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LOCALISED FACE PROCESSING BY THE HUMAN PREFRONTAL CORTEX: FACE-SELECTIVE INTRACEREBRAL POTENTIALS AND POST-LESION DEFICITS

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The patient described in the companion paper by Vignal, Chauvel, and Halgren (this issue) was studied with event related potentials (ERPs) recorded directly within the brain substance, as well as with neuropsychological tests before and after therapeutic cortectomy. Large ERPs were evoked in the prefrontal cortex to faces, as compared to sensory controls and words. The largest such ERPs were highly localised to the same right anterior inferior prefrontal site where direct electrical stimulation resulted in face hallucinations. Face-selective ERPs were also evoked in the right prefrontal sites that had shown projected activity during face hallucinations, and near the right anterior superior temporal sulcus. Selective responses began about 150msec after face onset. Words, but not faces or sensory controls, evoked large ERPs in distinct locations, mainly in the left hemisphere. A successful surgical therapy was performed by removing the cortex surrounding the right prefrontal site where face-selective responses were recorded and where face hallucinations were evoked by stimulation. This cortectomy resulted in a severe deficit in the recognition of emotional facial expressions, especially fear. No change was noted, however, in the recall of emotional words, or other tasks. The current results provide strong support for the early, specific, and sustained involvement of a multi-focal network in the right inferior fronto-temporal cortex in face-processing.

INTRODUCTION

In the companion paper by Vignal, Chauvel and Halgren, (this issue), a patient was described who had received implantation of electrodes in his left and right prefrontal, premotor, and anterior temporal cortices. Direct electrical stimulation of the right ventrolateral prefrontal cortex (VLPFC)

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resulted in face-related hallucinations and illusions. This result was felt to support a contribution of right VLPFC to face processing, and is consistent with models wherein VLPFC activates representations in working or declarative memories (Goldman-Rakic, 1995b; Ungerleider, Courtney, & Haxby, 1998).

However, there are some difficulties in interpreting stimulation-evoked hallucinations and illusions. First, although the focality of the response is supported by the fact that face hallucinations were evoked only at one location among the many stimulated, the localisation of the critical area is confounded by the possible spread of the afterdischarge evoked by stimulation to distant sites that may not have been recorded. In addition, the fact that VLPFC stimulation can evoke face hallucinations provides little information regarding the nature of the contribution of the VLPFC to *normal* face processing.

In this paper, the same patient was studied with two additional techniques. One method involved recording of local field-potentials evoked by faces, in comparison to words and sensory controls. Such data can reveal the timing and location of cognitive activity with great precision. Unlike scalp EEG, the neural generators of EEG recorded with electrodes directly implanted in the brain substance (for identification of the seizure focus) can be localised with certainty if the potential shows large gradients over short distances in all directions. Unlike PET/fMRI, which have temporal resolutions greater than a second, intracranial EEG has temporal resolution equal to the sampling rate (about 5msec in this case). The other method entailed testing the same patient before and after the involved cortex was removed surgically. Such data can provide more direct evidence as to what the essential contribution of the area to normal behaviour may be.

Using these methods, the current study obtains results that reinforce the conclusions of the companion paper: A network of small regions in the right ventral prefrontal, temporal, and occipito-temporal cortices appears to be specifically involved in face processing.

EXPERIMENT 1: INTRACEREBRAL EVENT-RELATED POTENTIAL (ERP) RECORDINGS DURING COGNITIVE TASKS

Methods

Intracerebral recordings in response to faces, words, and control stimuli were obtained while monitoring for spontaneous seizures from the patient described in the companion paper (Vignal et al., this issue), in a session that took place prior to the clinical stimulations described therein. During a visual face/pattern task, the patient was asked to attentively observe images presented on a videomonitor (stimulus duration: 240msec, interstimulus interval: 1066msec). The images were superimposed on a grey background and they consisted of photographs of human faces and their sensory controls (the same faces after being distorted into nonrecognisable patterns by randomly moving the pixels but with similar surface texture, intensity, and general shape—see Fig. 1). In addition, the following images were presented in the same oval-shaped frame: colour and grey contours, entire frames filled with different colours (equated for intensity and brightness), and white frames. Since no reliable differences were noted in the current study between colour and grey meaningless contours, nor between colour and white blank frames, they were averaged together. During a lexical decision task, the patient was asked to press a button to real words (120 items, 3 or 4 letters long, average lexical frequency equal to 9493 according to the word count of Content, Mousty, & Radeau, 1990), mixed randomly among an equal number of pronounceable nonwords matched for length. Stimuli were presented for 300msec with 3600msec interstimulus interval (onset-to-onset).

Field potentials were recorded from 105 contacts (2mm in length, separated by 3.5mm centre-to-centre) on the following probes implanted in the right: G, O, P, A and left hemisphere: G', O' A' [see Fig. 1 in Vignal et al., this issue, for electrode localisation]. The recordings were referenced to the tip of the nose and digitised every 4msec (face/contour task) or 6msec (lexical decision task) at 12-bit

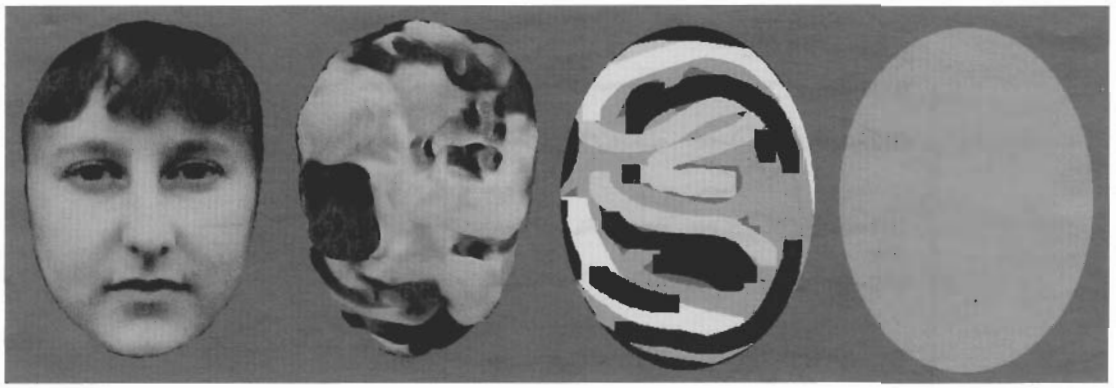

Fig. 1. *Examples of stimuli used.*

accuracy beginning 108msec before stimulus onset. The average ERPs were constructed from trials that were free of eye movements or epileptiform spikes.

