J Physiology (1994) 88, 51-80

Spatio-temporal stages in face and word processing. 2. Depth-recorded potentials in the human frontal and Rolandic cortices

E Halgren[a,b,c*], P Baudena[b], G Heit[b,d], J. M Clarke[a,e], K Marinkovic[a,f], P Chauvel[a,b]

[a]*INSERM CJF 90-12, Clinique Neurologique, CHRU Pontchaillou, 35033 Rennes;*
[b]*INSERM U 97, Centre Paul Broca, 2ter rue d'Alesia, 75014 Paris, France;*
[c]*Epilepsy Center, West Los Angeles Veterans Affairs MC, and Psychiatry and Brain Research Institute, UCLA, Los Angeles, CA 90024;*
[d]*Department of Neurosurgery, Stanford University, Stanford, CA 94305;*
[e]*Department of Psychology, University of North Texas, Denton, TX 76203;*
[f]*Department of Psychology, UCLA, Stanford, CA 94305, USA*

(Received 15 September 1993; accepted 28 December 1993)

Summary – Evoked potentials (EPs) were recorded directly from 650 frontal and peri-Rolandic sites in 26 subjects during face and/or word recognition, as well as during control tasks (simple auditory and visual discrimination). Electrodes were implanted in order to localize epileptogenic foci resistant to medication, and thus direct their surgical removal. While awaiting spontaneous seizure onset, the patients gave informed consent to perform cognitive tasks during intracerebral EEG recording. The earliest potentials appeared to be related to sensory stimulation, were prominent in lateral prefrontal cortex, and occurred at peak latencies of about 150 and 190 ms. A small triphasic complex beginning slightly later (peak latencies about 200–285–350 ms) appeared to correspond to the scalp N2–P3a–slow wave, associated with non-specific orienting. Multiple components peaking from 280 to 900 ms, and apparently specific to words were occasionally recorded in the left inferior frontal g. pars triangularis (Broca's area). Components peaking at about 430 and 600 ms were recorded in all parts of the prefrontal cortex, but were largest (up to 180 μV) and frequently polarity-inverted in the ventro-lateral prefrontal cortex. These components appeared to represent the N4-P3b, which have been associated with contextual integration and cognitive closure. Finally, a late negativity (650–900 ms) was recorded in precentral and premotor cortices, probably corresponding to a peri-movement readiness potential. In summary, EP components related to early sensory processing were most prominent in lateral prefrontal, to orienting in medial limbic, to word-specific processing in Broca's area, to eognitive integration in ventro-lateral prefrontal, and to response organization in premotor cortices. Thus, multiple frontal areas are involved in multiple stages of face and word processing, in a highly parallel but nonetheless differentiated manner.

N400 / P300 / memory / orbitofrontal / cingulate

Introduction

Although the human frontal lobe is thought to participate in the neural circuits underlying language, memory, attention, and other cognitive functions, its contribution is seldom essential for performance, and thus has been difficult to precisely define. Some hold that the frontal lobe contributes directly to the acquisition and interpretation of information, for example in directing attention to appropriate objects, or in understanding words. Alternatively, the frontal lobe may hold information (acquired from sensations or from memory) in an active state (termed 'primary' or 'working' memory), allowing contextual and strategic control of behavior. Finally, the frontal lobe may be conceived of as contributing mainly to response-selection, as the highest level of the motor (*ie* ventral) half of the neuraxis. These theories differ in their prediction of which part of the stimulus-response sequence involves the frontal lobe: stimulus, delay, or response periods, respectively. Of course, these theories are not mutually exclusive, and the frontal lobe may make different contributions even within the same task, and these contributions may be anatomically differentiated. The current study uses intracerebrally-recorded evoked potentials to localize and characterize the

* Correspondence and reprints to Rennes address

sequence of frontal lobe activation during word and face recognition.

Processing of both words (Morton and Patterson, 1980; Coltheart, 1987; Just and Carpenter, 1987) and faces (Bruce, 1988) appears to pass through formally similar stages: 1) sensory analysis; 2) feature detection; 3) integration of features; 4) individual identification; and 5) integration of the individual into the current context. Thus, the recording of responses to both words and faces allows the identification of areas where they share common processing stages, as well as those where they are distinctively processed.

Lesion and stimulation studies over the last 100 years have identified the dominant posterior inferior frontal gyrus (Broca's area) as essential for expressive language (Penfield and Roberts, 1959; Geschwind, 1965; Benson, 1979; Ojemann, 1990). In contrast, areas that are involved (but not necessary essential) in language may be revealed by PET measurements during cognitive tasks in normal subjects. In particular, in a series of studies Petersen *et al* (1989, 1990) have found that the left inferior frontal cortex is activated to words but not to non-words, even under passive task conditions. Semantic association (verb generation appropriate to the presented noun) activates (in addition to that activated by the motor output task) the anterior cingulate g bilaterally, and the left inferior prefrontal cortex. One also finds left inferior frontal activation to monitoring a list of words for an exemplar from a semantic category, and anterior cingulate g activation to various attention demanding tasks. Wise *et al* (1991), using a slightly different series of tasks, have found similar results with one major exception: reading tasks which accessed word meaning activated Wernicke's area rather than Broca's.

While PET is very useful, its sensitivity may be limited by the indirect and temporally-delayed relation between the physiological process measured by PET (glucose metabolism or bloodflow) and the brain activity that embodies cognitive information-transfer (synaptic current-flows). Furthermore, PET integrates the brain response over a 1.5–35-min period, whereas even complex information processing sequences usually last less than a second. For these reasons, it is important to make complementary measures in order to arrive at a functional view of the areas involved in language processing. In this regard, evoked potentials (EPs) have the advantages of fine temporal resolution and a direct relationship to synaptic current-flows (Halgren *et al*, 1992b). However, the generators of scalp EPs are difficult to localize to particular brain regions (Halgren, 1990b).

The best characterized scalp EP component evoked by words (and other potentially meaningful stimuli) is the N4 (or N400) (Halgren, 1990a). Previous depth recordings have demonstrated their generation in the medial temporal lobe (Smith *et al*, 1986), but the lack of significant change after unilateral temporal lobectomy implies that extratemporal N4 generators also exist (Smith and Halgren, 1989). Whereas earlier potentials are insensitive to sentence context, the N4 is very sensitive to context and in addition is modulated by recent episodic and remote semantic memory as well as lexical information (Halgren and Smith, 1987; Kutas and Van Petten, 1988).

Following the N4, a P3b (late positive component, or P300b), is usually recorded with a widespread scalp topography (Curran *et al*, 1993). Human intracranial recordings have demonstrated a very large P3b generated to words in the hippocampus (Smith *et al*, 1986). The same hippocampal field is activated by rare attended tones (Halgren *et al*, 1980, 1983, 1986; Stapleton and Halgren, 1987; McCarthy *et al*, 1989; Heit *et al*, 1990). Again, the P3 evoked by rare tones is not significantly affected by anterior temporal lobectomy, suggesting the existence of extra-temporal generators (Wood *et al*, 1982; Stapleton *et al*, 1987; Johnson, 1988). Depth recordings of P3s to rare tones have suggested the frontal lobe as a possible candidate for P3 generation outside of the hippocampus (Wood and McCarthy, 1985; Smith *et al*, 1990). However, these P3s have a short latency, and thus resemble a component associated with orienting and termed the P3a, rather than P3b. Similarly, scalp recordings in patients with unilateral pathology localized with CT suggest that the temporo-parietal junction is essential for P3b generation (Knight *et al*, 1989), whereas the frontal lobe plays an essential role in generation of the P3a (Knight, 1984).

In summary, both lesion and stimulation studies indicate that the left posterior inferior frontal lobe is important in reading tasks, and PET-activation studies find that visually-presented words also activate the anterior cingulate g. However, their roles and their sequence of activation are unknown, and it is highly likely that other structures are also activated. Finally, words evoke both early and late EP components, but their generators are largely unknown.

A similar patchwork of involved structures with unknown temporal sequence, and of involved

components with unknown localization, can be found for face processing. Specific deficits in face processing are not generally observed after frontal lesions (Meadows, 1974; Damasio *et al*, 1990; Sergent and Poncet, 1990). However, Sergent *et al* (1992) found metabolic activation in orbitofrontal cortex, especially on the right, to faces that were familiar and needed to be categorized by profession. In addition, unit-firing specific to faces has been recorded in the monkey ventrolateral prefrontal (*ie* lateral orbitofrontal) cortex (Pigarev *et al*, 1979; Skelly *et al*, 1992).

Like words, faces evoke a robust N4 which declines in amplitude when contextual integration is easier or more rapid due to the existence of a declarative memory trace (Smith and Halgren, 1987; Barrett *et al*, 1988), or due to priming by a categorically-related face (Barrett and Rugg, 1989). In the middle latency (150–180 ms post-stimulus onset), faces evoke a large positivity, that appears to be absent to non-face visual stimuli (Srebo, 1985; Jeffreys and Musselwhite, 1987; Botzel and Grüsser, 1989; Seeck and Grüsser, 1992), but with an unknown generator.

Thus, for the processing of faces as well as words, some structures are known to be necessary, and others are thought to be involved, but whether they process the information in parallel or in sequence, and in what order is unknown. This temporal information is inherent in the EP components that are also evoked by words and faces, but their generators are largely unknown. Like scalp EPs, intracerebral depth recorded EPs have a very high temporal resolution (limited by the sampling interval, about 5 ms) and a direct relation to synaptic communication. Unlike scalp EPs, depth EPs also have very high spatial resolution (effectively limited only by electrode size and spacing), and can unambiguously identify EP generators (Mitzforf, 1985; Arezzo *et al*, 1986). For example, if the locally-recorded EP component is much larger than in adjacent structures, and changes amplitude and polarity over short distances, then that component is without question generated locally. Depth recordings must be interpreted with caution, inasmuch as electrodes are only implanted for strictly clinical purposes in patients with long-standing epilepsy (Talairach *et al*, 1974). However, most such patients perform in the normal range on cognitive tasks, and their epileptiform activity is localized in time and space. Thus, it is possible for analyses to select patients, sites and epochs that appear to be normal. Depth recordings are also limited in that they are primarily sensitive only to locally-generated activity, and only a limited number of electrodes are implanted in each subject (determined entirely by clinical considerations). Thus, results from multiple subjects must be collated to arrive at an adequate sampling of cerebral activity.

In the current study, the time-course and task-correlates of the involvement of different frontal lobe regions are investigated using evoked potential (EP) recordings from electrodes directly implanted into the human brain. The insights possible from this technique are complementary to those obtained by metabolic imaging methods, in that the temporal sequence of the metabolically activated areas can be inferred from the EP method. Furthermore, the EP components can be tentatively identified with scalp EP components whose cognitive correlates have already been established over a large number of studies in normal subjects, allowing the functional significance of these activations to be inferred. Finally, the EP method does not require subtraction in order to observe activation (although subtraction is still useful as an interpretive method). Thus, areas of activation might be visible with EPs that are not apparent with PET. A series of EP components apparently related to sensory processing, cognitive integration and closure, and response selection were observed, localized to different parts of the frontal lobe.

Materials and methods

Patients

Adequate recordings were obtained from 26 patients suffering from epilepsy that had proved resistant to trials of all appropriate anticonvulsant medications (Talairach *et al*, 1974). Personality and intelligence were within the normal range. Electrodes were implanted for 4 to 14 days in order to localize the sites of seizure onset, at the Neurosurgical Services at Hôpital Sainte-Anne in Paris (Pr JP Chodkiewicz, Chief), or at Hôpital Pontchaillou in Rennes (Pr J Faivre, Chief). While awaiting spontaneous seizure onset, recordings were obtained during cognitive tasks (table 1). Patients were not recorded if they were having frequent or major seizures, or within 1 h after a complex partial seizure. Data were rejected from patients and/or sites which exhibited chronic slow waves or interictal spikes, or when a patient was unable to perform within the normal range in speed and accuracy on the cognitive tasks. Selection of patients and sites to implant, as well as the duration of implantation, were made without reference to the experimental protocol. Cognitive recordings were made only after fully informed consent monitored by the appropriate human subject protection committees.

