral insula (Ins)

Left lingual gyrus (L)

Left pallidum (P)
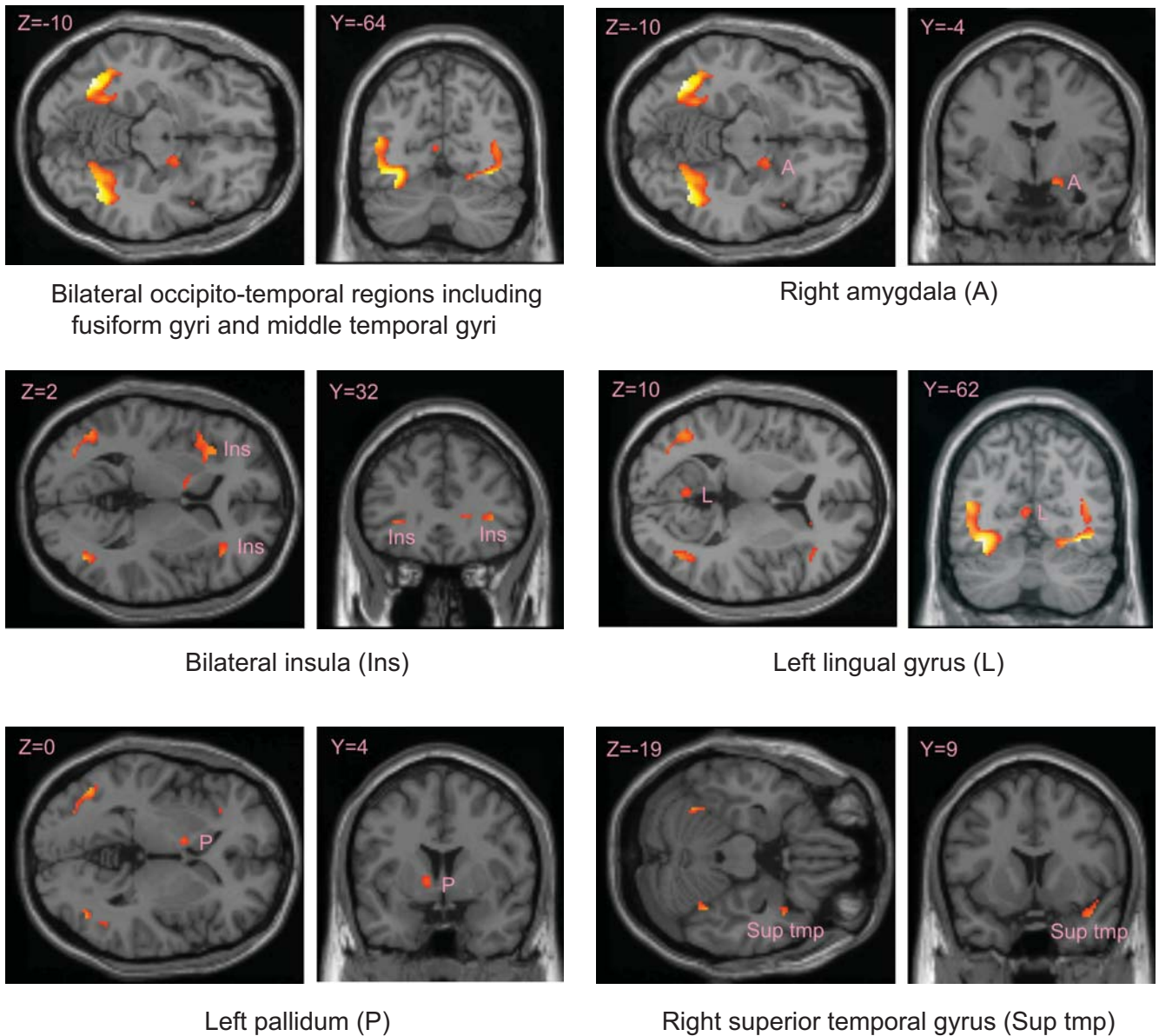
Right superior temporal gyrus (Sup tmp)

Fig. 3. Regional brain activations yielded by conjunction analysis of box-car function and HR changes while watching negative and neutral slides. Areas of significant activity ($P<0.0001$) are mapped onto template structural MRI scan. Coordinates are given in standard space of Talairach and Tournoux 1998.

temporal gyri, right occipital gyrus, left lingual gyrus). Less pronounced, but still significant, activations were apparent in the right amygdala, bilateral anterior insula with right insula activation extending to the inferior frontal gyrus, right superior temporal gyrus and left pallidum. All these activations, yielded by conjunction analysis of box-car function with HR changes in the negative *versus* the neutral condition, are given in Table I and are illustrated in Fig. 3.