Results

ERPs obtained during sensory-cognitive tasks from 19-right hemisphere and 19-left hemisphere sites are presented in Figs. 2 and 3, respectively. For each site, potentials evoked by faces (averaged waveform based on 47 trials) vs. nonfaces (57 trials) are shown superimposed in the first column; to contours (101 trials) vs. blank ovals (103 trials) in the centre column; and to words (112 trials) vs. nonwords (113 trials) in the right column. An oscillating potential was preferentially evoked by faces (thick line in the left column). The waveform had four phases of alternating polarity (positive-negative-positive-negative) with approximate latencies from stimulus onset to peak of 180, 240, 330, and 430msec. This waveform was widely distributed bilaterally within the anterior prefrontal area (contacts on probes G, O, P, G', and O'). The oscillating potential was also evoked by nonfaces, but with a much smaller amplitude (Figs. 2 and 3, left columns, thin lines), and by contours and blanks (Figs. 2 and 3, centre columns). Words and nonwords evoked potentials from these contacts differing in distribution, latency and waveform from those evoked by faces or sensory controls (Figs. 2 and 3, right columns).

A diffusely distributed potential is indicative of a diffusely distributed generator, or of a distant source. In contrast, steep *gradients* in the locally recorded potential imply a local neural generator. Such gradients in face-selective potentials were most prominent in G11, O5, and O9 (all in the right VLPFC), and A9 (in the right anterior temporal lobe). In G11, O5, and A9, the gradient appeared to be produced by the superposition of a sustained potential beginning before 200msec and lasting at least 500msec. In all cases, the sustained potential is absent in the immediately adjacent contacts medially and laterally. Since adjacent contacts are separated by only 1.5mm, this suggests local generation by a small area.

Statistical comparisons of the face vs. nonface average waveforms were performed across trials on the mean amplitudes within 200 to 600msec latency window. These average amplitudes were measured for the four contacts revealing face-selective ERPs (G11, O9, O5, and A9; left column of Fig. 2), as well as their immediately adjacent contacts that were paired during bipolar electrical stimulation reported in the companion paper. Univariate ANOVA revealed a significant interaction between the face/nonface factor and the amplitudes measured for the four pairs of channels, [$F(7,693) = 15.7$, $P < .0001$]. For each of the eight channels, pairwise comparisons between the face and nonface conditions were performed. Tukey post hoc procedure (Woodward, Bonett, & Brecht,

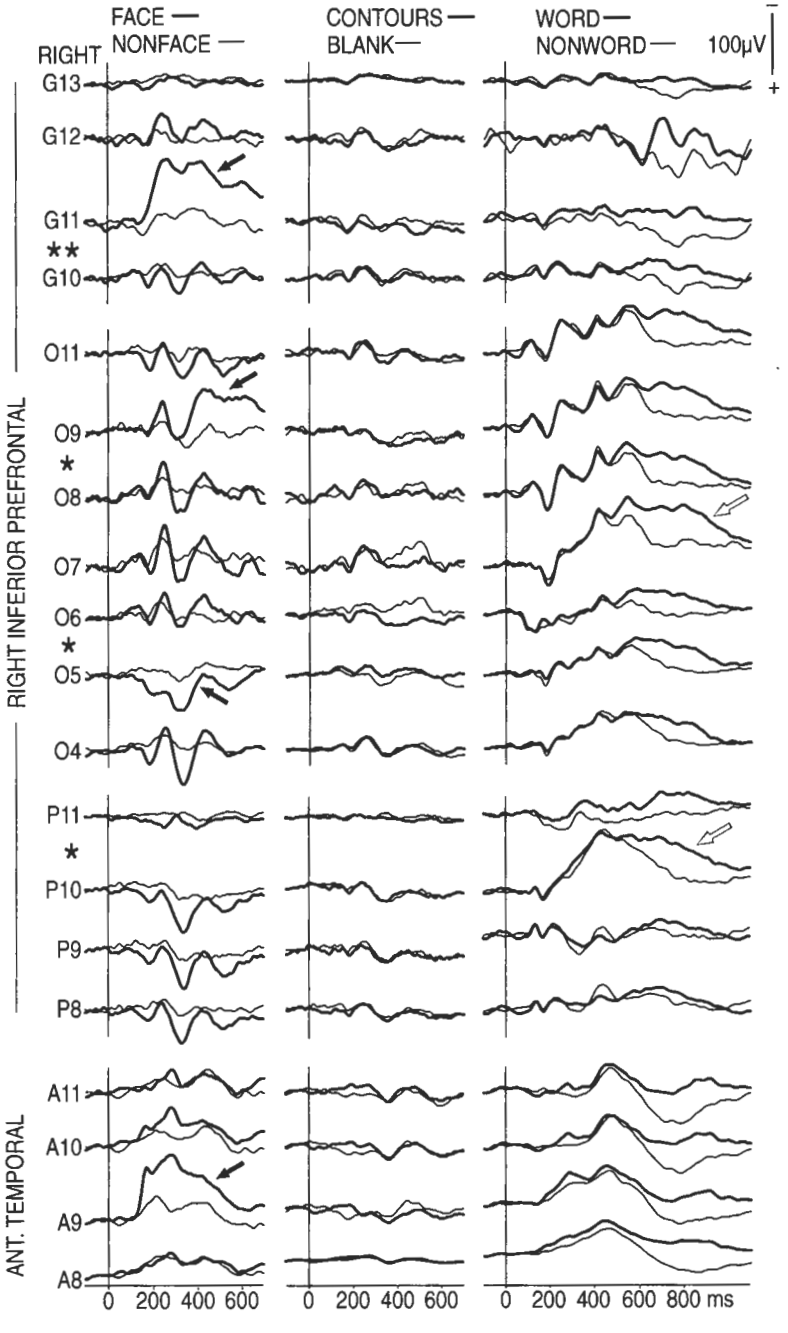

Fig. 2. *Potentials evoked in the right prefrontal and perirhinal cortices to faces. Large face-selective potentials (filled arrows) are evoke the inferior frontal gyrus in the same contact (G11) where stimulation subsequently evoked hallucinations of faces (**), as well as the sit that showed projected activity during the face hallucinations (*: O5–6, O8–9, P10–11). A smaller triphasic face-selective response is no diffusely in other prefrontal sites. A large face-selective response is also noted in a contact located just superior to the fundus of the inferio temporal sulcus (A9). In general, the focal responses are not seen in the immediately adjacent probes, separated by only 1.5mm. Details o electrode locations are shown in Fig. 1 of the companion paper (Vignal et al., this issue).*