Table I. Patient characteristics

Pt no	*Sex*	*Age*	*Implanted sites*[a]	*sz focus*[a]	*Dominance man (hem)*[b]	*Tasks*[c]
2	F	34	RTPCF	RT	R	F,W,A
3	M	20	RPCF, LCP	RFP, LFC		F,W,A,V
5	F	39	RTPCF	RT	R	F,W,A
6	M	50	RTPCF	RT	L(L)	F,A,V
7	M	29	RPRF	RF	R	F,A,V
8	M	21	RTPF	RTP	R	F,W,A,V
9	M	37	RTPCF	RT	R	F,W,A
10	M	40	RTPF	RT	R	W,A,V
12	M	32	RTOPF	RT	L(R)	F,W,A,V
14	M	35	LTPCF	LT	R	F,W,A,V
16	F	26	RTF	RT	R	F,A,V
17	M	26	RTOPCF	RT	R	F,A
18	M	39	RTCF	RT	R	F,A
20	M	22	RTOCF	RT	R	F,W,A,V
21	M	31	RTOCF	RT	R	F,W,A,V
22	M	30	RTPF	RT	R	F,W,A,V
23	M	28	RTOPCF	RJ	R	F,W,A
24	M	24	RTF	RT	R	F,A
27	M	24	RTPCF	RT	R	F,W,A
28	M	26	LTOF	LT	L(L)	F,A
31	F	24	LTF, RTF	BF	R	W,A,V
32	M	20	RTF	RT	R	W,A
35	F	35	LTPOCF, RC	LC	L(R)	W,A
36	F	28	LTPF, RTPF	BP	R	W
37	F	32	LTF	LT	R	W,A
38	F	18	LCF, RF	LF	R	W,A
48	F	30	LPF, RPF	BF	R	W,A

[a]T, temporal; O, occipital; P, parietal; F, frontal; C, central; J, junction of TPO; R, right; L, left; B, bilateral.
[b]man, manual dominance; hem, hemispheric dominance, as determined by language function after unilateral intracarotid amytal (Wada test) in left handed subjects.
[c]F, face recognition; W, word recognition; A, auditory discrimination; V, visual discrimination.

Electrodes and localization

Each patient received 1–6 electrodes in the frontal lobe or lobes (total 71 electrodes, 17 left, 54 right). Electrodes were 0.8 mm in diameter, with a rounded blunt tip, and had five, 10 or 15 recording contacts. Each contact was 2.0 mm in length, and successive contacts were separated by 1.5 mm. Provisional electrode trajectories are chosen using the method of Talairach *et al* (1967): a standard baseline (the anterior commissure-posterior commissure (AC–PC line), and a proportional grid system partially compensate for variations in the size and shape of the brain, allowing the average location and statistical variation for the major neocortical gyri and telencephalic subcortical structures to be specified. *(Throughout the text, electrode contact location is indicated in relation to the axes defined by the Talairach system using the format '(x,y,z)' where: (x) lateral, mm to midline, positive right hemisphere; (y) anteroposterior, mm to the AC line, positive anterior; (z) vertical, mm to the AC–PC line, positive dorsal (up). Electrode contacts are indicated by the letter of the electrode, followed by a prime if the electrode is in the left hemisphere, followed by the number of mm from the center of the contact to the interhemispheric plane.)* Brodmann areas (Brodmann, 1909) are also indicated, as mapped in Talairach (Talairach *et al*, 1967; Talairach and Tournoux, 1988), but it must be emphasized that these are only approximate: cytoarchitectonic boundaries obviously cannot be confirmed *in vivo*.

Statistical localization was confirmed and refined by direct visualization of vessels tracing the structure's outlines, using stereoscopic stereotactic angiography (Szikla *et al*, 1977). Angiograms were made in the same stereotaxic frame as was used for electrode implantation, and at a distance of 4.85 M (thus eliminating significant parallax). This method also allowed avascular trajectories to be chosen for the electrodes. Stereotactic MRI, with planes parallel to the interhemispheric plane and with the AC–PC line indicated, was obtained in some patients after electrode withdrawal. This allowed direct visualization of electrode tracks, albeit at a lower

Recording and analysis

For each patient, simultaneous recordings were made from 29 to 108 depth contacts, 0–6 EEG electrodes (including one placed between Cz and Pz in 21 patients) and a vertical EOG derivation. Bandpass was 0.1 to 40 or 100 Hz. Waveforms were digitized at 12 bit accuracy, every 5 or 6 ms, for 1200 ms beginning 117 ms before face onset. In most patients, a second 1200 ms digitization epoch was collected beginning 100 ms before the feedback tone. Only trials without wrong responses, eye movements or epileptiform EEG spikes were used in constructing averages. Eye movements were detected by amplitude criteria applied to the EOG channel. Epileptiform EEG spikes and other large transients were rejected on amplitude criteria set individually for each patient's data. The effectiveness of these artifact rejection routines was carefully monitored by visual inspection of the graphics display. Channels contaminated by frequent epileptiform abnormalities were excluded from analysis. Peak measurements were made by finding the maximum or minimum in each channel within the appropriate latency window, and subtracting the average value of that channel during the period prior to the stimulus onset (*ie* baseline period). The contact in each structure with the largest amplitude EPs was chosen for measurements.

Behavioral tasks

The principle tasks, Face and Word, required declarative recognition memory. Simple auditory (AD) and visual (VD) discrimination tasks with infrequent target and non-target distractor stimuli (*ie* auditory and visual 'oddball' tasks) were presented for comparison purposes. During all tasks, the patients reclined on a bed or chair, and maintained fixation on a target. Stimulus presentation was controlled and behavioral responses were monitored for latency and accuracy using a microcomputer.

Face (21 patients)

The faces were presented every 3 s as color slides on a back projection screen tachistoscopically for 300 ms each. The images subtended a visual angle of 5.5 degrees horizontal by 8.3 degrees vertical. The patient was required to press a microswitch held in the dominant hand within 1200 ms after presentation of a repeating face. At 1200 ms post-stimulus, a 55 ms sawtooth feedback tone was presented indicating whether the response (or lack thereof) had been correct (1000 Hz) or wrong (200 Hz). Feedback tones evoked responses similar to those evoked by 'auditory oddball' tasks. The face stimuli consisted of photographs of previously unfamiliar young adults of European descent who lacked beards or mustaches. The background was black, and the clothing was obscured by a black drape. Glasses, jewelry and other unnatural identifying objects were removed, and hair was pulled back from the face prior to photography. Subjects posed in each photograph as happy, sad, or neutral, according to instructions and after practice.

Six hundred slides from 260 individual subjects were included, divided into two equivalent sets. In each set, 10 individuals were chosen to be targets and presented repeatedly ('repeats'), with the remaining 120 presented only once ('non-repeats'). During the input phase, each of the repeating individuals was shown six times (twice each for each of three emotions), and the subject was required to rate the valence and intensity of the facial expression with a joystick. During the output phase, 240 slides were presented every 3 s with rests after 80 and 160 slides. Of these 240 slides, 120 were the non-repeats, and the remainder were 12 repetitions of each of the 10 target faces. Repeats and non-repeats were presented in random order, except that no individual could be presented on two successive trials, no more than three repeats or three non-repeats could follow each other in a row, and each of the 10 targets occurred exactly once in each block of 20 slides. Consequently, the delay between successive presentations of a given face was filled with distractors, and had a duration of 6 to 117 s (average 61.5 s). The faces were 1/2 male and 1/2 female, and no more than five male or five female faces were presented in a row. The faces were 1/3 of each emotional expression, and no more than three faces with the same expression were presented in a row. Repetition, gender and expression were all completely crossed with each other. The influence of gender, and expression on the waveforms, as well as the results of the input task, will be presented in another paper.

Word (20 patients)

The words were presented as proportionally-spaced white letters on a computer monitor for 300 ms, where each subtended a visual angle of 1.24 to 1.49 degrees horizontal by 0.36 degree vertical. The 4–7 letter words were 1/2 of moderately low (31 to 162 occurrences per 10 million, average 100), and 1/2 of moderately high frequency (> 3193 occurrences per 10 million, average 15 000). 260 individual words were used, divided into two equivalent sets. In each set, 10 words were chosen to be targets and presented repeatedly ('repeats'), with the remaining 120 presented only once ('non-repeats'). During the input phase, each of the repeating words was shown for 10 s, and the subject was required to attempt to memorize it. Timing and response requirements during output were exactly identical to those in Face.

AD (25 patients), VD (12 patients)

In the auditory and visual oddball tasks with distractors, the patient responded to rare target rare stimuli by incrementing a silent count and by pressing a microswitch in the patient's dominant hand. Frequent stimuli and non-target (but rare) distracting stimuli were also presented, and were to be ignored. In AD, a 48 ms sound (including a 12 ms rise and 12 ms fall) was presented every 1 600 ms at a comfortable level binaurally

through a speaker located 2 meters behind the patient's head. Rare target (11% of trials), frequent (78%), or distractor (11%) stimuli occurred in random order. In VD, single letters or symbols subtending 0.43 degrees of visual angle were presented in white on a video monitor for 200 ms every 1600 ms. Details of these tasks and the potentials evoked by them are presented elsewhere (Baudena *et al*, submitted; Halgren *et al*, submitted). We present these results here only inasmuch as they help explicate the potentials evoked by faces and words.

Results

Behavioral

Average reaction time was 628 ± 75 ms to correctly identified repeating faces, and 640 ± 63 ms to repeating words. Of the repeating faces, 80 ± 14% were correctly identified ('hits'), and 23 ± 19% of the non-repeating faces were falsely identified as being repeated ('false positives'). Performance for the words was 84 ± 19% hits and 11 ± 10% false positives.

Physiological

Visual inspection of the waveforms revealed a regular series of evoked potential components from 110 to 1000 ms peak latency after stimulus onset. Whereas most EP components tended to be similar in latency and localization for faces and words, some early components were quite distinct, and will be discussed separately.

Components evoked by faces

N150–P190–N220

A negative-positive-negative EP sequence was recorded in several sites. The three peaks could occur together, or the initial negative peak or second positive peak could predominate. In nearly all cases, the initial two potentials are evoked only by faces, not by words. However, the N220 had a wider distribution than the N150–P190, and appeared to be less specific for faces (as compared to words). These potentials did not change with repetition of the face (table II).

Inferior frontal g. A large somewhat focal N150 component was evoked by faces in the inferior frontal gyrus pars triangularis (area 46: table II; fig 2, 34; fig 3, F'42; fig 8, 30; fig 11, G39; coordinates about 45, +33, +12).

Orbitofrontal cortex. Very clear P190 components (sometimes preceded by an N120) were recorded in the orbitofrontal cortex (area 11: fig 8-37; coordinates about 25, +36, −18). Often, these potentials were very focal, and in two orbital recordings, possible polarity inversions were observed, with P150 or P160 laterally, and a slightly earlier negativity in the next medial lead 7 mm away (fig 5-24 to 17 to 10; fig 6-33 to 26). These components were apparent only to faces. A small face-specific N220 was sometimes recorded in the orbitofrontal cortex (area 11: fig 5-10, 24, 38; fig 8-37).