In the positive *versus* the neutral session significant ($P<0.001$, uncorrected) activations, similar to these seen in the negative *versus* neutral session, were detected in the visual areas. That means bilaterally in the fusiform gyri, the inferior temporal gyri and the lingual gyri. Another activation seen in both sessions was detected on the border between the right anterior insula and the inferior temporal gyrus. A noticeable activation in the hypothalamus was unique for the positive *versus*

the neutral session. Activations yielded by conjunction analysis of box-car function with HR changes in the positive *versus* the neutral condition are given in Table II and are illustrated in Fig. 4.

Table I

Areas activated by both course of experimental run and HR changes (negative vs. neutral slides)

	Brodman area	Side	Number of voxels	Z-score	Talairach coordinates x	y	z
Fusiform Gyrus, Middle Temporal Gyrus	37,19	L	942	(Inf)	-36	-61	-9
Fusiform Gyrus,Inferrior Temporal Gyrus,Middle Occipital Gyrus	37,19	R	758	(Inf)	42	-59	-7
Insula	47	L	71	(5.16)	-34	23	3
Amygdala		R	35	(4.76)	18	-4	-12
Inferior Frontal Gyrus/Insula	47	R	34	(4.72)	38	31	2
Superior Temporal Gyrus	38	R	33	(4.63)	42	9	-19
Pallidum		L	25	(4.09)	-10	4	0
Lingual Gyrus	17	L	43	(4.09)	-4	-62	10

Bilateral occipito-temporal regions including fusiform gyri and inferior temporal gyri

Hypothalamus (HT)

Right inferior frontal gyrus extending to insula (Inf front/Ins)
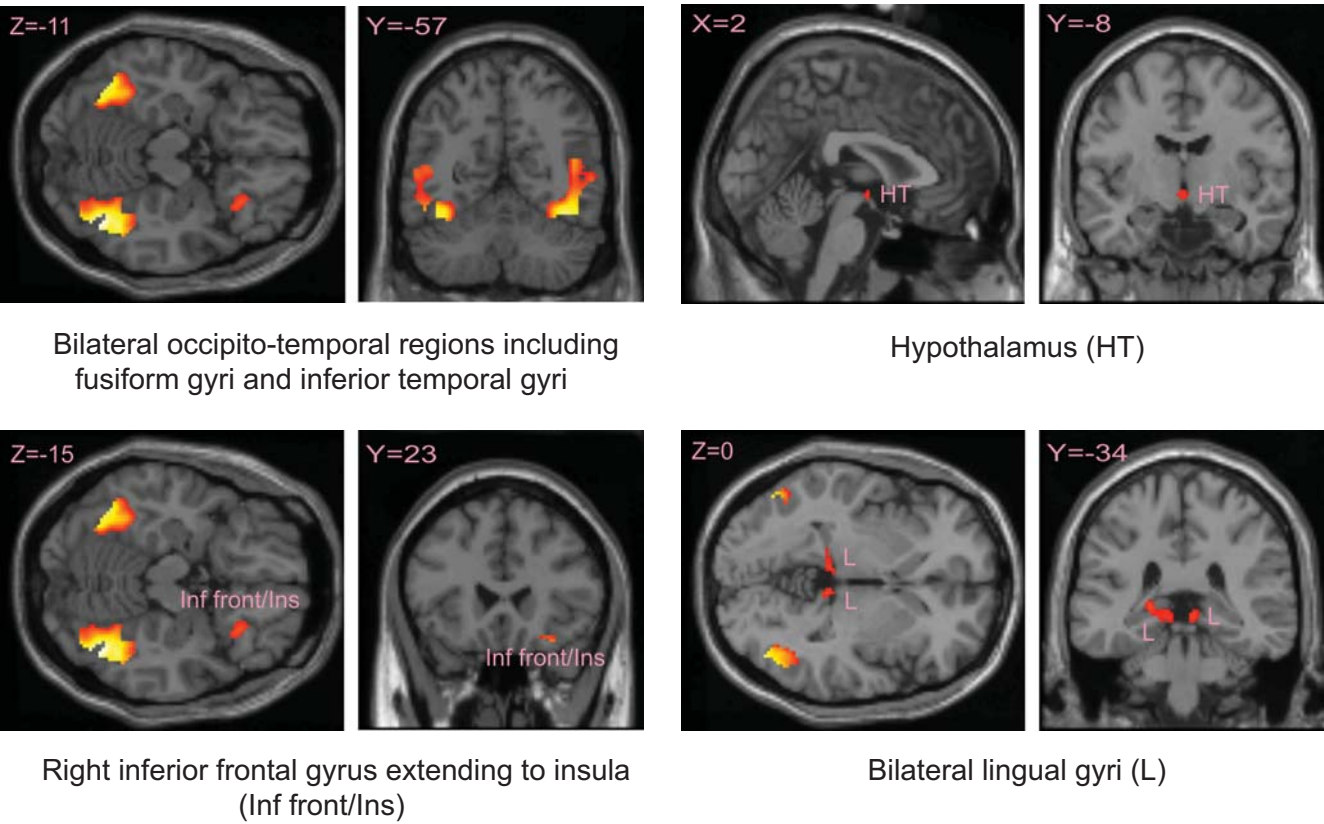

