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We examined neural activity associated with selectively attending to subjective emotional responses in a study where subjects viewed emotional picture sets. During picture viewing when subjects attended to their subjective emotional responses, highly significant increased neural activity was elicited in rostral anterior cingulate (BA 32) ($Z = 6.87$, $p < 0.001$, corrected). By contrast, under the same stimulus conditions when subjects attended to spatial aspects of identical picture sets activation was observed in the parieto-occipital cortex bilaterally ($Z = 5.71$, $p < 0.001$, corrected). The findings indicated a specific role for the anterior cingulate cortex in representing subjective emotional responses and are consistent with a suggested role for associated medial prefrontal structures in representing states of mind.

Key words: Anterior cingulate cortex; Attention; Emotion; Functional imaging

Neural activation during selective attention to subjective emotional responses

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Introduction

There are two divergent concepts relating to the neural basis of emotional behaviour and experience. One view holds that emotional experience is a by product of neural computations associated with processing of value-laden stimuli.[1] An alternative view proposes a specific functional anatomy based on observations that deficits in emotional experience may ensue in patients with specific brain lesions.[2] However, little is known about how subjective aspects of emotion are represented in the intact brain.

Selective visual attention can modulate task-specific neural activity in early visual pathways as seen, for example, during visual processing.[3,4] In this experiment we tested the hypothesis that selectively attending to subjective emotional responses, in the context of processing emotional stimuli, would modulate neural activity supporting the representation of emotional experience. We addressed this hypothesis by creating emotional picture sets and comparing the neural responses under conditions when the subjects attended to either the evoked emotional response or to spatial aspects of the depicted scenes.

Materials and Methods

The subjects were 10 healthy right-handed males with a mean age of 23.9 years (s.d. = 5.5) without a history of medical, neurological or psychiatric disorder. None of the subjects were taking medication or had a history of substance abuse. All subjects had normal visual acuity.

Picture sets were created from the International Affective Picture System[5] using normative valence (pleasure) and arousal ratings obtained from several hundred male subjects. Six types of emotional picture sets were created which varied in the percentage of neutral pictures contained within each set. This variation spanned from 10% to 90% in increments of 16%. The variation in emotional content within sets was introduced so that subjects would not adopt a fixed-response mode with respect to the type of emotion they were processing. Neutral stimuli included neutral faces, household objects and complex scenes such as a freeway. Remaining pictures (i.e. the emotional picture sets) in each picture set were equally divided between pleasant and unpleasant. Pleasant pictures included stimuli such as flowers, ice cream, female nudes and skydivers. Unpleasant pictures included stimuli such as a cemetery, a mangled face, a snake and a gun aimed at the viewer. Two versions of each picture set were created

and the two versions were counterbalanced across subjects with respect to their occurrence in either of the two experimental conditions.

The stimuli in each condition consisted of 30 pictures with the sequence typically beginning about 9 s prior to the onset of a scan. Each picture was presented for 500 ms with an interstimulus interval of 3.0 s. Three hundred milliseconds after picture offset, a visual guide for keypad responses, as described below, appeared on the screen for 1500 ms.

The experimental conditions involved varying attentional focus in relation to the picture sets. In the internal focus condition subjects indicated whether the picture evoked a pleasant, unpleasant or neutral feeling via corresponding word prompts which appeared on the screen. Subjects were explicitly instructed to make this rating based on their emotional response to the picture. In the external condition subjects indicated whether the picture depicted a scene which was 'indoors', 'outdoors' or 'either', again prompted by the respective words on the screen. Responses in both conditions were made via a manual keypad.

During a familiarization session, in advance of scanning, subjects practised responses on the internal and external focus conditions. During a debriefing session all subjects indicated that emotional responses were evoked during both conditions but reported more enduring awareness of this response in the internal condition.

Twelve PET derived measures of regional cerebral blood flow (rCBFr), six in each attentional condition, were obtained using $H_2{}^{15}O$ were obtained using a Siemens/CPS ECAT EXACT HR+PET scanner operated in high sensitivity 3-D mode. Subjects received a total of 350 MBq of $H_2{}^{15}O$ (about 8 mCi) over 20 s through a forearm cannula. Images were reconstructed into 63 planes, using a Hanning filter, resulting in a 6.4 mm transaxial and 5.7 mm axial resolution (full width at half maximum, FWHM). The data were processed and analysed with statistical parametric mapping (SPM97)[6] using SPM software from the Wellcome Department of Cognitive Neurology, London, implemented in Matlab (Mathworks, Sherborn, MA). After initial realignment, the scans were transformed into standard stereotactic space. The scans were smoothed using a Gaussian filter set at 16 mm FWHM. The regional cerebral blood flow (rCBF) equivalent measurements were adjusted to a global mean of 50 ml/dl/min by performing an analysis of covariance on a subject-specific basis. MRI scans of the head of each subject were co-registered with PET data for purposes of anatomical localization and transformed into this stereotactic space. Local maxima are reported in this stereotactic space.