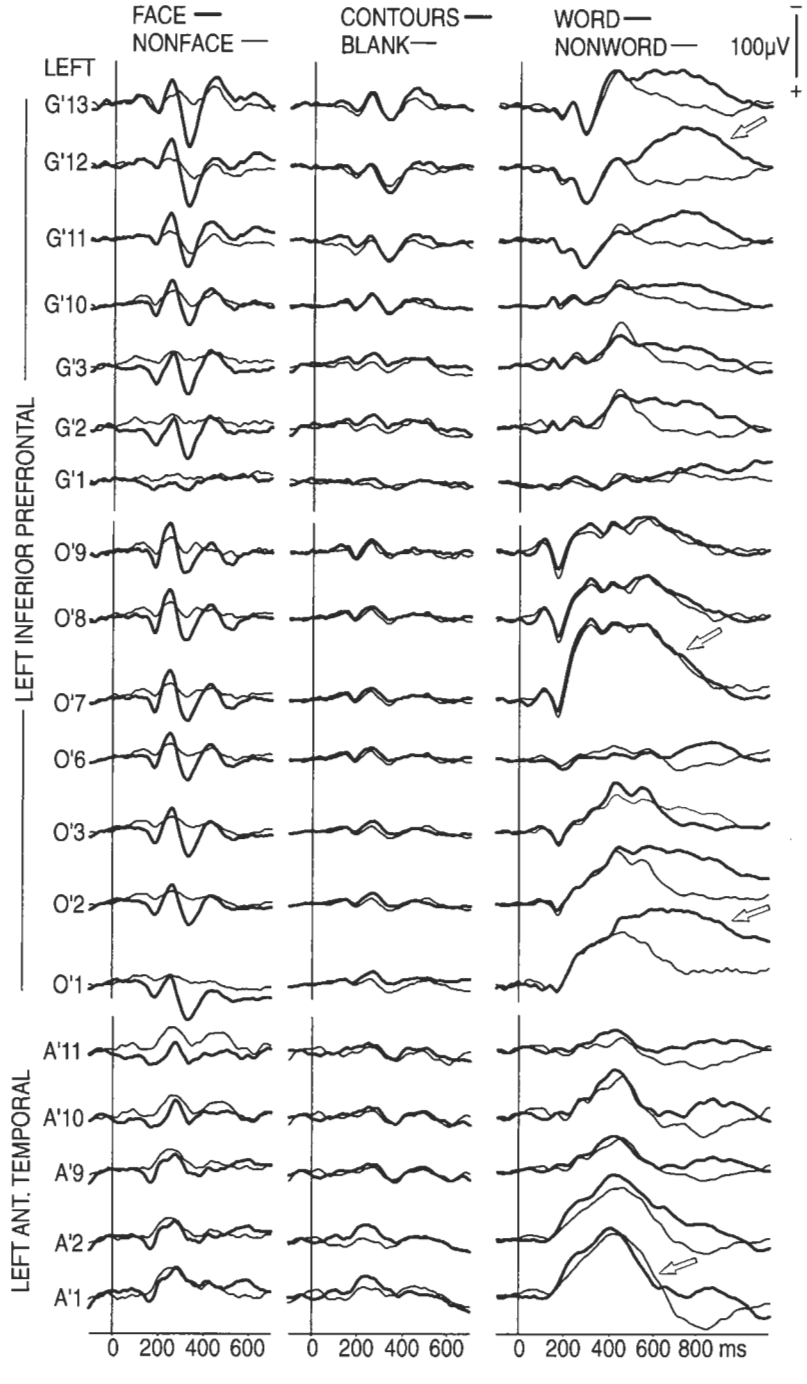

Fig. 3. *Potentials evoked in the left prefrontal and perirhinal cortices to words. Large word-selective potentials (open arrows) are recorded in several left inferior prefrontal sites (G'13, O'7, O'1), as well as the left amygdala (A'1, probably generated in periamygdaloid or perirhinal cortex). Comparison with Fig. 2 demonstrates a double-dissociation in the material-specificity of ERPs in the left and right ventral frontotemporal cortices, with large face-selective responses in the right hemisphere, and large word-selective responses in the left.*

1990) was utilised as a protection against inflated probability values and the corrected *P*-values are reported throughout. Large differences between the ERPs to faces vs. nonfaces that can be observed in Fig. 2, left column, (marked with filled arrows), turned out to be statistically significant for the four contacts [G11: $F(1,99) = 38.6$, $P < .001$; O9: $F(1,99) = 17.6$, $P < .05$; O5: $F(1,99) = 11.3$, $P < .05$; A9: $F(1,99) = 12.3$, $P < .05$]. These effects were highly focal as none of the differences observed at immediately adjacent contacts approached significance (*F* values ranging from 0.05 to 2.7).