Inferior precentral cortex. N150–P190 sequences were often observed in the precentral and premotor cortices, evoked by faces (table II; fig 11-M42, R48, P41). In one patient, a clear and partially face-specific N150–P200–N270–N370 was evoked by faces (and clearly less to words) in the right inferior Rolandic cortex (fig 9-R43), in the area devoted to face sensation and movement. It appeared that a broad underlying N400 component was evoked only by faces in this electrode (fig 9-R64).

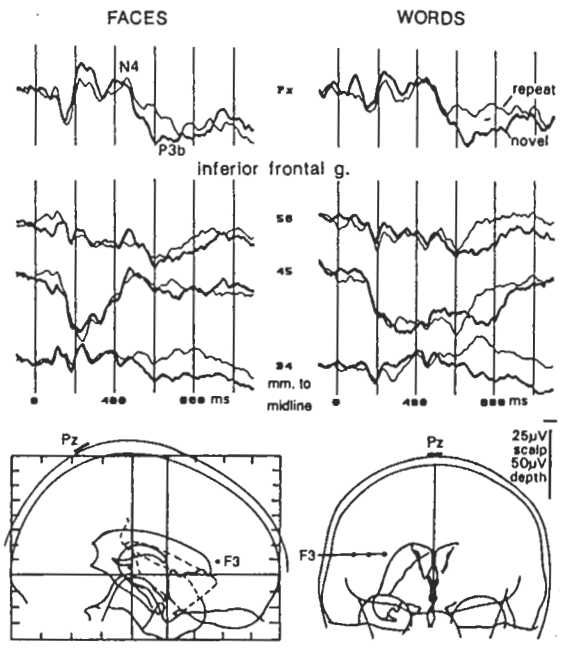


Fig 2. Early frontal face and word potentials. A focal P190 is evoked by both words and faces in the pars triangularis of the right inferior frontal g (filled square: 45 mm). This local positive potential continues until about 400 ms to faces, and until 700 ms to words. Patient no 20.

Table II. Average latency and amplitude of potentials evoked by faces in each region

Components	*Site*	*oFc*	*abs oFc*	*aCg*	*F3t*	*pCM*	*CPz*
N150	N	2		5	7	6	8
	LAT	160		146	146	146	118
	NEW	−27		−13	−30	−24	−3.2
	RPT	−29		−12[e]	−32[e]	−25[e]	−3.9[e]
P190	N	1		4	7	5	10
	LAT	194		190	200	188	180
	NEW	16		7	22	23	5.6
	RPT	13		7	21[e]	22[e]	4.8[e]
N240	N			6	3		9
	LAT			268	220		235
	NEW			−21	−29		−4.1
	RPT			−16[d]	−19		−3.3[e]
N310	N	3			8	6	8
	LAT	307			309	316	307
	NEW	−26			−21	−35	−6.3
	RPT	−27			−17[e]	−30[e]	−5.1[e]
N430	N	7		6	9	4	13
	LAT	423		397	443	481	437
	NEW	0	41	−23	−34	−37	−4.6
	RPT	−5[e]	47	−16[d]	−26[e]	−35	−4.7[e]
P630	N	6			7		12
	LAT	600			591		617
	NEW	12	44		−4		4.5
	RPT	28[a]	43		−10[e]		6.3[e]
N740	N					7	
	LAT					730	
	NEW					−13	
	RPT					−34[c]	

N, number of electrodes measured; LAT, latency in ms; NEW, amplitude in μV to non-repeated faces; RPT, amplitude to repeated faces; abs, absolute value; Components are listed according to usual polarity (positive or negative) and approximate mean latency across sites (including also posterior sites); oFc, orbitofrontal cortex; aCg, anterior cingulate gyrus; F3t, inferior frontal g, pars triangularis; pCM, precentral, premotor, supplementary motor cortices; CPz, scalp midline between Cz and Pz.
Statistical significance of differences between NEW and RPT faces tested with paired *t*-test (two-tailed): [a]$P < 0.001$; [b]$P < 0.01$; [c]$P < 0.02$; [d]$P < 0.05$; [e]ns. Only tested for $n > 4$.

Components evoked by words

P280

Inferior posterior prefrontal. In one patient, a clear P280 was evoked by words but not by faces in the left inferior frontal g, pars triangularis (fig 3-F'42, 49; area 46; coordinates −42, +29, +15). In the right inferior frontal g, pars triangularis, of another patient, a P270 was also evoked by words but not faces (fig 4-42, 45).

N310–N460–N600

Broca's area. A large (60 μV peak amplitude) negativity extending from 350 to 900 ms post-stimulus onset, and with peaks at 400 and 600 ms, was evoked by words but not by faces in the left inferior frontal g, pars triangularis (fig 3-F'49: area 46: coordinates −49, +29, +15). Interestingly, the N3-N4s recorded by more medial leads of the same electrode failed to differentiate between words and faces. More posteriorly, in pars opercularis, a focal positivity peaking at about 400 ms was also observed (fig 10-R'38), but since faces were not recorded in this patient the specificity of this response is unknown.

Components evoked by both faces and words

N150–P200–PN260

Early components evoked both by words and by faces were usually small, and often were obscured by larger N150–P190–N220 potentials evoked by

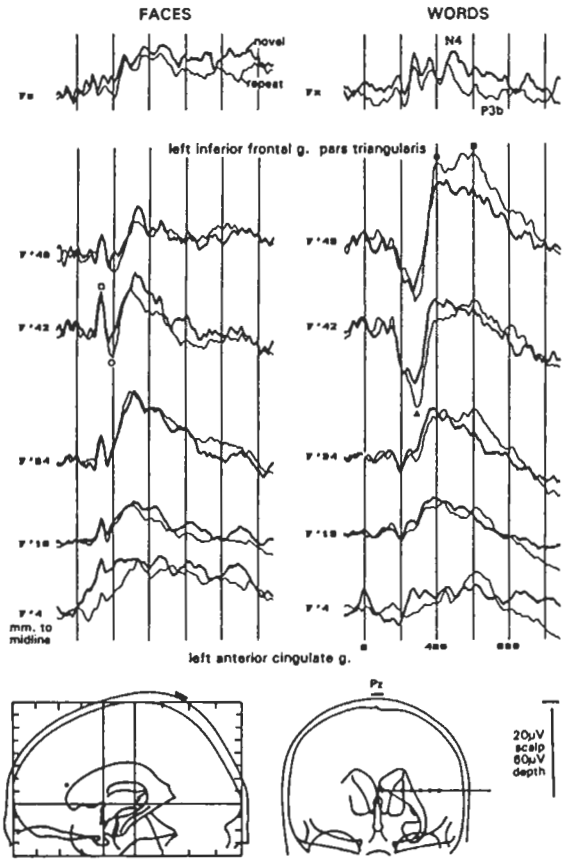


Fig 3. Left frontal word potentials. In the left inferior frontal g (F'49, in the pars triangularis, near the sulcus separating it from the middle frontal g, corresponding to Brodman's area 46), words but not faces evoke a large focal positivity at 280 ms (▲), followed by large negativities at 400 ms (●) and 600 ms (■). Conversely, only faces evoke an N120 (□: F'42). Both faces and words evoke positivities at about 200 ms (○), and similar broad negativities peaking at about 340 ms, in sites near the sulcus separating the inferior and middle frontal g (F'42, 34), and ending in the anterior cingulate g (F'4). Patient no 14.

faces only. In addition, the N150–P200–PN260 did not constitute a widespread characteristic waveform like the N150–P190–N220, and many sites lacked one of its components, as noted below. Clearly, given the substantial overlap in latency between these potentials, as well as apparently intermediate forms with partial face-specificity, their division into face-specific and non-specific potentials is sometimes arbitrary.

Anterior cingulate g. (approximate coordinates ± 6, +35, +9; area 24 or 32). An N150–P200–N250 sequence was recorded in the acg of seven subjects in response to faces, and in two subjects in response to words (table II). In all cases, this sequence was small (less than 25 μV and usually about 10 μV), with no significant voltage gradient. In some cases, the P200 only brought the wave back to baseline, but not to positive polarity. This sequence was larger to faces (< 25 μV) than words (< 10 μV), and was more easily evoked by faces (seven out of 12 subjects) than words (three out of eight subjects). The N250 appeared to slightly decrease as faces were repeated (table II).

Inferior posterior prefrontal. (N140–P200). In the inferior frontal g, pars triangularis, a negativity at about 140 ms followed by a positivity at about 200 ms was commonly evoked by both words and faces (fig 4-45: area 46: coordinates 42, +31, +7). Commonly, the positive component was much more prominent than the negative (fig 2-45; fig 3-F'42). This P200 component was large in leads within about 15 mm of the surface, and then abruptly disappeared in more medial leads. This topography is consistent with generation in a nearby horizontally-oriented sulcus, and indeed the sulcus between the medial and inferior frontal gyri passed just superior to the sites where this potential was recorded. A similar potential, with a possible polarity-inversion (N200–P220) was observed in a slightly more posterior and superior site (fig 10-M36, M15).

N200–P280–N350

Anterior cingulate g, orbitofrontal cortex, and inferior posterior prefrontal. In the same latency range and in many of the same regions as the sensory N150–P200, a small N200–P280–N350 sequence was often observed. These sequences could be distinguished by the more lateral topography of the N150–P200, and by comparison with the EPs evoked in the same sites in an auditory discrimination task. Rare target and non-target sounds in the auditory task evoke an N200–P280–N350 sequence, which has been identified with the N2–P3a–slow wave EP complex observed at the scalp to stimuli that evoke orienting (Baudena *et al*, submitted). This sequence was observed rather diffusely and in multiple sites (figs 4, 8). Rather than decrease in amplitude precipitously in contacts medial to the middle frontal sulcus, these potentials tended to maintain their amplitude, and even to increase as the anterior cingulate g was approached.

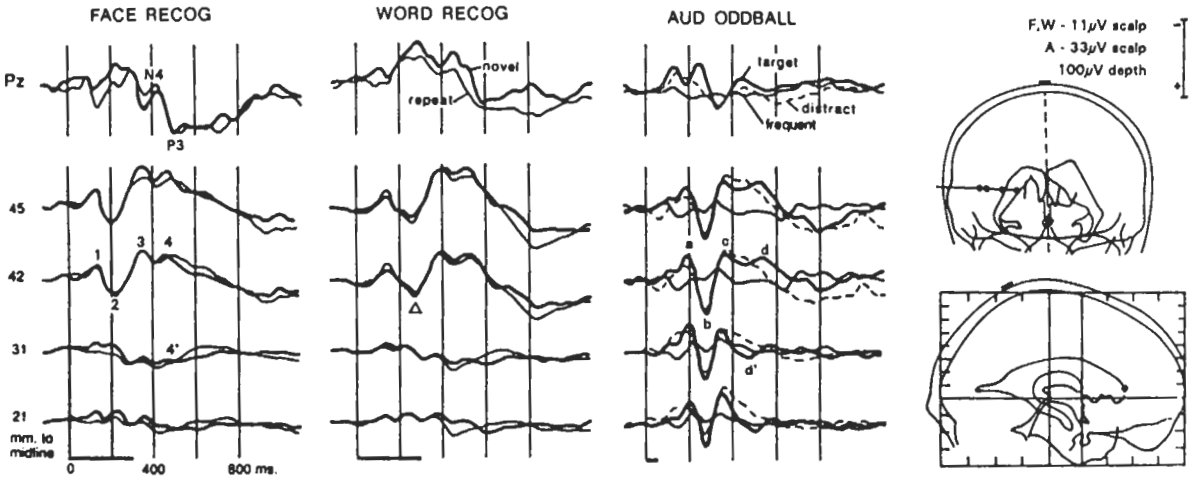
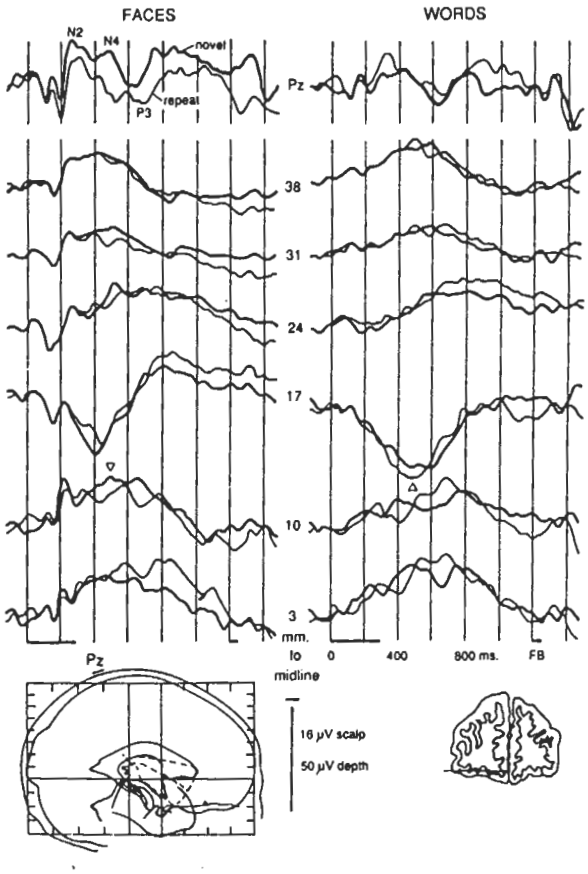