Results

Across all picture sets the percentage of pleasant (mean (± s.d.) 31.5 ± 5.5%), unpleasant (31.5 ± 6.8%) and neutral (37.0 ± 9.6%) keypad responses did not differ. These results indicate that the emotional arousal induced by the pictures influenced how neutral pictures were perceived with a greater number being rated emotional than expected on the basis of normative ratings. Reaction times during the six internal (1.38 ± 0.1 s) and six external (1.36 ± 0.1 s) conditions did not differ, indicating that the categorization judgments in the two conditions were comparable.

The first comparison involved that of the internal focus with the external focus of attention condition. This comparison revealed increased neural activity that was maximal in anterior cingulate cortex (BA32; $Z = 6.74$; $p < 0.001$, corrected) and extending into medial prefrontal cortex (BA9; Fig. 1). Other areas of significant rCBF increase in this comparison included the right temporal pole (BA 38) extending into the medial aspect of the right temporal lobe and a homologous area on the left with peaks of activation in the frontal operculum ($Z = 5.13$, $p < 0.05$, corrected) and insula ($Z = 4.79$, $p = 0.05$, corrected). An activation of lesser magnitude was evident in the vicinity of the left ventral cingulate. The coordi-

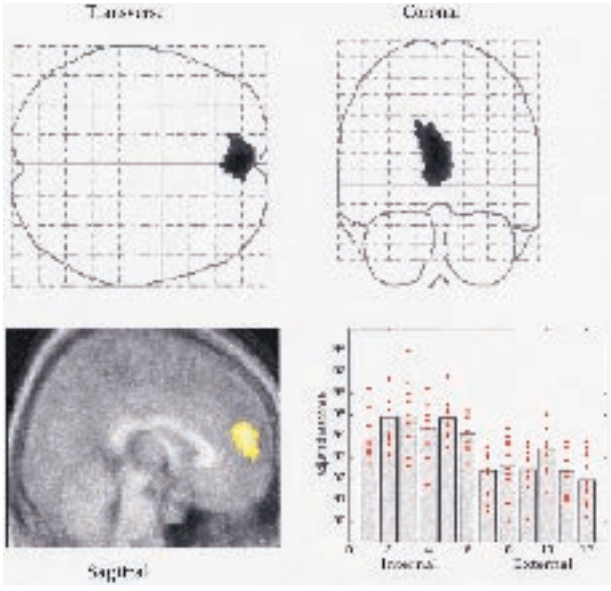

FIG. 1. A statistical parametric map (SPM) showing significant rCBF increases in anterior cingulate cortex (BA32)/medial prefrontal cortex (BA9) during selective attention to subjective emotional responses (minus activations specific to the internal condition). The figures in the upper and lower left are projection images in the transverse and coronal planes, respectively. The sagittal view in the upper right depicts the spatial distribution of the activation in the internal focus condition ($Z = 6.87$, $p < 0.001$, corrected) superimposed on the average structural MRI of the 10 male subjects. The figure in the lower right demonstrates blood flow values in each condition (internal: 1–6; external: 7–12).

Table 1. Areas of significant activation during selective attention for the two main contrasts

Structure	Brodmann's area	x	y	z	Z score
Internal minus external emotional conditions					
Anterior cingulate cortex	32	0	50	16	6.74
Temporal pole	38	42	8	–30	5.87
Frontal operculum/insula		–46	14	6	5.13
Ventral cingulate	25	–8	10	–8	4.92
External minus internal emotional conditions					
Left parieto-occipital cortex	19/37	–40	74	28	5.71
Rightparieto-occipital cortex	39	44	–70	20	4.25

nates of the foci of maximal activation are shown in Table 1.

The opposite comparison of the external focus with the internal focus of attention (i.e. activations associated with attention to the spatial aspect of the depicted scenes) revealed increased neural activity in the left parieto-occipital cortex ($Z = 5.71$, $p < 0.001$, corrected; see Fig. 2). A similar activation was identified ($Z = 4.25$, $p < 0.001$, uncorrected) in an homologous area on the right. The coordinates of the foci of maximal activation are shown in Table 1.