A closer examination of latencies suggests that the anterior temporal response leads that in the VLPFC. Univariate ANOVAs were performed across trials for the average amplitudes measured at four 20msec latency windows spanning 120 to 200msec post stimulus for the contacts A9 and G11 and the simple comparisons protected with Tukey procedure. The response in A9 begins at about 124msec after stimulus onset, and its first peak appears at 168msec [face vs. nonface difference significant within 160–180msec latency window, $F(1,103) = 21.8$, $P < .01$, with a strong trend within 140–160msec, $F(1,103) = 8.4$, $P < .1$], with a second broader peak at 280msec. In contrast, the G11 response begins at about 152msec,with peaks at 244 and 268msec. The face vs. nonface difference does not attain reliable significance until the 180–200msec latency window, [$F(1,103) = 9.9$, $P < .05$]. In O9, the sustained potential began at about 300msec, peaked at 430msec, and lasted at least 400msec. These responses were completely absent to sensory controls and verbal stimuli.

Smaller oscillating potentials were observed to faces in P11 and G'1, as compared to adjacent sites. In both cases, smaller potentials were also seen in the same contacts to other stimuli (contours, blanks, words, and nonwords), suggesting a general decrease in amplitude due to biophysical factors, such as possibly being external to the cortex laterally (P11) or medially (G'1).

As has been detailed in the companion paper (Vignal et al., this issue), the patient reported seeing faces during direct electrical stimulation between contacts G11–12 in the right inferior frontal gyrus. These stimulations evoked a propagated spike/slow-wave discharge recorded between contacts O5–6, and propagated slow-waves between contacts O8–9 (shown in Figs. 2 and 3 of that paper). Thus, the clear face-specific focal ERP in the inferior prefrontal area was seen only in the contacts that were directly stimulated (electrode G), or where prominent propagated activity was evoked (electrode O).

The focal face-selective activity described earlier was seen only in the right hemisphere. In contrast, the large and focal potentials elicited by verbal stimuli were bilateral, but predominantly in the left hemisphere (Figs. 2 and 3, right columns). VLPFC sites with large amplitude and relatively steep voltage gradients to words and nonwords include O7 and P10 in the right, and G'12, O'7, and O'1 on the left. Large amplitude potentials to words without steep gradients were recorded in the left amygdala (A'1). None of these contacts showed any large or focal activity to faces or sensory controls. In the same contacts, face or contour visual stimuli evoked nonfocal distributed bimodal potential as described earlier. Overall, the meaningless contours evoked very small potentials bilaterally without indications of local generation.

In summary, focal face-selective activation was found in three locations in the right VLPFC, and in a site in the right anterior inferior temporal sulcus. The VLPFC locations corresponded to the precise locations where electrical stimulation either provoked hallucinations of faces, or where prominent propagated activity was recorded during the face hallucinations. A double-dissociation was demonstrated between these sites showing focal ERPs to faces, and the predominantly left fronto-temporal sites showing word-selective ERPs.

EXPERIMENT 2: BEHAVIOURAL TESTS BEFORE AND AFTER CORTECTOMY

Methods

As the final step in the surgical treatment of his seizures, the patient underwent a selective resection of the right prefrontal/orbital cortex. The cortectomy

encompassed the right orbitofrontal and opercular area including the locations of electrodes O, P, and G, and extending to electrode F (see Fig. 1 in Vignal et al., this issue). Ventromedially, the cortectomy extended to (but did not include) the optic chiasm and branch A1 of the anterior cerebral artery, uncovering the corpus callosum at the medial end of the G electrode. As is often the case in frontal lobe epilepsy, no pathology was found in the surgical specimen. The patient remains seizure-free more than 4 years after the operation.

The patient was tested before and after the surgery with two equivalent versions of the following behavioural tests: Recognition of Facial Affect (Ekman & Friesen, 1976) and Recall of Emotional Words (adapted from Lieury, Boissiere, Jamet, & Marinkovic, 1997). The tests were administered 2½ months (Recognition of Facial Affect) or 2 days (Recall of Emotional Words) prior and 14 days after the selective cortectomy. In addition to these two testing occasions, the patient was retested with the Facial Affect task 3 years after surgery. The patient's performance on these behavioural tests is compared to the results of normal controls ($N = 5$, 3 females) that were matched in age, educational level and socioeconomic status. The patient was treated with comparable levels of antiepileptic medications on all three testing occasions.

Recognition of Facial Affect (Ekman & Friesen, 1976). On each of the two testing occasions (before and after surgery), and after familiarisation with the task and the list of emotions, the patient was presented with a randomised sequence of 55 photographic slides of 7 facial expressions (joy, sadness, fear, surprise, disgust, anger, and no emotion). The two versions of the test each contain from 7 to 10 pictures from each of the facial expression categories. After observing the picture for 2 seconds, the patient was prompted to give an answer by choosing the best fitting response among the 7 expressions.

Recall of Emotional Words. On each testing occasion, the patient was shown six lists of words, each consisting of nine items: three rated as emotionally positive (e.g. romance), three as negative (e.g. suicide), and three as neutral (e.g. scenario) in a counterbalanced order. The words were presented on a computer screen for 240msec with 2700msec ISI. The patient was instructed to memorise the words in the list and was subsequently asked to recall as many words as possible after each list. The words were equated for their length and frequency based on the French language norms (Content et al., 1990). In addition, the emotional word categories were balanced for their valence as determined in a previously conducted study (Lieury et al., 1997) in which 239 independent judges rated their emotional characteristics.

General Neuropsychological Tests. A short neuropsychological battery was administered before and then 15 days after the surgery. This battery included naming (50 images of objects from Imagier Père Castor, France), verbal fluency (letters, furniture and animals, from the Batterie de Fluidité Verbale, 1989; Cardebat & Doyon, 1990), reading and writing from the Boston Diagnostic Aphasia Examination (Mazaux & Orgogozo, 1981), nonsemantic language comprehension (tested with the Token Test; DeRenzi, 1979), and arithmetic (from the Wechsler Adult Intelligence Scale: Wechsler, 1989). Verbal recent memory including immediate and delayed free recall of 12 words, as well as nonverbal recent memory, including immediate and delayed free recall of 12 abstract designs, were tested with the BEM 144: Batterie D'Efficience Mnésique (Signoret, 1991). The Test of Facial Recognition (Benton & Van Allen, 1968) was only administered 3 years after surgery.