Fig 4. Comparison of components evoked by words, faces and tones in the prefrontal cortex. Faces and works evoke an N120–P200–N350–N460 (1, 2, 3, 4) well-localized to lateral leads (45, 42). Words only evoke an additional positivity at 270 ms (Δ). In contrast, rare target and distractor tones evoke an N190–P280–N360 sequence in both lateral and medial leads, identified elsewhere with the N2–P3a–SW (a, b, c). This triphasic waveform is preceded by a diffuse negativity at about 110 ms, and followed by a negativity at 530 ms (d) in lateral leads only. Patient no 21.



N300–N450–P600

This triphasic complex was recorded in several frontal sites, especially ventrally and laterally (tables II, III; fig 12). This distribution was clearly more lateral than that observed for the P3a evoked by rare auditory stimuli (Baudena *et al*, submitted).

Anterior cingulate g was recorded in 14 patients (approximate coordinates ± 6, +35, +9: area 24 or 32). In 11 subjects, a negativity peaking at about 400 ms was recorded (tables II, III). No subsequent positivity was observed in the aCg. Rather, in nine out of 11 patients the aCg was negative at the latency of the P600. The amplitude of the aCg N400 was small (5–33 μV), and a voltage gradient was observed in only one subject (fig 11, G4 to 11). No difference between faces and words could be observed in either the size of the response, or the proportion of subjects

Fig 5. Right orbital face and word potentials. A focal double-inversion of the N460 to faces and words is seen in the right orbitofrontal cortex (at triangles). Passing from lateral to medial, the N460 is negative (38, 31, 24 mm), then positive (17 mm), then negative (10, 3 mm). Less well-defined are an N680 (10 mm) and N850 (17 mm). Preceding the N460, especially to faces are a P150 (17 and 24 mm with possible inversion at 10 mm) and a N220 (maximal at 10 mm). Patient no 9.

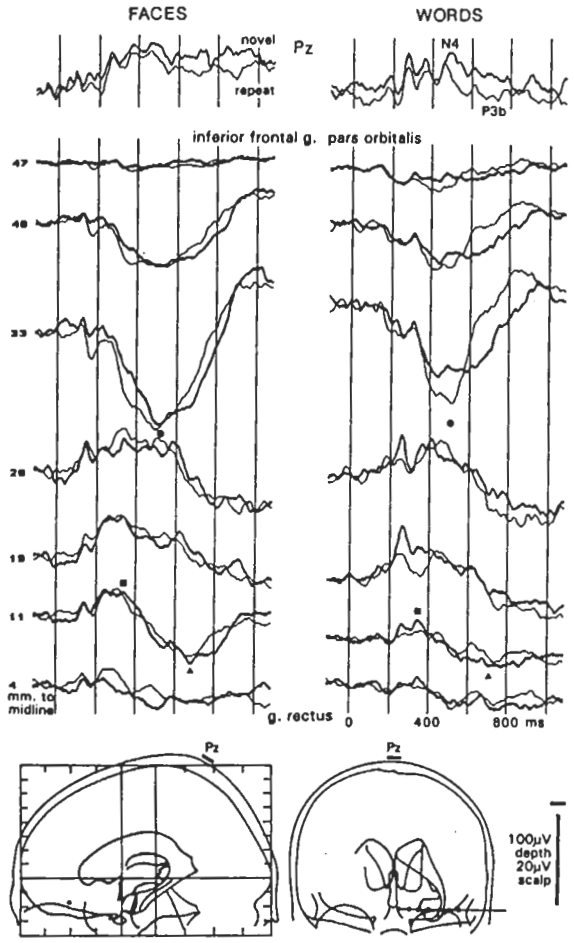


Fig 6. Left orbital face and word potentials. A 100–μV P510 (●) is evoked by words and faces in the pars orbitalis of the left inferior frontal g (33 mm). This potential declines in amplitude more laterally (40, 47 mm), and inverts polarity more medially (26, 19 mm) on the same electrode track. Words and faces also evoke an N330 (■) and a large late N950, both with a topography similar to that of the P510, and a P680 with a more medial topography (▲: 11 mm). Faces only evoke an earlier N134–P160 (26, 33 mm), whereas words only evoke an N260 (19, 26 mm). Patient no 14.

which exhibited it. However, the N400 to faces in aCg did significantly decrease in amplitude with repetition (table II).

Inferior frontal g, pars triangularis was recorded in 16 patients, and showed endogenous responses in 11 (tables II, III; fig 3–F'34; fig 4–45). Multiple components were evoked by faces, fewer by words. Responses were small with the N310 attaining a maximum amplitude of 52 μV to faces and 40 μV to words, a maximal N430 of 61 μV to faces and 51 μV to words, and a maximal P630 of 54 μV to faces and 50 μV to words. Nonetheless, the responses were usually focal, and in four cases inverted to slightly positive over the course of the electrode track. In all four cases, the N430 was involved in the inversion, and in two the inversion also involved the N310 and P630 (fig 4).

Orbitofrontal cortex. In addition to the earlier components discussed above, two components were observed in the orbital cortex of most patients: an NP430, falling within the latency range of 380 to 460 ms, and a PN630, between 500 and 700 ms (figs 5–8). In some recordings, an earlier N300, between 240 and 370 ms, and/or a very late NP1000, from 800 to 1400 ms was also found (fig 6).

N300s were observed in 12 out of 15 electrodes, commonly near the midline (10–30 mm). They were small (maximal 30 μV to faces, 34 μV to words) and could be of either polarity (fig 6–19). Voltage gradients were small, although occasionally polarity inversions could occur (4/12). Potentials in this latency range were observed in two cases in the ventrolateral prefrontal cortex (about 40 mm from midline), but due to overlap with the NP430, they did not form a separate peak and it was not possible to determine if they were actually distinct potentials.

In 12 of 15 orbital electrodes (14 patients), a peak at about 420 ms was observed, of either polarity. In seven of these patients, the NP430 was observed to polarity invert across successive contacts of electrodes traversing the orbitofrontal cortex from lateral to medial (fig 5–10 to 17 to 24). The orbitofrontal NP430 was often quite large (maximal 85 μV to faces and 189 μV to words). This maximum amplitude was typically positive, and was attained 32 to 43 mm from the midline (fig 12). Maximal amplitude could be more lateral in more superior placements, presumably corresponding to the curvature of the ventrolateral prefrontal cortex. Negative potentials tended to be smaller (30 to 100 μV), and maximal between 22 and 33 mm from the midline. Electrodes recording the largest responses tended to enter the cortex a small distance superior and anterior to the usual placement (in the first division below AC–PC, and 2.5 divisions anterior to AC, as compared to the second division below AC–PC and 1.8 to 2.2 divisions anterior to AC). Consequently, the coordinates of the maximal responses was about ± 38, +43, –5, for the positive, and ± 28, +43, –5, for the negative. This corresponds to area 11 in the orbital part of the middle frontal g, slightly anterior to the sulcus separating it from the anterior frontal g.

Table III. Average latency and amplitude of potentials evoked by words in each region

Components	*Site*	*oFc*	*abs oFc*	*aCg*	*F3t*	*abs F3t*	*pCM*	*CPz*
N310	N	2			4		2	8
	LAT	281			328		287	311
	NEW	−3			24		−20	−5.3
	RPT	8			20		−8	−1.1[d]
N430	N	9		3	4		6	12
	LAT	457		428	453		433	470
	NEW	52	80	−23	1	41	−36	−3.8
	RPT	44[e]	69	−16	7	35	−20[b]	−2.5[e]
P630	N	7			3			11
	LAT	584			563			612
	NEW	62	68		−7	29		5.7
	RPT	65[e]	68		8	34		6.3[e]
N740	N						6	
	LAT						750	
	NEW						−10	
	RPT						−41[b]	

For abbreviations see legend to table II.

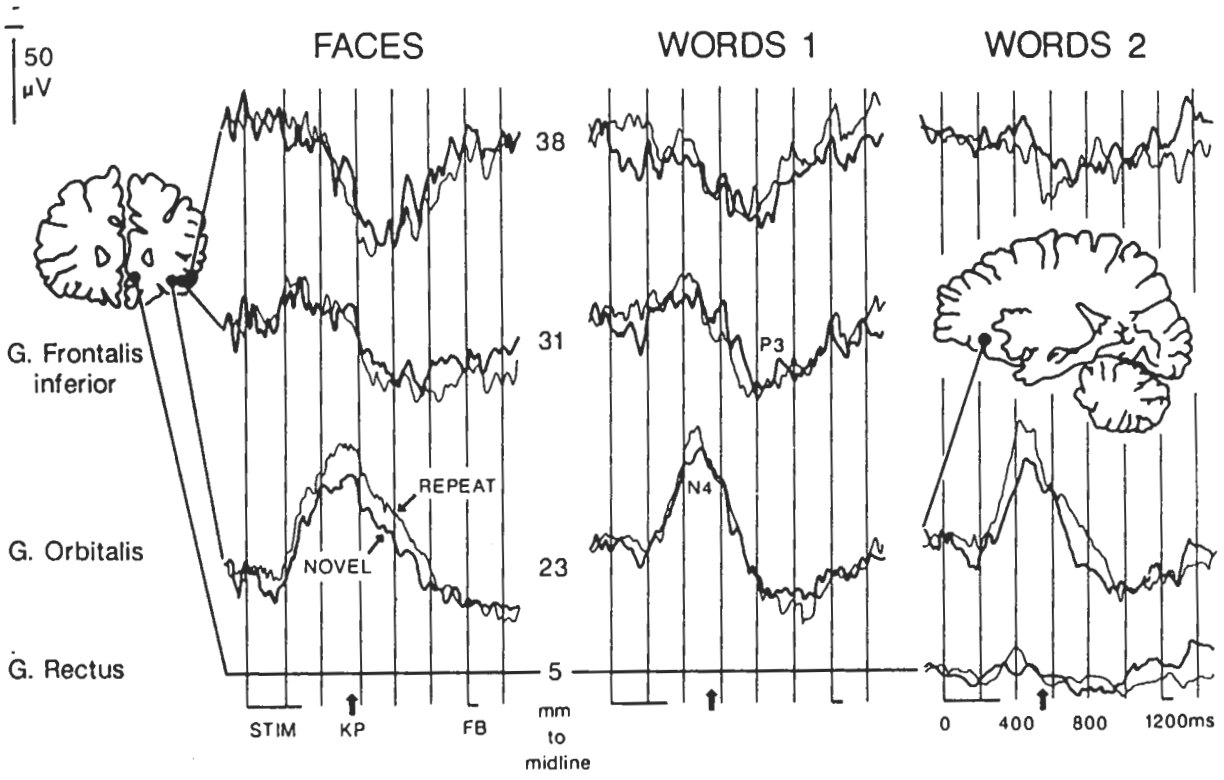


Fig 7. Right orbital face and word potentials. Focal large (−75 µV) N460 evoked by faces and by words (on two different days, Words 1 and Words 2), in the pars orbitalis of the right inferior frontal g (by the electrode contact 23 mm from the midline). In the same tasks, the P800 is relatively more prominent more laterally (31, 38 mm). Patient no 5.