Bilateral lingual gyri (L)

Fig. 4. Regional brain activations yielded by conjunction analysis of box-car function and HR changes while watching positive and neutral slides Areas of significant activity (*P*<0.0001) are mapped onto template structural MRI scan. Coordinates are given in standard space of Talairach and Tournoux 1998

Table II

Areas activated by both course of experimental run and HR changes (positive vs. neutral slides)

	Brodman area	Side	Number of voxels	Z-score	Talairach coordinates		
					x	y	z
Fusiform Gyrus, Inferior Temporal Gyrus	19,37	R	1291	(Inf)	42	-65	-9
Fusiform Gyrus, Inferior Temporal Gyrus	37	L	500	(Inf)	-42	-55	-11
Inferior Frontal Gyrus/Insula	47	R	34	(5.42)	32	22	-16
Lingual Gyrus	27	L	67	(4.46)	-8	-31	-2
Lingual Gyrus	27	R	27	(4.06)	8	-33	0
Hypothalamus			11	(3.64)	2	-8	-5

DISCUSSION

In the current experiment we managed to identify areas of the brain involved in alterations of HR during the processing of emotionally relevant stimuli. The session in which subjects watched negative and neutral stimuli revealed activations in extrastriate visual areas, in the insulae, the right amygdala, the right superior temporal gyrus and the left pallidum. Session with positive and neutral pictures also activated the extrastriate visual areas, the right insula and additionally the hypothalamus. The results indicate, therefore, that the control of HR changes during affective processing depends on the valence of the stimulus. Hence the conclusion must be that autonomic regulation during positive and negative affect is governed by different central structures. In the negative affect condition autonomic regulation of HR most likely depends on the activity of the amygdala. Conversely, in the positive affect condition the role of the amygdala is negligible and the changes in HR most probably depend upon the activity of the hypothalamus. Animal studies have pointed to both, the amygdala and the hypothalamus as being critically involved in HR regulation in emotions (Kapp et al. 1992, LeDoux 1995, Smith et al. 1990). This parallels our result in rats, showing that activity of the amygdala correlates with HR deceleration as a reaction to a CS+ but not a CS- (Kuniecki et al. 2002).