Results

Recognition of Facial Affect. As can be observed in Fig. 4, the patient's performance before the surgery was somewhat impaired, but generally within the normal range (about 8% decrease in correct responses as compared to the controls, z-score = -0.6). However, a much larger deficit in the patient's ability to recognise emotional expressions was seen 14 days after the frontal cortical resection (overall decrease of about 24%, z-score = -1.75). Particularly striking was the patient's inability to recognize fear (0% correct), as all of the eight

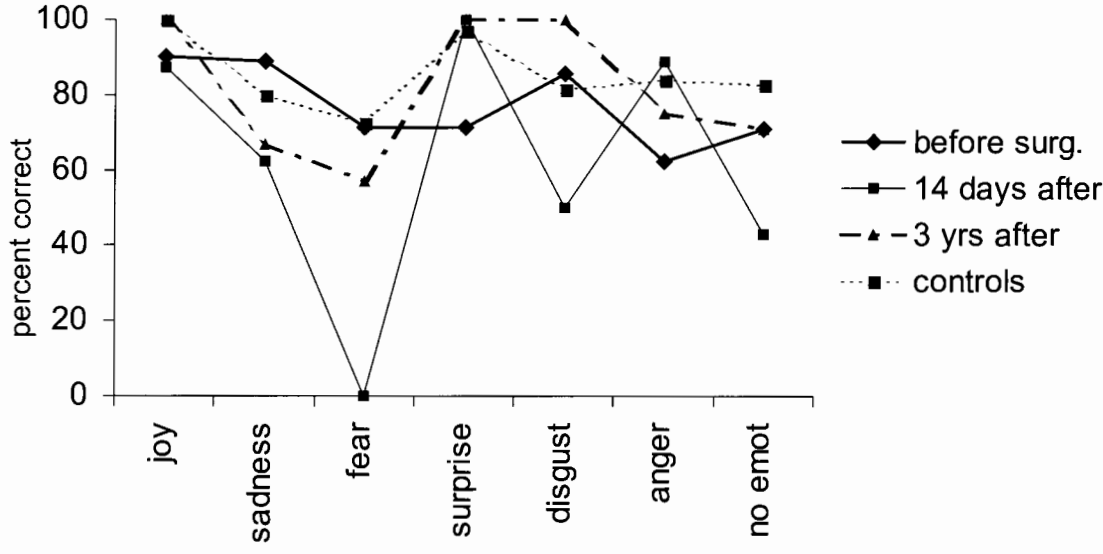

Fig. 4. *Behavioural recognition of emotional face expressions before and after therapeutic removal of right inferior prefrontal cortex. Performance is at near-normal levels before surgery to remove the epileptogenic focus. When retested 14 days later, the emotion of fear was not recognised on any of the eight presented faces with fearful expressions. Substantial recovery is apparent at testing 3 years after surgery.*

presented fear expressions were attributed to surprise. Recognition of disgust was at 50%, with 37.5% of the disgust expressions also mistaken for surprise. Three years later, there was a significant improvement in the patient's performance on this task (overall z-score = − 0.35): disgust was recognised 100% correctly. However, the residual deficit in recognition of fear was still present: The expression of fear was correctly recognised 57% of the time, and was misattributed to surprise on 28.5% of the trials. One may note that in normal controls, the most common misattribution of fearful facial expressions is also as surprise (Ekman & Friesen, 1976). Recognition of the expression of sadness did not improve significantly 3 years after the surgery: 63% vs. 67% correct responses. The patient did not report being aware of any problems in emotional processing in general, nor in recognising emotional expressions in particular. Upon completion of the post-surgery testing session, the patient was queried about the apparent absence of the reported expressions of fear. Similar to other patients with frontal lesions (Marinkovic, Trebon, Halgren, & Chauvel, 1997), the patient commented that such expressions were shown "the last time, but not today."

Recall of Emotional Words. When compared to the normal controls, the patient's performance on this task was overall low before surgery (z-score = − 1.07). However, it improved slightly after surgery (z-score = − 0.6). This recall task was followed by a recognition task, wherein the 54 words used in the recall part were presented again, semirandomly mixed among 27 new (9 words in each emotional category), previously unseen words. The patient was instructed to press one of two keys for each repeated or new word with no emphasis on speed. The results of the recognition task are comparable to those from the recall portion. The patient's correct recognition rate increased by 8% and his error rate by 3% postoperatively. In addition, no significant psychomotor slowing was observed after the surgery as the reaction times increased only slightly, from 1346msec before to 1363msec after surgery. In summary, no change in recall or recognition memory for emotional words was observed after surgery.

General Neuropsychological Performance (Table 1). Naming, verbal fluency, reading, writing, and arithmetic, as well as verbal and nonverbal recent

Table 1. *Neuropsychological performance*

Tests:	*Before Surgery*	*15 days after Surgery*	*6 months after Surgery*
Naming (50 items)	98%	100%	100%
Fluency (animals, furniture) 60"	21	18	18
Fluency (letters b, s) 60"	26	24	23
Token test (max 156)	152	146	147
Reading: BDAE (max 10)	10	10	10
Writing: BDAE (max 12)	10	10	12
Arithmetic: WAIS (max 4)	3	4	4
Verbal Recent Memory: BEM144			
Immediate recall (max 12)	11	11.5	11
Delayed recall, 10'	11	11	12
Nonverbal recent memory: BEM144			
Immediate recall (max 12)	9	11	11
Delayed recall	11	11	12

memory, were normal before surgery, and unchanged when tested 15 days and 6 months after the surgery. The only possible exception to this pattern of normal and unchanged performance was a low-normal presurgical score on the Token Test, which deteriorated slightly after the surgery. Taken within the context of the other results, little significance can be ascribed to this finding. Importantly, performance on the Test of Facial Recognition was normal when tested 3 years after surgery (score on the long form of 43, normal range 41–54).

DISCUSSION

In this and the companion paper (Vignal et al., this issue), three lines of converging evidence are presented for an area related to faces in the right VLPFC of a single patient. Electrical stimulation of a single location resulted in hallucinations of faces. Large focal face-selective potentials were recorded from the same location and from two other VLPFC locations where the stimulation had resulted in projected activity. Surgical removal of this area and surrounding tissue led to a profound deficit in recognising certain emotional facial expressions, but no deficit in a variety of verbal tasks, including the recall and recognition of emotion-laden words. Although these observations were made in a patient with epilepsy, there was no indication that any of these responses represented abnormal cortical organisation. Nonetheless, this possibility cannot be eliminated.