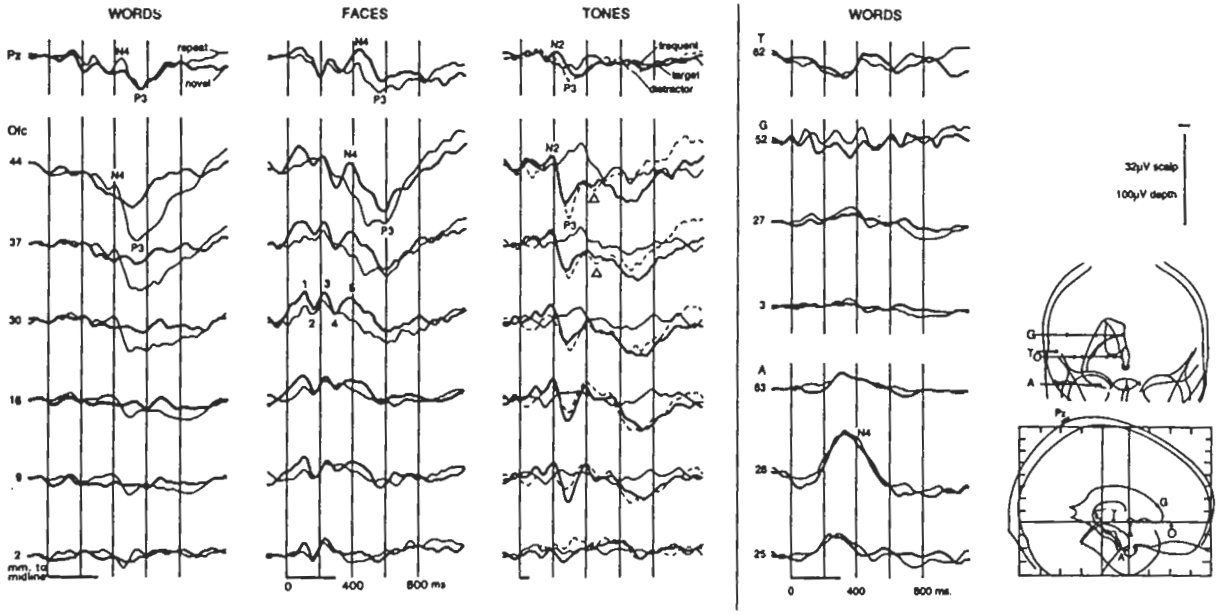


Fig 8. Comparison of P3a and P3b topographies in the orbitofrontal cortex. A large (+ 70 μV) P3b at 500–600 ms to Words and Faces is maximal in the most lateral orbitofrontal (Ofc) lead (44 mm from the midline), and nearly absent in the most medial leads (16, 9, 2). The N2/P3a/SW complex to rare target and distractor Tones has a clearly different (more diffuse and medial) distribution than the P3b to repeating words and faces. Using these topographies, it is possible to identify what appear to be a small P3b in lateral leads during Tone (Δ), and a small N2–P3a–SW in Face (3, 4, 5), and possibly Word. Note also the early N120–P160 to faces only in both medial and lateral leads (1, 2). Also shown are recordings from: area 47 inferior/medial frontal g (G52); anterior cingulate g (G3); superior temporal g (T62); anterior middle temporal g (A63); and amygdala (A28). The absence of response in these channels during Words provides further evidence that the activity in VLFC is not volume-conducted from surrounding areas. Patient no 22.

In one patient, recordings were obtained from two electrodes implanted in the orbital cortex, one posterior (14 mm anterior to AP), and the other anterior (in the usual placement, 37 mm anterior to AP: both in area 11; fig 6). The posterior electrode first penetrated the temporal pole, and then passed through the cisterna ambiens into the orbitofrontal cortex about 35 mm from the midline. In this more posterior track, the N450 was noted to invert between 17 mm (negative) to 24 mm (positive), and again from 31 mm (positive) to 38 mm (negative). Recordings were of the same order of magnitude as those simultaneously obtained more anteriorly, where the N470 inverted from 26 mm (negative) to 33 mm (positive). Examination of the MRI shows that in the regions of the inversions that the electrode was passing through vertically-oriented sulci rising from the orbital surface of the frontal lobe, or the electrode was exiting through the lateral orbital surface. Thus, the orbital generator appears to engage a large cortical area.

In seven of 15 orbital electrodes (14 patients), a peak at about 600 ms was observed, of either polarity (tables II, III; maximal 112 μV to words, 154 μV to faces). Two voltage maxima were observed for the PN600 in the orbitofrontal cortex: a medial focus about 12 mm to midline, and a lateral about 40 mm to midline (fig 12). The amplitude of the lateral focus was about 100 μV (range 35–154 μV), whereas that of the medial focus was about half as large, 50 μV (range 25–60 μV). Polarity inversions were seen in three subjects, most often laterally (figs 6–11 to 19). However, in four electrode tracks (three subjects), the PN600 decreased and then increased again passing from lateral to medial, strongly suggesting two generators. Again, the orbital PN600 tended to be larger in the more superior and anterior electrode placements. The orbital PN600 was significantly more positive to repeated faces (table II).

The large amplitude, focal topography, and frequent polarity inversions of the NP420/PN600

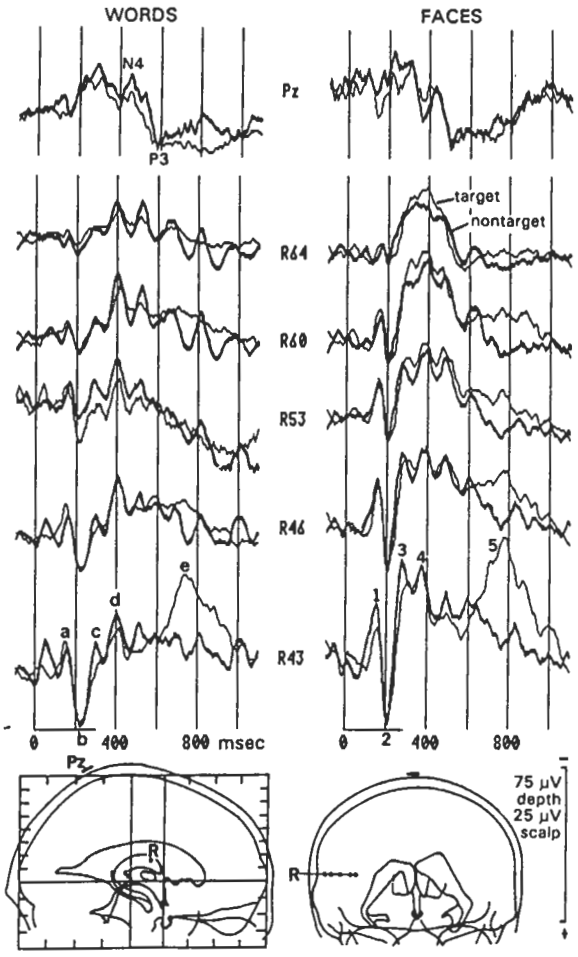


Fig 9. Apparent movement-related potentials in motor cortex. A series of potentials are recorded in the face area (*ie* inferior part of the Rolandic sulcus: R43) to words and faces. Similar peaks are observed at 150, 205, 290, 390 ms (a, b, c, d) to words, 1, 2, 3, 4 to faces). The initial components (1, 2, 3) are more prominent to faces, and underlying these peaks is a slow negativity to faces only peaking at about 400 ms. In both tasks, a focal late negativity from 620 to 990 ms is observed (e, 5) to targets only. Patient no 21.

strongly imply local generation within the orbital cortex. This inference was confirmed by comparison with simultaneously recorded potentials in surrounding structures. In all cases, the NP420/PN600 recorded in the orbital cortex was larger than that recorded more superiorly, for example, by electrodes that entered the inferior frontal g pars triangularis and ended in the anterior cingulate g. Similarly, the orbital NP420/PN600 could not be generated in the hippocampal formation, because: 1) the orbital NP420/PN600 could occur in the absence of any discernable activity in this latency range in the hippocampal formation; 2) when the NP420/PN600 were recorded simultaneously in both structures it was often much larger in the orbitofrontal cortex; 3) when large amplitude NP420/PN600s were present in both structures, they were often found to be smaller in the amygdala, which lies in between the two structures.

Motor cortex (pre-central, pre-motor, supplementary motor, frontal eye field, and motor cingulate. These areas were recorded in 11 patients (16 electrodes). In nine of these patients, two endogenous components were observed, an N310 peaking between 270 and 350 ms, and an N430 peaking between 375 and 565 ms (tables II, III, figs 9-11). Electrodes recording these components were located in the precentral gyrus (area 4 or 6: face area, 2/5 electrodes; hand area, 0/1 electrode; trunk area, 0/2 electrodes), where they tended to show mild voltage gradients, and thus probably represented far-field recordings. These components were also recorded in premotor cortex (area 6: face area, 1/1; hand area, 3/3; trunk area, 1/1), supplementary motor cortex (area 6: 2/4 electrodes), and motor cingulate (area 24: 3/3 electrodes), where they tended often to be focal in their distribution. Two possible inversions of the N4 were observed, one in the motor cingulate (fig 10, R'7), and one in the supplementary motor

Fig 10. N4 in pre-motor cortex. Recordings in two subjects (patients no 48 left and 35 right) from premotor cortex in response to words. A small positivity at 400 ms is focal in the most external lead of the patient on the left (R'38), located in Broca's area (area 44: inferior frontal g, pars opercularis). More medially (R'28), a late negativity is observed to target words beginning about 300 ms post-stimulus and continuing until after 1000 ms (1). This inverts near the midline (2) in the central cingulate g (area 24: R'10). In the external lead on the right, a large positivity at 210 ms (M36, M39, 3) appears to undergo a double polarity inversion more medially (4: M11, M15, M22, M32). These contacts lay near the sulcus separating the precentral g from the middle frontal g. The maximal response to medial n stimulation in this electrode occurred in this region (M26) but with a clearly different topography. In the most medial leads (between the middle cingulate g and the supplementary motor cortex) a late positivity is visible to target stimuli from about 400 ms to over 1000 ms post-stimulus (M1; 6). The later part of this potential may polarity-invert more laterally (M11; 5). Note that this patient had a large post-central lesion that may have altered the functional organization of the recorded area. Patients no 38, 48.