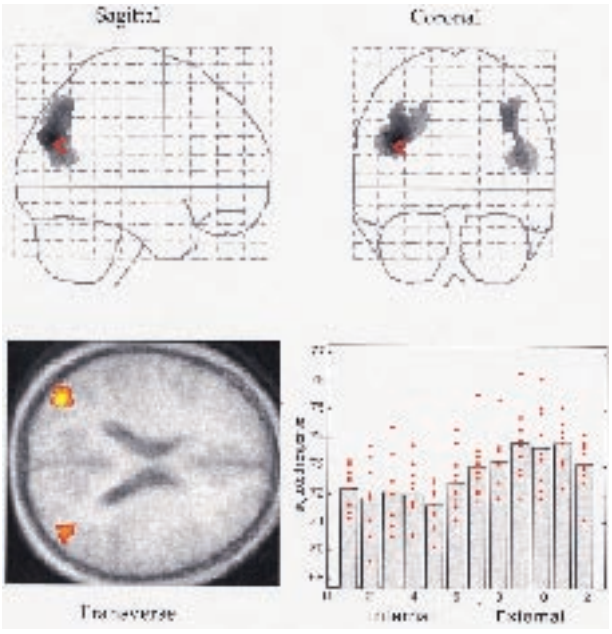

FIG. 2. An SPM showing rCBF increases in left ($Z = 5.71$; $p < 0.001$, corrected) and right ($Z = 4.25$; $p < 0.001$, uncorrected) parieto-occipital cortex in the external condition (minus activations in the internal condition). The figures in the upper and lower left represent projection images in the sagittal and coronal planes, respectively. The figure in the upper right depicts the spatial distribution of the activation superimposed onto the co-registered averaged brain MRI from 10 healthy male subjects. The figure in the lower right demonstrates blood flow at the point of maximum activation in the left parieto-occipital cortex for both conditions (internal: 1–6; external: 7–12).

Discussion

These data indicate that selective attention to emotional experience activates the anterior cingulate cortex. The anterior cingulate has a known role in both motor attention and response selection.[7] However, these aspects of attention do not provide a sufficient explanation for the current findings. First, the area of anterior cingulate cortex activated in this study is anterior to that typically associated with attention.[8,9] Second, the response time data indicate that the internal and external attention tasks were comparable in attentional demands. Third, in our control condition, selective attention to the location of the scene was associated with bilateral activation in a region known to participate in the evaluation of spatial relationships.[10,11] Our interpretation of the data is that activation in anterior cingulate is related to the emotional processing and representation emphasized in the internal condition. This interpretation is consistent with Papez' suggestion that this region is "the seat of emotional experience."[12]

The maximum activation during the internal focus condition is localized to the cingulate sulcus, the anatomical border between the anterior cingulate (BA32) and the medial prefrontal cortex (BA9). While this area (BA32) can also be described as paracingulate cortex we followed the conventions of Vogt and colleagues in calling this region cingulate cortex.[13] Vogt *et al.*[13] have determined that the cytoarchitectonic characteristics of pregenual Brodmann's area 32 is transitional from anterior cingulate to medial prefrontal cortex. Similarly, Barbas and Pandya[14] have described a gradual change, from caudal to rostral direction, in laminar characteristics from limbic periallocortex toward isocortical areas in medial prefrontal cortex. This suggests that a rigid distinction between this portion of the anterior cingulate cortex and the medial prefrontal cortex is misleading. Given that the observed activation extended into both anterior cingulate and medial

prefrontal cortex it most likely reflects processes characteristic of these two regions.

Activation of right anterior temporal region, medial prefrontal cortex and anterior cingulate cortex has been reported during retrieval of affect-laden autobiographical memories.[15] We interpret our activation as reflecting the likelihood that evaluation of the emotional significance of a novel stimulus necessarily involves reference to previous experience. The activation of the insula is also of interest in that this region participates in visceral sensation, autonomic regulation[16] and emotion.[17] The current finding suggests that interoceptive cues are preferentially amplified during selective attention to emotional experience.

The picture sets were invariant across the two study conditions with the sole difference being instruction to subjects and task response. Thus the contrasted conditions (internal and external foci) share implicit aspects of emotional processing and possibly early explicit emotional responses. Structures known to be involved in emotional processing such as the amygdala[18] may well have been activated in both conditions and are consequently not evident in the current study. In this regard it is striking that the condition requiring a spatial analysis of the presented scenes, and where the emotional content was not the focus, activated regions known to be involved in spatial aspects of attention.[10,11,19] As the content of the visual input was balanced across conditions this indicates that the differential response we observe in the anterior cingulate is susceptible to a modulatory attentional effect.