Multi-focal Activation to Faces

Two patterns of face-selective potentials were recorded within the prefrontal cortex in the current study, a nonfocal oscillation and a focal sustained ERP. Both patterns have been previously recorded in human frontal cortex, but sustained focal face-selective potentials were limited to the right premotor area (Halgren et al., 1994b). In addition, large sustained focal *word*-selective potentials were recorded in the left VLPFC in that study. Given that the responses in the current study were highly focal, it is likely that Halgren et al. failed to record large sustained focal face-selective potentials in the right VLPFC due to incomplete sampling. Furthermore, the location of most electrodes in that study were somewhat posterior to the VLPFC contacts showing focal face-selective responses in the current study. Finally, since bilateral prefrontal recordings with both words and faces were never obtained in the Halgren et al. study, it was not possible to demonstrate the within-patient double-dissociation between prefrontal areas with focal responses to faces *versus* those responding focally to words, as was done in the current study. The laterality and latencies of these prefrontal face-selective activations are consistent with those found in normal patients using whole-head magnetoencephalography (Marinkovic et al., 1999) and scalp EEG (Marinkovic & Halgren, 1999).

It should be noted that Halgren et al. (1994b) found a number of sites in the VLPFC that produced large focal sustained potentials to both faces *and* words, but not to simple visual or auditory stimuli (Baudena, Heit, Clarke, & Halgren, 1995). Halgren et al. used the same task for words and faces (delayed recognition), while the current study confounded task and material (the face task was "attentively observe" and the word task was lexical decision). Owen (1997) has criticised the activation

evidence for material-specificity in the frontal lobe on just these grounds, asserting that when different materials were presented in different tasks, task rather than material differences could be the source of the different localisations. In the current study, no activation in either hemisphere was observed to the "attentively observe" instructions when contours or randomised faces were presented. Thus, the large responses to faces using the same instructions could not be due simply to the instructions, but some of the specificity could be related to the combination of the task and the stimulus.

In any case, combining the current results with the previous studies of Halgren et al. (1994b), large sustained focal face-selective potentials have been recorded in humans with depth electrodes in the ventrolateral, orbital, and premotor regions of right prefrontal cortex. These localisations are similar to those found for face-specific unit-responses in the macaque, possibly corresponding to ventrolateral (Ó Scalaidhe, Wilson, & Goldman-Rakic, 1997), orbital (Booth, Rolls, Critchley, Browning, & Hernadi, 1998; Ó Scalaidhe et al., 1997), and arcuate sulcal regions of prefrontal cortex (Ó Scalaidhe et al., 1997), respectively.

Although multiple areas contain locations with large focal face-selective responses, most locations within those areas are *not* focally responsive to faces. This suggests that face-selective processing is embodied in a distributed network of focal sites. Some indication of the size of these sites is suggested by the observation that typically no focal activity was recorded by contacts separated by 1.5mm medially or laterally from the active site. Spatial resolution in the anteroposterior or dorsoventral dimensions is limited by the electrode spacing of 15–20mm. In macaques, face-selective unit responses may show a similar pattern. Although such responses are highly localised to specific prefrontal regions, within any given region only a very small proportion of cells (1 to 5%) show face-selectivity (Booth et al., 1998; Ó Scalaidhe et al., 1997). These authors did not comment on whether face-responsive cells are clustered in the prefrontal sites. However, such clustering has been reported in the temporal lobe (Perrett, Hietanen, Oram, & Benson, 1992).

An alternative explanation for the multi-focal pattern of large face-selective responses would be that they are actually generated by all cortex, but fail to propagate due to their particular laminar distribution of sources and sinks (e.g., a tripolar rather than bipolar configuration). In this case, contacts would record the focal signal if and only if they lay in the cortical grey matter. We consider this explanation unlikely for several reasons. First, other contacts on the same electrodes showed large focal sustained responses to words but not to faces. Furthermore, neither a face nor word response was seen in some sites that according to anatomical criteria seemed to be in grey matter.

The most prominent prefrontal sites showing focal sustained face-selective responses were orbital site O5 and VLPFC site G11. The hallucinations evoked by stimulation of G10–11 also evoked spike-wave complexes in O5–6, suggesting that these sites are anatomically-connected parts of the same network. However, stimulation of O5–6 did not evoke face hallucinations, but rather resonating distortions of the physician's voice (Vignal et al., this issue). Vocal intonation is, of course, highly related to facial expression at many levels, suggesting the intriguing possibility that the network identified by these recordings may have a broader role than face-processing, for example the interpretation of communications from conspecifics.

Several studies have found face-selective prefrontal PET or fMRI activation, usually in the right hemisphere (for review see Ungerleider et al., 1998). However, the localisation of this activation across studies has not been highly consistent, nor clearly differentiated from other material. The multi-focal organisation of face-selective areas found in the current study can provide a partial explanation for these results. Given that the focal face-selective areas identified with intracerebral recordings and stimulation in the current papers are probably smaller than the spatial resolution of PET or fMRI, and that the focal face-selective areas are distributed across several regions and intermixed with word-selective areas, it is not surprising that PET/fMRI studies would sometimes fail to find significantly different distributions for different materials.

In sum, the current data from stimulation and recordings, together with earlier studies, suggests that specialisation for face-processing may be multi-focal, i.e. distributed across areas but highly localised within each area. Ojemann (1992) made a similar suggestion based on the pattern of disruption of function with stimulation of the exposed prefrontal cortical surface.

Fronto-temporal Interactions in Face Processing

In addition to the prefrontal activations, the current study found a large focal sustained face-selective potential in the most anterior part of the right middle temporal gyrus. Face-selective unit activity has been recorded in the apparently homologous area in monkeys, the lower bank of the superior temporal sulcus and subjacent cortex (Perrett et al., 1992). Furthermore, also in monkeys, these temporal areas project anatomically to the VLPFC locations where face-selective cells were recorded (Barbas, 1988; Ó Scalaidhe et al., 1997). In addition, the response properties of the face-selective cells in the VLPFC resemble those in the anteroventral temporal lobe (Ó Scalaidhe et al., 1997), as do the VLPFC and anteroventral temporal waveforms recorded in the current study. Finally, as noted later, VLPFC and anteroventral temporal lesions have similar effects on the judgement of facial emotional expressions. Thus, anatomical, physiological, and neuropsychological evidence suggests that these areas may participate in the same functional circuits.