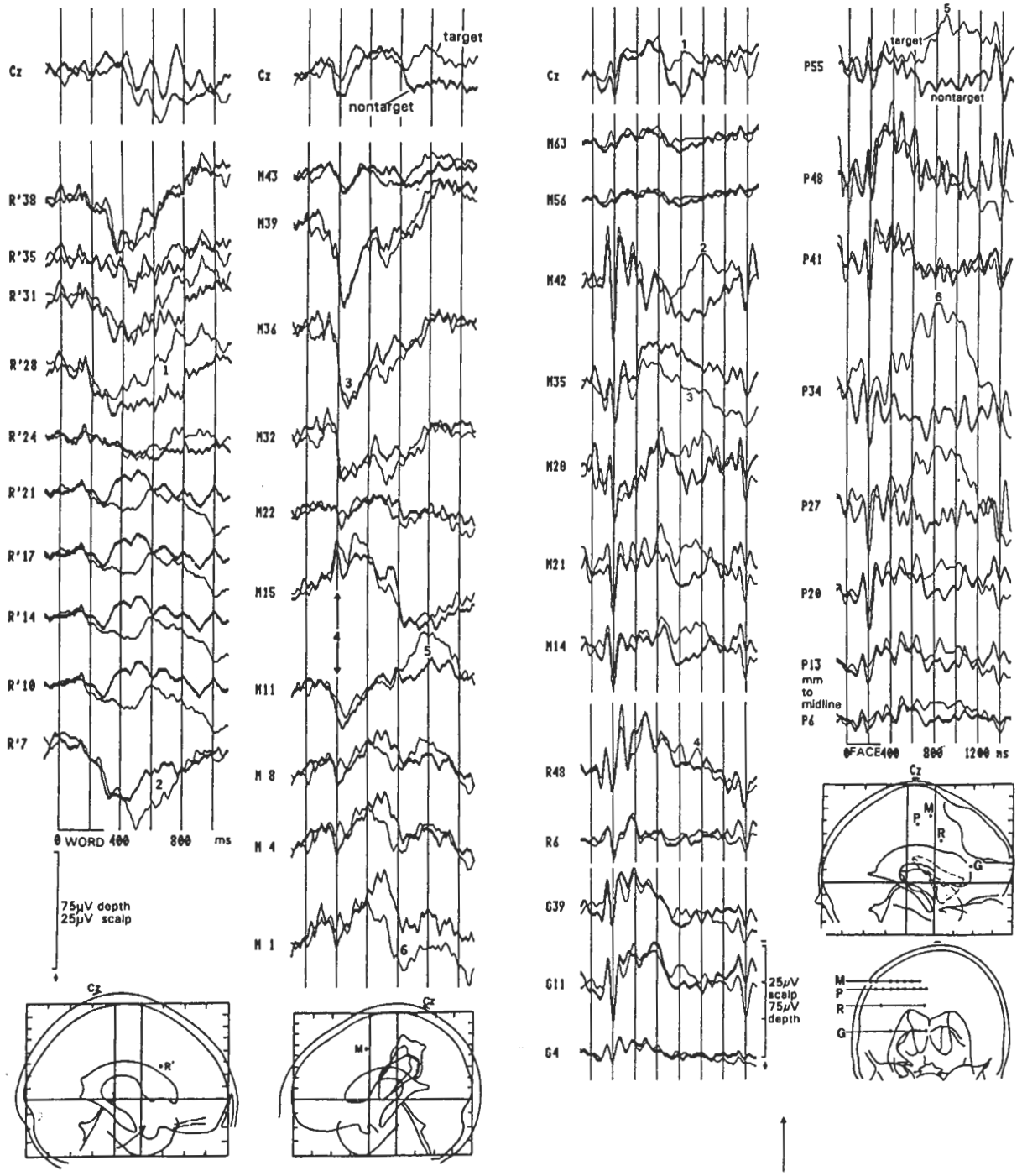


Fig 11. Early and late potentials to faces in Rolandic and premotor cortices. Faces evoke an N140–P200–N260–N400 in the premotor cortex (M42, R48), and less prominently, in the Rolandic (P41), anterior cingulate (G11), and supplementary motor (M14) cortices. Electrode P was demonstrated by stereotaxic stereoscopic arteriography to pass through the Rolandic sulcus, and was further localized using somatosensory evoked potentials. A large slow negativity evoked only to target faces, and peaking at about 800 ms is focal in leads lying in the Rolandic fissure (6: P34) and postcentral cortex (5: P55), and appears to polarity-invert in the premotor cortex, area 6 (2: M42, to 3: M35). Smaller negativities to targets are possibly present in premotor (4: R48) and supplementary motor (P6) cortices. Note that the potential in precentral cortex (5) begins later than that in the central fissure (6) consistent with it representing somatosensory feedback. Patient no 7.

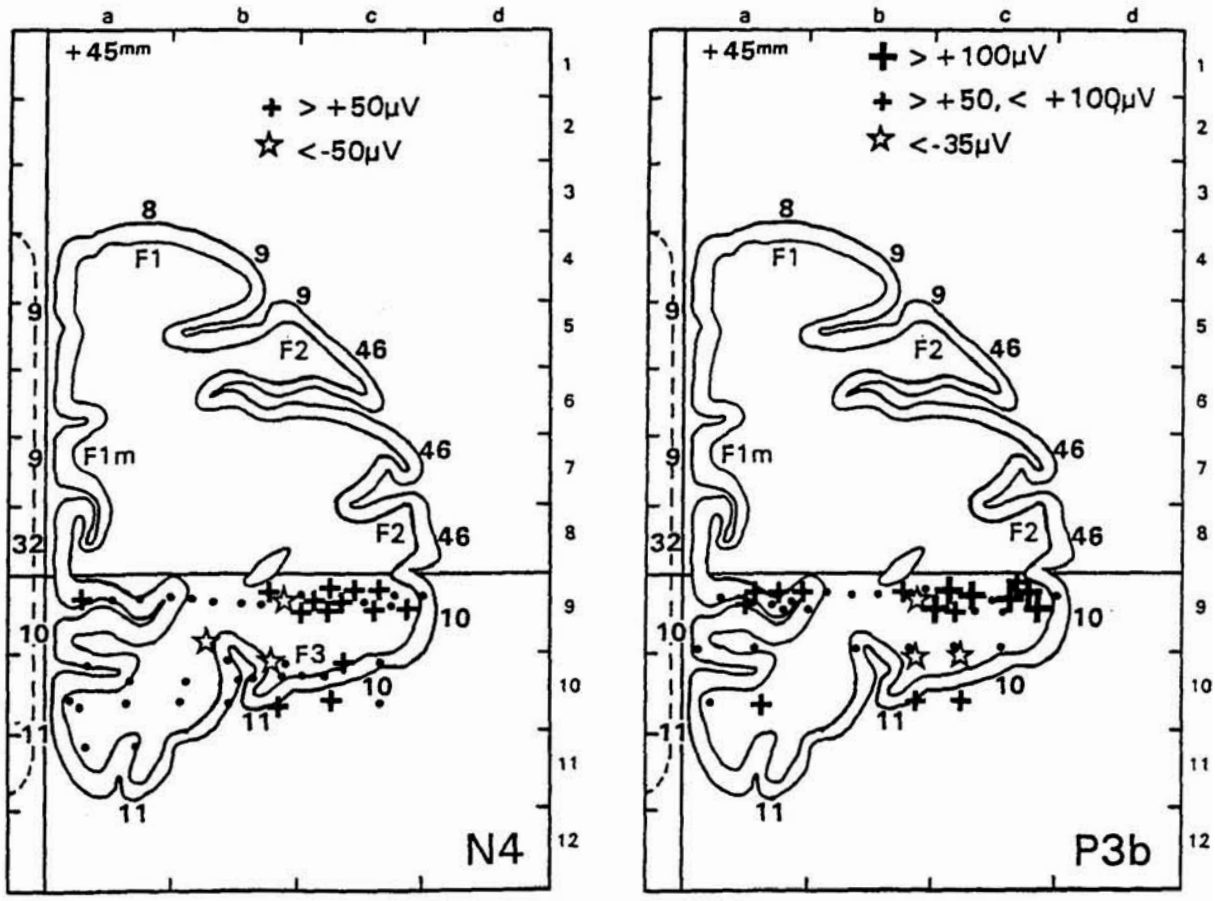


Fig 12. Distribution of endogenous potentials in basal prefrontal cortex. Amplitudes of the N4 and P3b recorded from electrodes implanted into the orbitofrontal cortex were plotted on a section from the atlas of Talairach and Tournoux (1988). The large amplitude (in absolute terms and compared to surrounding structures), focal topography, and frequent polarity inversions of the N4/P3b strongly imply local generation within the orbital cortex. In contrast to the N4/P3b, the P3a was found to have a more diffuse distribution (Baudena *et al*, submitted). N4 attained maximum positive amplitude (60–180 μV) at 32–43 mm from midline in area 11 (stereotaxic coordinates ± 38 mm to midline, + 43 anterior to AC, –5 inferior to AC–PC). Negative potentials were less common, tended to be smaller (30–100 μV), and were maximal between 22 and 33 mm from the midline (coordinates ± 28, +43, –5). The apparent generating area was very large (22 to 43, 14 to 50, –2 to –26). P3b voltage maxima were observed both laterally (35–125 μV) about 40 mm to midline, and medially about 12 mm to midline (25–60 μV). Although polarity inversions were all lateral, in four electrode tracks, the PN650 decreased and then increased again passing from lateral to medial, strongly suggesting two generators. Maximal amplitude of both the N4 and P3b tended to be in more anterior, lateral and superior placements. The VLFC N4–P3b was usually larger than simultaneously recorded potentials in the inferior frontal g pars triangularis, anterior cingulate g, and amygdala. It could be recorded in the absence of any discernable hippocampal activity in this latency range. Note that the localization shown on these sections is only approximate, due to inter-individual variation in cerebral anatomy, as well as the fact that electrodes at different anterioposterior levels were all plotted on a single plane.

cortex (fig 10, M11). However, in most cases, these potentials were small, usually 20 to 40 μV (49 μV maximum N310 to faces, 24 μV to words; 48 μV maximum N410 to faces, 80 μV to words).

The two electrodes in one patient that seemed to lie within the frontal eye fields (area 8) did not display these potentials. However, the probable FEF electrode in the right (healthier) hemisphere did show a 50 μV focal positivity to words at 230 ms (fig 10-M36).

Anteromedial superior frontal g. This region, anterior to the supplementary motor cortex, was implanted in 6 patients (11 electrodes). In three patients (four electrodes) a clear focal response,

40 to 80 μV in amplitude and about 500 ms in latency, was recorded in response to both words and faces. In two patients, the potential was positive, and was greater to repeated words and faces. In one patient, the potential was negative, and was larger to nonrepeated stimuli. This potential could be related either to the N460 commonly recorded in premotor cortex (see above), or to the late negativity recorded in precentral and premotor cortex.

Comparison of N2–P3a–SW with N4–P3b. The N2–P3a–SW in the simple auditory discrimination task (AD), and the N4-P3b in the face recognition task (Face) were often recorded by the same electrode, each with a characteristic topography (*ie* different relative amplitudes at different anatomical sites, and different locations of polarity-inversions: figs 4, 8). In particular, the P3a's distribution was more diffuse than the N4-P3b's, which tended to polarity-invert and be largest in lateral recording sites (fig 12). However, a small P3b sometimes occurs in AD, and a small N2–P3a–SW in Face and/or Word. Potentials were measured in patients with a small P3b in AD, or a small N2–P3a–SW in Face and/or Word. In four such patients the amplitude of the P3b was about three times larger in Face or Word than in AD, and across seven patients the P3a was about three times larger in AD.