Activations of anterior cingulate cortex, involving both BA24 and BA32, have been observed in functional neuroimaging studies that span a wide range of cognitive contexts including selective attention and memory (for review see Ref. 20). Modulation of pain-related neural activity in anterior cingulate cortex (BA32) as a function of self-reported affective unpleasantness has recently been described.[21] Furthermore, depressed patients show significant activity decreases in anterior cingulate cortex suggesting that this structure plays a fundamental role in the regulation of mood.[22] The activation we observed when subjects attended to their own internal emotional responses, is more anterior to the foci reported in these studies which is suggestive of a distinct functional role.

A hypothesis that this region of anterior cingulate/medial prefrontal cortex is crucially implicated in the representation of emotional experience is supported by neuropsychological studies. Lesions of the anterior cingulate cortex produce akinetic mutism, a condition associated with blunting of emotional experience.[23] As noted above, patients with lesions in ventromedial prefrontal cortex have deficits in the capacity to experience emotion and to utilize that information in decision making.[4] Follow-up studies of patients with prefrontal leucotomies reveal that they are unable to anticipate the emotional consequences of their actions to self and others, leading to behaviour which at times is socially inappropriate.[24] Thus, neuropsychological and functional imaging data provide converging evidence that the anterior cingulate cortex/medial prefrontal cortex are key structures in the representation of emotional experience. This contention is also in line with other evidence that related medial prefrontal structures are involved in representing other aspects of states of mind.[25]

Conclusion

This study indicates that the anterior cingulate cortex and medial prefrontal cortex play a specific role in representing subjective emotional responses. Other areas which participate in this function include the right temporal pole, insula and ventral cingulate cortex. This region of the anterior cingulate cortex is close to an area of medial prefrontal cortex which has been shown to play a role in representing the mental states of others.[25]

References

1. LeDoux JE. *The Emotional Brain*. New York: Simon and Shuster, 1996.
2. Damasio AR. *Descartes' Error: Emotion, Reason and the Human Brain*. New York: G.P. Putnam, 1994.
3. Fink GR, Halligan PW, Marshall JC *et al. Nature* **382**, 626–628 (1996).
4. Corbetta M, Miezen FM, Dobmeyer S *et al. Science* **248**, 1556–1559 (1990).
5. Lang PJ, Bradley MM and Cuthbert BN. *The International Affective Picture System (IAPS): Photographic Slides*. University of Florida: The Center for Research in Psychophysiology, 1995.
6. Friston KJ, Holmes AP, Worsley KJ *et al. Hum Brain Mapp* **2**, 189–210 (1995).
7. Posner MI. Attention in cognitive neuroscience: an overview. In: Gazzaniga MS, ed. *The Cognitive Neurosciences*. London: MIT Press, 1995: 615–624.
8. Paus T, Petrides M, Evans AC *et al. J Neurophysiol* **70**, 453–469 (1993).
9. Petersen SE, Fox PT, Posner MI *et al. Nature* **331**, 585–534 (1988).
10. Corbetta M, Miezin FM, Shulman GL and Petersen SE. *J Neurosci.* **13**, 1202–1226 (1993).
11. Fink GR, Dolan RJ, Halligan PN *et al. Brain* 1997, in press.
12. Papez JW. *Arch Neurol Psych* **38**, 725–734 (1937).
13. Vogt BA, Nimchinsky EA, Vogt LT *et al. J Comp Neurol* **359**, 490–506 (1995).
14. Barbas H and Pandya DN. *J Comp Neurol* **236**, 353–375, 1989.
15. Fink GR, Markowitsch HJ, Reinkemeier M *et al. J Neurosci* **16**, 4275–4282 (1996).
16. Augustine JR. *Brain Res Rev* **22**, 229–244 (1996).
17. Lane RD, Reiman EM, Ahern G *et al. Am J Psychiatry* **154**, 926–933.
18. Morris J, Frith CD, Perrett D *et al. Nature* **383**, 812–815 (1996).
19. Heilman KM, Pandya DN and Geschwind N. *Trans Am Neurol Assoc* **95**, 259–261 (1970).
20. Cabeza R and Nyberg L. *J Cogn Neurosci* **9**, 1–26 (1997).
21. Rainville P, Duncan GH, Price DD *et al. Science* **277**, 968–971 (1997).
22. Bench CJ, Friston KJ, Brown RG *et al. Psychol Med* **22**, 607–615 (1993).
23. Damasio AR and Van Hoesen GW. In: Heilman KM and Satx P, eds. *Neuropsychology of Human Emotion*. New York: Guilford Press 1983: 85–110.
24. Hoffman JL. *New Engl J Med* **241**, 233–236 (1949).
25. Happe F, Ehlers S, Fletcher P *et al. NeuroReport* **8**, 197–201 (1996).

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