Previous intracranial recordings have identified face-selective waveforms in the right fusiform gyrus (Halgren, Baudena, Heit, Clarke, & Marinkovic, 1994a). The probably homologous area in monkeys (part of TEO or TF: Halgren, Dale, Sereno, Tootell, Marinkovic, & Rosen, 1999), projects to the anterior temporal areas that in turn project to the VLPFC (Barbas, 1988). Like the face-specific response in the anterior temporal lobe reported here, those in the fusiform gyrus generally have a shorter latency to onset and to peak than those in the VLPFC. With intracerebral recordings, Klopp, Halgren, Marinkovic, Nenov, and Chauvel (1999b) found a strong phasic face-selective increase in 40Hz coherence at latency of about 180–200msec between the fusiform gyrus and VLPFC. These responses show a consistent phase lag, with the VLPFC following the fusiform gyrus by about 15msec. These data suggest that the fusiform gyrus may participate in the same functional network with the face-selective anterior temporal and ventral prefrontal sites, and furthermore, at short latencies, the fusiform gyrus may lead the more anterior areas. The fusiform gyrus ERP continues for several hundred milliseconds, and thus is co-active with the prefrontal and anterior temporal sites. However, in the 300–700msec time window, the ventrolateral prefrontal cortex shows a wideband *increase* in power to faces, whereas the fusiform cortex shows a profound *decrease*, suggesting that the prefrontal sites may take a lead role during the later period of re-entrant processing (Klopp, Halgren, Marinkovic, & Nenov, 1999a). This interpretation is consistent with the ability of prefrontal stimulation to inject images of faces into awareness demonstrated in the companion paper (Vignal et al., this issue). In conclusion, the current study provides evidence that face processing involves multiple interacting highly focal locations in both temporal and prefrontal cortices.

Removing the region where focal face-selective responses were recorded produced a profound deficit in recognising the facial expression of fear and, to a lesser degree, impaired recognition of disgust. Recognition of other emotional face expressions appeared to be unchanged. The deficit in recognising fear, while unusually profound in this patient, is also seen in many patients with right prefrontal and/or temporal lesions (Adolphs, Damasio, Tranel, & Damasio, 1996; Marinkovic et al., 1997; Peper & Irle, 1997). A comparably profound deficit was found in a single patient with bilateral amygdala lesions (Adolphs et al., 1995), and amygdala stimulation commonly evokes fear in humans (Halgren, Walter, Cherlow, & Crandall, 1978). Intracerebral (Halgren & Marinkovic, 1995) and scalp ERPs (Marinkovic & Halgren, 1999) also have found evidence for differential responses to emotional facial expressions in both temporal and prefrontal areas. The fact that the

patient in the current study recovered much of his ability to recognise fear when tested 3 years later is consistent with the contribution of multiple areas to this ability.

There appears to be no special requirement of the Recognition of Facial Affect test for working memory, response selection, semantic access, or other "executive functions." Furthermore, any requirement of the test for these faculties would appear to be equivalent across different emotional expressions. Thus, it is difficult to reconcile this result with theories that subsume all prefrontal functions under these rubrics. On the other hand, prefrontal lesions clearly produce deficits in many nonemotional tasks. For example, right prefrontal lesions may produce false recognition of unfamiliar faces (Rapcsak, Polster, Glisky, & Comer, 1996), as well as impaired recall (but not recognition) of famous faces (Shimamura, 1995). It thus appears that the prefrontal cortex may embody several distinct functions, even for face processing.

Implications for the Functional Organisation of Prefrontal Cortex

The current results strongly support the existence of material-specific processing in localised prefrontal areas, and thus are generally consistent with models of prefrontal function that posit such localisation, with processing of spatial material more dorsal, and that of object identity more ventral (for reviews see Goldman-Rakic, 1995a; Ungerleider et al., 1998). Recently, alternative models for prefrontal function have been proposed, in which the dorsal/ventral specialisation in prefrontal cortex is based on the nature of processing rather than the material that it is performed upon (Owen, 1997; Petrides, 1995). Ventral activation is thought to occur whenever working memory processes are required by the task, and more dorsal prefrontal cortex becomes involved when the task requires more complex executive processes, such as holding more information simultaneously in mind, needing simultaneously to process information and hold it in mind, and/or needing to decide amongst multiple response alternatives. Although the deficit in our patient did not appear to result from an impairment in any of these functions, the distinct effects of stimulating different focal face-selective locations suggests that they may also have a functional specialisation based on processing requirements. The totality of our results are best accounted for in a model that posits multi-focal prefrontal and posterior areas specialised for both material and processing.

REFERENCES

Adolphs, R., Damasio, H., Tranel, D., & Damasio, A. R. (1996). Cortical systems for the recognition of emotion in facial expressions. *Journal of Neuroscience, 16*(23), 7678–7687.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. R. (1995). Fear and the human amygdala. *Journal of Neuroscience, 15(9)*, 5879-5891.

Barbas, H. (1988). Anatomic organization of basoventral and mediodorsal visual recipient prefrontal regions in the Rhesus monkey. *Journal of Comparative Neurology, 276*, 313–342.

Batterie de Fluidité Verbale. (1989). Paris: Les Editions du Centre de Psychologie Appliquée.

Baudena, P., Heit, G., Clarke, J.M., & Halgren, E. (1995). Intracerebral potentials to rare target and distractor auditory and visual stimuli: 3. Frontal cortex. *Electroencephalography and Clinical Neurophysiology, 94*, 251–264.

Benton, A.L., & Van Allen, M.W. (1968). Impairment in facial recognition in patients with cerebral disease. *Cortex, 4*, 344–358.