N740 (Late negativity 650–900 ms)

Pre-central/pre-motor. In all 18 electrodes implanted into the precentral or premotor cortex, a late slow focal negativity was evoked to faces and words (tables II, III; fig 9–R43; fig 10–M1, R'28; fig 11, M42, P34). In 16 of these 18 electrodes, the response was clearly larger to target stimuli (repeated words or faces, requiring a key-press response) as opposed to non-target stimuli (in one case, in the left face precentral cortex, the response to non-targets was larger, and in one case, in the hand premotor cortex, they were equal). Across sites, the N740 was significantly larger to both face and word target stimuli (tables II, III). This response was maximal at about the same time as the key-press, or up to 100 ms thereafter (*ie* from 600 to 830 ms). It has a broad waveform and can begin as early as 300 ms post-stimulus onset. Often, this response was the only one recorded by electrode contacts in this region. It was usually about 30 to 60 μV in amplitude, but could be as large as 150 μV, and in one patient inverted in polarity in the trunk region of the premotor area (fig 11, area 6: approximate coordinates +43, –4, +65). However, focal responses were observed in all regions. Responses with similar latency and waveform were observed medially, in the supplementary motor cortex and the central cingulate g, but they were much more variable: in three patients a late negativity, targets > non-targets; in two patients, a late positivity, targets > non-targets; in one patient, a late negativity, targets > non-targets; and in one patient, no response.

Discussion

Summary of results

Several EP components, each with its own anatomical topography, were observed during face and/or word recognition in the frontal lobe. Amongst the earliest potentials was an N150–P190, which appeared to be specifically evoked by faces as opposed to words. These potentials were recorded most commonly in the dorsolateral prefrontal cortex (in the inferior frontal g near the sulcus separating in from the middle frontal g: estimated area 46), and in the orbital cortex, where possible polarity inversions were observed. Interestingly, these potentials were also recorded in precentral, premotor face cortices, where apparently face-specific activity continued with an N400. An N220, less specific for faces and more widespread, was often associated with the N150–P190. These early potentials did not change with repetition. Potentials that were specific for words as opposed to faces were most prominent in Broca's area (a P280–N310–N460–N600). The early part of this sequence could also be observed in the homologous region on the right. In addition to these possibly specific potentials to words and faces, there was a nonspecific N150–P190–N220 in the anterior cingulate g, and, most prominently, in area 46. A polarity inversion in this region was observed at about 200 ms latency.

Distinguished from these potentials by its more widespread (and especially medial) topography, was a small N200–P280–N350. This was recorded in multiple sites, including the anterior cingulate g, area 46, and orbitofrontal cortex (especially in its medial part, the gyrus rectus). It appeared to have the same topgraphy as potentials recorded

by the same electrodes in simple signal detection tasks, where it has been associated with orienting.

The largest potentials evoked by words and faces in the frontal lobe are the N300–N450–P600 complex. It again was recorded in multiple areas, including the anterior cingulate g, and area 46 and premotor cortex. In these areas, it is small but can be somewhat focal or even show slow inversions. Clearly, however, the N300–N450–P600 are most prominent in the ventral prefrontal cortex (*ie* lateral orbitofrontal), where they commonly polarity invert over short distances and attain large amplitudes.

Characteristic of the potentials recorded by all electrodes penetrating the motor cortex (central, premotor, and supplementary motor) was a broad late negativity peaking at about N740 (*ie* about 100 ms after the key-press). These responses were clearly correlated with the behavioral response.

These data can be tentatively interpreted as reflecting: 1) stimulus processing (sensory in area 46, word in Broca's area, face in ventrolateral prefrontal and inferior Rolandic cortices); 2) orientation (diffuse but mainly in area 46, anterior cingulate g and the g rectus); 3) cognitive integration and closure (diffuse but mainly ventrolateral prefrontal cortex); and 4) response choice (motor, premotor and supplementary motor areas). These interpretations are elaborated below in view of: 1) where each component is generated, as revealed by this and other studies; 2) the anatomical relation of these areas to other areas, as revealed by anatomical tracer studies of the corresponding areas in lower primates; 3) the function of the generating area, as revealed by lesion and stimulation effects, and PET studies in humans, as well as lesion effects and unit-recordings in monkeys; and 4) the function of the EP component, as revealed by scalp recordings of the corresponding component in normal subjects.

Methodological considerations

Insensitivities of the method

Before discussing the implications of these data, it is important to recognize that there are several possible reasons why all of the electrophysiological response stages evoked by the task in the frontal lobe may not have been detected. First, the most dorsal and anterior convexity of the frontal lobe, as well as the most inferior and posterior portions of the g rectus, were inadequately sampled. Furthermore, synaptic activity that is crucial to task performance may nonetheless be too dispersed spatially or temporally to result in a significant extracellular field-potential. Conversely, it is conceivable that an unimportant processing stage may evoke a relative large potential. More generally, interpretation of the physiological significance of these potentials is limited by the fact that the specific synaptic pathways generating them is unknown, even if the general location of the anatomical structures where they are generated can be deduced from the data reported here.

Relation to pathology

Given that all recordings were obtained from patients who had suffered from uncontrolled seizures for several years, it is possible that the data reported here have been distorted by pathology. However, the patients had a general intelligence within the normal range, and could adequately perform the tasks, indicating their brains retained the processing capabilities that were probed physiologically. Furthermore, every effort was made to eliminate recordings from sites or time periods contaminated by epileptiform activity. While epileptiform EEG spikes can be evoked by cognitive stimuli, such responses are quite rare and would have been eliminated from the current data (Altafullah and Halgren, 1988; Clarke *et al*, 1993). Abnormal connections have also been demonstrated near the epileptic focus in the medial temporal lobe (Buser and Bancaud, 1983; Houser *et al*, 1990), but not thus far in the frontal lobe (Buser *et al*, 1992). A lack of cognitive EPs is common in the epileptogenic hippocampal formation (Squires *et al*, 1983; Wood *et al*, 1988; Puce *et al*, 1989) and anecdotally was noted also in the current studies in the frontal lobe. Thus, it seems likely that these data have underestimated the responsiveness of the frontal lobe to faces and words. In any case, both the absence or excess of cognitive response in a given structure due to epileptiform pathology are idiosyncratic, reflecting the organization of the individual patient's focus. In contrast, the principal findings reported here were all found in several subjects with dissimilar pathophysiologies.

Orienting response

Rare target and distractor stimuli in the auditory and visual modalities have been observed to evoke a characteristic negative-positive-negative triphasic EP complex in the frontal lobe with peaks at about 200, 280 and 350 ms after stimulus

onset, respectively (Wood and McCarthy, 1985; Alain *et al*, 1989; Smith *et al*, 1990). In separate studies, these peaks were found to be generated in widespread cortical areas, especially in the supramarginal g, posterior and anterior cingulate gyri, inferior frontal g, pars triangularis, and g rectus (Halgren *et al*, submitted; Baudena *et al*, submitted). They were thought to correspond to the N2a/P3a/SW complex, recorded at the scalp in normal subjects under the same task conditions. The N2a/P3a/SW complex has been associated with a cortical component of the orienting response, inasmuch as it is evoked by unusual stimuli which also evoke a galvanic skin response, regardless of modality, and regardless of whether the stimulus is task-relevant (Squires *et al*, 1975; Naatanen and Gaillard, 1983; Donchin *et al*, 1984; Marinkovic and Halgren, in preparation).

In the current study, a small (10–25 μV) triphasic complex was also observed during face and, less commonly, during word recognition. This complex was identified with the N2/P3a/SW complex on the basis of its similar waveform, latency, and above all, anatomical topography, to the depth N2a/P3a/SW recorded at the same electrode contacts in simple auditory discrimination control task. The cortical action associated with orienting is the direction of attention, and the anterior cingulate g, the g rectus, and the inferior frontal g, pars triangularis, are all key sites in the interconnected network proposed on the basis of PET, lesion and primate studies to subserve directed attention (Mesulam, 1990; Vogt *et al*, 1992). This network also includes the posterior sites where the N2/P3a/SW are generated (*eg* supramarginal g: Halgren *et al*, submitted).

In any case, the functional contribution of the N2/P3a/SW to the face and word recognition tasks was presumably quite small, given that all stimuli were presented foveally, at regular time intervals. In contrast, real-life social situations require the appropriate direction of attention to spatially dispersed faces (Bruce, 1988), and competent reading implies the rapid sequential transfer of attention to words (Just and Carpenter, 1987). This direction of attention may receive contributions related to cognitive context and strategy from area 46, and related to socio-emotional context from the g rectus, integrated and funneled through the aCg to the pCg and sMg, thus modulating processing in posterior association cortex. The interactions of this network would circulate during the N2/P3a/SW, to control immediately subsequent stimulus processing.

Stimulus processing (sensory, word and face)

Sensory

A striking observation of the present study was the early responses to visual stimuli, peaking at about 140–150 ms after stimulus onset, and most prominent in the inferior frontal gyrus, pars triangularis (F3t). Epileptiform spikes were observed to be evoked with approximately the same latency by simple visual (117 ms) and auditory (87 ms) stimuli in the same area in one patient (Clarke *et al*, 1993). Furthermore, single neurons in area 46 have been noted in macaques to respond to visual stimuli to such an extent that Felleman and VanEssen (1991) include area 46 as a visual association area. This component may correspond to the scalp potential termed the visual N1 (Regan, 1989). Although this component has mainly occipital generators (Hillyard, 1993), the visual N1 recorded over the frontal scalp can be distinguished from simultaneously-recorded occipital potentials by peak-latency as well as the effects of brain lesions (Spitz *et al*, 1986).

Area 46 receives direct projections from several visual areas, including: V4, TF/TH, AITd, PIT, CIT, STPa, STP_P, LIP, DP, 7a and FEF (Barbas and Mesulam, 1985; Goldman-Rakic, 1988; Seltzer and Pandya, 1989; Fellemand and Van Essen, 1991; Barbas, 1992). Of these areas, potentials with similar latency and task correlates have been recorded in the lateral occipitotemporal cortex (corresponding to V4 and/or PIT) and the supramarginal gyrus (near areas possibly homologous to STP_P, LIP and a7) (Halgren *et al*, 1994). Despite the long distance from these juxtaoccipital to frontal sites, the lack of a clear difference in latency is not necessarily disturbing. Assuming that the transmission time from posterior visual areas to area 46 is about the same as between primary sensory areas of the two hemispheres, a delay of only about 8–13 ms may be expected (Salamy, 1978; Saron and Davidson, 1989). This is consistent with the conduction velocity of a myelinated fibre of about 1 μ diameter over an 8–cm distance (Patton, 1982).

Although F3t contained EP responses that appeared to be related to both orienting as well as simple sensory input, these responses had a somewhat distinct topography, suggesting that they are generated by separate subdivisions of this cortex. This may correspond to the anatomical observation that area 46 (sulcus principalis region) of macaques contains multiple sub-regions related to different sensory modalities and probably other

factors (Goldman-Rakic, 1988; Barbas and Pandya, 1989; Cavada and Goldman-Rakic, 1989; Seltzer and Pandya, 1989).

Faces

Early responses predominaly to faces were also observed in the prefrontal cortex, especially in its ventrolateral aspect. These responses usually had a triphasic waveform with peaks at about N120–P170–N220, and thus resembled a large triphasic N100–P150–N190 response to faces recorded in several posterior cortical sites (Halgren *et al*, 1994). This complex was largest, focal, and polarity inverted in the fusiform g, in the basal occipito-temporal cortex, possibly corresponding to ventral areas 19 and 37. In both fusiform and orbital recordings, the middle peak is maximal, and it may be the only clearly discernable peak in the ventrolateral prefrontal cortex. The VLFC responses are probably locally generated, given that they can be quite focal, and in two patients the middle peak appeared to polarity invert. The interpretation of these responses as face-specific must be considered as tentative, especially in view of the fact that the face stimuli were larger and brighter than the word stimuli. On the other hand, it should be noted that the fusiform area generating these responses is also the area where lesions cause specific deficits in face recognition (Meadows, 1974; Sergent and Poncet, 1990; Damasio *et al*, 1990), and that scalp EPs with about the same latency have been found to be specific to faces (Srebo, 1985; Jeffreys and Musselwhite, 1987; Botzel and Grüsser, 1989; Seeck and Grüsser, 1992).