It is noteworthy that Lane et al. (1997), using a similar design but without HR as an independent variable, not only reported hypothalamic activation in a positive *versus* neutral condition comparison, but also hypothalamic activation along with amygdala activation in the

negative *versus* the neutral comparison. It might therefore appear that we failed to register the activity of the hypothalamus in the negative condition. However, Lane et al. (1997) used only females, while we used only male subjects. This might suggest that the central regulation of autonomic changes in emotions are not only valence specific but also gender specific. This suggestion, however, requires further investigation.

We did manage to identify commonalities in the central mechanisms of HR regulation during emotions. The anterior insula was apparently activated in both sessions. This region was also shown by Critchley et al. (2000a, b) to be related to arousal, as indicated by skin conductance and tonic HR changes. However this arousal was not caused by emotional stimuli. Other authors report an activation in this region as being related to skin conductance changes related to emotional arousal (Bechara et al. 1995, Büchel et al. 1998, LaBar et al. 1998). It seems therefore that the insula is involved in generalized arousal reactions, more than arousal in specific emotional conditions.

In both sessions we detected enhanced processing in occipito-temporal locations (extrastriate visual areas) consisting of fusiform gyri, lingual gyri, medial and inferior temporal gyri. The activated structures closely match the location stream of cortical visual information processing serving fine object analysis. Therefore, these structures are most likely related to a more intensive evaluation of the emotional stimuli regardless of their valence in comparison with neutral checkerboard stimuli. Intensive occipito-temporal processing of emotional stimuli was widely described in brain imaging as well as in Event Related Potential (ERP) studies

(Adolphs 2002, Carretié et al. 2001, Critchley et al. 2000a, Keil et al. 2001, Lane et al. 1997, Lang et al. 1998, Paradiso et al. 1999, Simpson et al. 2000, Taylor et al. 2000). The ERP studies, having a sufficient time resolution, showed that the mechanism underlying this observation is an example of top down processing or using Lang's words: "reentrant processess from sites more anterior in the brain" (Lang et al. 1998).

Regions located in frontal lobe make a judgement about the relevance of the incoming stimulus, based on the crude information obtained from primary sensory areas as well as subcortical nuclei including the amygdala. If it is determined that the stimulus might be significant and hence requires further inspection, appropriate commands are passed back to the primary and secondary sensory fields calling for more refined analysis. It is also feasible that the amygdala by itself is capable of recruiting primary and secondary sensory cortices, including the visual cortex (Calder et al. 2001, Lane et al. 1997, Morris et al. 1998, Paradiso et al. 1999, Tabert et al. 2001, Taylor et al. 2000).

The activation in the superior temporal gyrus found in the negative *versus* the neutral condition comparison agrees with an earlier report by Iidaka et al. (2001). These authors interpret this activation as related to higher order visual processing.

There are two additional issues, currently debated in the field of emotional processing, which seem to be addressed by the current experiment. The first issue is an ongoing controversy as to whether the amygdala processes both positive and negative affect or only negative affect. The animal experiments leave this question open, as there are researchers arguing for an engagement of the amygdale in both negative (LeDoux 1995) as well as positive (Everit et al. 1991) emotion. In human brain imaging studies the situation seems to be much the same with some researchers opting for an involvement of the amygdala in both valences (Taylor et al. 2000), whereas others argue that the amygdala processes only negative and not positive emotions (Paradiso et al. 1999). Our results seem to support the latter option. A second issue concerns lateralisation effects in the processing of emotions. In the present study we detected an activation only in the right amygdala. This might support the common notion about a greater involvement of the right hemisphere in processing of affective information. This, however, would be a premature conclusion as the functional imaging studies have so far yielded mixed results in this respect (Tabert et al. 2001).

Finally, we would like to address the problem of lack of activation in the cingulate gyrus. Such activation is often reported in imaging studies dealing with emotions (Berthoz et al. 2002, Bush et al. 2000, Lane et al. 1998, Taylor et al. 1998, Whallen et al. 1998). Our failure to find such activation might be explained by the phasic character of the HR changes in current experiment. As pointed out by Critchley et al. (2000a) transient physiological changes might not be correlated with anterior cingulate activity.

CONCLUSIONS

We have shown that the central control of heart rate changes in emotions depends on the valence of emotions. Heart rate is regulated primarily by an amygdala in negative emotions and the hypothalamus in positive emotions.

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