Booth, M.C.A., Rolls, E.T., Critchley, H.D., Browning, A.S., & Hernadi, I. (1998). Face-sensitive neurons in the primate orbitofrontal cortex. *Neuroscience Abstracts, 24*, 898.

Content, A., Mousty, P., & Radeau, M. (1990). Brulex: Une base de données lexicales informatisées pour le français écrit et parlé. *L'Année Psychologique, 90*, 551–566.

DeRenzi, E. (1979). A shortened version of the Token Test. In F. Boller & M. Dennis (Eds.), *Auditory comprehension: Clinical and experimental studies with the Token Test*. New York: Academic Press.

Ekman, P., & Friesen, W.V. (1976). *Pictures of facial affect*. Palo Alto, CA: Consulting Psychologists Press.

Goldman-Rakic, P.S. (1995a). Architecture of the prefrontal cortex and the central executive. *Annals of the New York Academy of Sciences, 769*, 71–83.

Goldman-Rakic, P.S. (1995b). Cellular basis of working memory. *Neuron, 14*, 477–485.

Halgren, E., Baudena, P., Heit, G., Clarke, J.M., & Marinkovic, K. (1994a). Spatio-temporal stages in face and word processing. 1. Depth-recorded potentials in the human occipital, temporal and parietal lobes. *Journal of Physiology (Paris), 88*, 1–50.

Halgren, E., Baudena, P., Heit, G., Clarke, J.M., Marinkovic, K., & Chauvel, P. (1994b). Spatio-temporal stages in face and word processing. 2. Depth-recorded potentials in the human frontal and Rolandic cortices. *Journal of Physiology (Paris), 88*, 51–80.

Halgren, E., & Marinkovic, K. (1995). Neurophysiological networks integrating human emotions. In M. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 1137–1151). Cambridge, MA: MIT Press.

Halgren, E., Dale, A.M., Sereno, M.I., Tootell, R.B.H., Marinkovic, K., & Rosen, B.R. (1999). Location of human face-selective cortex with respect to retinotopic area. *Human Brain Mapping, 7*, 29–37.

Halgren, E., Walter, R.D., Cherlow, D.G., & Crandall, P.H. (1978). Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala. *Brain, 101*, 83–117.

Klopp, J.C., Halgren, E., Marinkovic, K., & Nenov, V.I. (1999a). Face-selective event-related spectral changes in the human fusiform gyrus. *Clinical Neurophysiology, 110*, 677–683.

Klopp, J.C., Halgren, E., Marinkovic, K., Nenov, V.I., & Chauvel, P. (1999b). *Coherence evidence for early widespread cortical distribution of fusiform face-selective activity.* Manuscript submitted for publication.

Lieury, A., Boissiere, I., Jamet, E., & Marinkovic, K. (1997). Les mots grossiers et sexuels sont-ils mieux mémorisés que des mots neutres? *Le Langage et l'Homme, 32*, 17–37.

Marinkovic, K., & Halgren, E. (1999). Human brain potentials related to the emotional expression, repetition and gender of faces. *Psychobiology, 26*, 348–56.

Marinkovic, K., Halgren, E., Rabbel, C., Dhond, R. P., Paulson, K., Fischl, B., & Dale, A. (1999). Anatomically-constrained MEG activity to emotional expressions of faces. *NeuroImage, 9*, S363.

Marinkovic, K., Trebon, P., Halgren, E., & Chauvel, P. (1997). Effects of temporal and frontal cortectomies on emotional judgements of facial expressions and memory for emotional words. *Society for Neuroscience Abstracts, 23*, 1317.

Mazaux, J.M., & Orgogozo, J.M. (1981). *Boston Diagnostic Aphasia Examination: Echelle française*. Paris: Editions Scientifiques et Psychologiques, EAP.

Ojemann, G. (1992). Localization of language in frontal cortex. In P. Chauvel, A.V. Delgado-Escueta, E. Halgren, & J. Bancaud (Eds.), *Advances in neurology, Vol.57. Frontal lobe seizures and epilepsies* (pp. 361–368). New York: Raven Press.

Ó Scalaidhe, S., Wilson, F.A., & Goldman-Rakic, P.S. (1997). Areal segregation of face-processing neurons in prefrontal cortex. *Science, 278(5340)*, 1135–1138.

Owen, A.M. (1997). The functional organization of working memory processes within human lateral frontal cortex: The contribution of functional neuroimaging. *European Journal of Neuroscience, 9*, 1329–1339.

Peper, M., & Irle, E. (1997). The decoding of emotional concepts in patients with focal cerebral lesions. *Brain and Cognition, 34(3)*, 360–387.

Perrett, D.I., Hietanen, J.K., Oram, M.W., & Benson, P.J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 335*, 23–30.

Petrides, M. (1995). Functional organization of the human frontal cortex for mnemonic processing. Evidence from neuroimaging studies. *Annals of the New York Academy of Sciences, 769*, 85–96.

Rapcsak, S.Z., Polster, M.R., Glisky, M.L., & Comer, J.F. (1996). False recognition of unfamiliar faces following right hemisphere damage: Neuropsychological and anatomical observations. *Cortex, 32*(4), 593–611.

Shimamura, A.P. (1995). Memory and the prefrontal cortex. *Annals of the New York Academy of Sciences, 769*, 151–159.

Signoret, J.L. (1991). *BEM 144: Batterie D'Efficience Mnésique*. Paris: Collection Esprit & Cerveau, Elsevier.

Ungerleider, L.G., Courtney, S.M., & Haxby, J.V. (1998). A neural system for human visual working memory. *Proceedings of the National Academy Sciences USA, 95*(3), 883–890.

Vignal, J.P., Chauvel, P., & Halgren, E. (1999). Localised face processing by the human prefrontal cortex: Stimulation-evoked hallucinations of faces. *Cognitive Neuropsychology, 16*, 281–291.

Wechsler, D. (1989). *Wechsler Adult Intelligence Scale-Revised: Version française*. Paris: Editions du Centre de Psychologie Appliquée.

Woodward, J. A., Bonett, D.G., & Brecht, M.L. (1990). *Introduction to linear models and experimental design*. San Diego, CA: Harcourt Brace Jovanovich.