A possible pathway that the N100–P150–N190 in the fusiform g may follow to result in the N120–P170–N220 in the ventrolateral prefrontal cortex is suggested by anatomical studies in macaques. The fusiform area where the P150 is generated appears to be homologous to the ventral part of area V4, which receives projections directly from V1 (Felleman and VanEssen, 1991). V4 projects directly to 21 cortical areas, including lateral and inferomedial temporal cortex, which in turn projects to orbital cortex (Morecraft *et al*, 1992).

Early as well as later responses to faces were also prominent in one patient with recordings in the precentral cortex, in or near the area specialized for faces. These unexpected responses suggest a link between the perception of others' faces, and the motor control of one's own face. This is consistent with studies showing a powerful tendency toward the imitation of facial expressions, even in newborn humans (Meltzoff and Moore, 1977; Field *et al*, 1982).

Words

A prominent clear positivity to words only, and peaking at about 280 ms post-stimulus onset was observed in F3t of two patients. Again, confirmation of the specificity of this response to words requires testing with additional stimulus types. However, the large amplitude of the response evoked by words, and the absence of any response to faces, which were brighter and larger stimuli, encourages the interpretation of this response as non-sensory. In one patient, the recording was in the left hemisphere, where F3t is often considered to constitute part of Broca's area. This early response may be projected, like the early response to faces, from the left fusiform g or angular g, where large focal peaks to words with latencies to peak of about 200 ms can be observed (Halgren *et al*, 1994). This component would then arrive in F3t *via* the pathways described above.

Scalp recordings have also demonstrated a positive potential at about the same latency in response to visually-presented words. This potential is larger to words that are subsequently recallable (Paller *et al*, 1987; Smith, 1993), and is found to decrease with immediate repetition of the word (Rugg, 1987; Van Petten *et al*, 1991; Paller and Kutas, 1992). Although the brain generator of this potential cannot be unambiguously inferred from scalp recordings, the current study suggests that it could arise in F3t, and further studies are in progress to determine if their task correlates correspond.

Also recorded in the left F3t, to words but not to faces, was a sustained negativity, with peaks at 400 and 600 ms post stimulus onset. This component provides further evidence for early word-related processing in this area. It may correspond to a potential recorded at the same latency over the frontal lobe which is modulated by syntactic discrepancies (Münte *et al*, 1993; Rösler *et al*, 1993). This potential will be discussed further below, in the context of responses that are similar except that they are evoked by both words and faces.

Fried *et al* (1981) have also shown electrophysiological responses in the left postero-inferior frontal lobe to verbal stimuli. However, these responses were recorded from the cortical surface in tasks that required a vocal output (naming), and were much longer latency. It must be emphasized

that the responses observed in the current study were in a task that required no vocal output, and visual and auditory monitoring of the patients during the task revealed no lip movements or whispering that could suggest subvocalization.

The exact function of F3t, and of Broca's area more generally, remains controversial. Electrical stimulation of the left F3t results in naming errors at about 40% of sites tested, a comparable proportion to that found in the classical Broca's area, just posterior to F3t (Ojemann, 1992). In general, both receptive and expressive language function are disturbed by stimulation of F3t (Penfield and Roberts, 1959; Ojeman, 1990). While some authors have found a strong correlation between lesions (localized with CT) in left F3t and the classical symptoms of Broca's aphasia (Popovici *et al*, 1987), others have failed to find a clear-cut relationship (Poeck *et al*, 1984), and no correlation was found between hypometabolism in this region and any specific aphasic deficit (Karbe *et al*, 1990). Furthermore, Broca's aphasics often have severe reading disturbances (Benson, 1979). Similar data led Liberman *et al* (1967) to suggest that speech production and perception use a common model (see also Caramazza, 1988; Damasio, 1988). These data are consistent with the presence of early EPs to words in F3t described here. As a whole they imply that Broca's area makes a contribution to silent reading.

The conclusion of PET studies regarding this question remain controversial. On the one hand, some studies have found metabolic activation of the left inferior frontal lobe (coordinates: –29, +55, 0) in response to the passive presentation of words, but not in response to non-words (Petersen *et al*, 1989). The hypothesis that this represents semantic activation, rather than activation due to either sensory input or word-output, is also supported by the left inferior frontal metabolic activation in response to passively listening to auditory speech syllables (coordinates: –54, 24, –5 and –50, 22, 11) (Zatorre *et al*, 1992). However, contrasting results have been reported by Wise *et al* (1991), who found that categorical judgements on heard words evoke no specific frontal activation, suggesting that subvocal output is essential for this response. Both groups agree that semantic association (*ie* verb generation appropriate to the presented noun) activates the inferior lateral prefrontal cortex, but with differing coordinates (–28, +50, –6, according to Petersen *et al*, 1990, *versus* –40, +14, 16, according to Wise *et al*, 1991). This could suggest that subvocal output is essential for metabolic activation of the left inferior prefrontal cortex.

The EP responses at 280, 400 and 600 ms to words but not faces were recorded at coordinates –49, 28, 14, near the passive listening area of Zatorre *et al* (1992), but about 20 mm lateral, 27 mm posterior and 14 mm superior to the passive reading area of Petersen *et al* (1989). Similarly, this region is about 14 mm anterior to the silent verb generation area of Wise *et al* (1991), and 22 mm posterior to the verb generation area of Petersen *et al* (1990). These different localizations between the EP recording site and metabolic activation centers could indicate activation in different cortical areas, due to differences in the cognitive tasks used, or to different loci of metabolic *versus* electrophysiological activity. Alternatively, these differences could simply represent non-systematic effects of subject selection, electrode placement, and noise. Indeed, the differences amongst the PET studies themselves for a given task (verb generation) are greater than the differences in PET *versus* EP localization. In any case, the current results, if replicated with a more extensive stimulus set, support the interpretation of the metabolic activation of left F3t as representing semantic activation by the presented word, rather than verbal output processing, inasmuch as the EP response is very short latency, and occurs without any apparent verbal output.

Cognitive integration and closure

The largest and most regular potentials evoked in the frontal lobe by words and faces were those peaking at about 420 and 650 ms in the ventrolateral prefrontal cortex (lateral orbitofrontal cortex). These potentials were clearly locally generated, in view of: 1) their very large amplitude, in absolute terms as well as in comparison to superior and posterior neighboring structures; and 2) their steep voltage gradients including common polarity-inversions. The coordinates of the maximal responses suggested a generator in area 11, in the orbital part of the middle frontal g, slightly anterior to the sulcus separating it from the inferior frontal g. Preceding these potentials is often another peak at about 300 ms that, while smaller, also appears to be locally-generated.

Due to the frequent polarity-inversions, the components at 420 and 650 ms could be of either polarity. However, their latency, general task correlates and correspondence with potentials recorded simultaneously in more posterior sites in

the same patients, suggest that they may be identified with the N4 (or N400), and P3b (or P300, or late positive component), respectively. One of the major generators of these potentials is the medial temporal lobe, where the N4 appears to be generated in the hippocampus, parahippocampal g and periamygdaloid region, and the P3b is probably generated in the hippocampus proper (Halgren *et al*, 1980, 1983, 1986; Stapleton and Halgren, 1987; McCarthy *et al*, 1989; Heit *et al*, 1990).

The P3b was about three times larger (at a given recording site) in response to repeating faces or words, in comparison to rare target or distractor tones. This finding is in striking contrast to what has been observed in the hippocampus, where the large negativity termed 'P3b' is approximately the same size to repeated words (Smith *et al*, 1986; Halgren *et al*, 1994) as compared to rare tones (Stapleton and Halgren, 1987; Halgren *et al*, submitted). Although these potentials have very different latencies to peak (360 ms for rare tones, 620 ms for repeated words), they have the same topography and waveform, and thus very likely share the same generator, with the latency difference being due to the increased latency necessary to reach closure on the cognitive encoding of the event.

This finding in the hippocampus has given rise to the hypothesis that the P3b was generated in a circuit with multiple sites that were always linked (Halgren and Smith, 1987; Halgren *et al*, 1986). For example, even if the P3b were locally generated in multiple structures, they may be rigidly linked if each local generator reflected the synaptic input from a shared distant trigger structure. This hypothesis predicts that different task conditions would manipulate P3b amplitude equally across all of its generators, *ie* that the relative amplitude of the P3b across different generating structures would remain constant. The current results imply that this hypothesis is not tenable, but rather that the P3bs in multiple generators are to at least some degree a local phenomenon that depends upon local calculations in each generator, even if that generator may still be modulated and synchronized by a shared trigger structure. In any case, it appears that the ventrolateral prefrontal cortex is only partially engaged in the P3b by simple stimuli, and that more complete engagement requires a stimulus and task with a greater level of complexity and meaningfulness.

The orbital cortex lies in close proximity dorsally and medially to the anterior medial temporal lobe. Very often, orbitofrontal leads record potentials to words and faces that have a similar waveform to those observed in the temporal pole. In three of four patients with simultaneous recordings in both structures, these potentials were larger in the temporal pole. However, clear polarity inversions were observed in VLFC but not in the temporal pole. In any case, the most likely generator in the temporal pole is the rhinal cortex and, given the dense anatomical interconnections of the orbital and rhinal cortices (Barbas and De Olmos, 1990; Amaral *et al*, 1992; Morecraft *et al*, 1992), generation in both structures could be expected.

Large N4s are also observed in the fusiform g where they may be specific to words or faces (Halgren *et al*, 1994). In addition to these major generators small but apparently locally-generated N4s were noted in this study in every structure that was extensively sampled, including F3t (area 46), aCg, premotor and supplementary motor cortices, and, apparently in medial F1 and F2 as well. Similarly, recordings in posterior cortex found small N4 generators in several structures, including the supramarginal g, posterior cingulate g, and superior temporal sulcus (Halgren *et al*, 1992a, 1994).

The cognitive task correlates, timing, and anatomical extent of the N4 suggest that it embodies the global integration of the stimulus with the current cognitive context, in order to neurally-encode the event (see Halgren *et al*, 1994 for review). In particular, the N4 is only evoked by potentially meaningful stimuli such as words or faces, and N4 amplitude is modulated by the ease of integrating that event into the current cognitive context (Halgren and Smith, 1987; Halgren, 1990a, 1994). The current study (together with Halgren *et al*, 1994) demonstrates that the N4 has a very extensive anatomical distribution, including probable generators in most or all supramodal association cortex areas, and thus engages a sufficiently broad neural substrate to encode all of the knowledge domains that contribute to an encoded event. In general, this anatomical extent is identical for words as compared to faces, as would be predicted given that their integration seems to have access to much the same information. This corresponds to the position in cognitive neuropsychology that the semantic knowledge base is, to a large degree, unified. However, specialized knowledge bases supporting 'modular processing' also exist in the brain (McCarthy and Warrington, 1988). Indeed, this is how we interpret the N4

that was evoked by words but not by faces in the left F3t. The finding that the N4 was generated in both frontal lobes to both faces and words is not inconsistent with previous studies of the effects of lateralized frontal lobe lesions, and of 'split brain' patients. These studies have shown that, although word recognition is somewhat lateralized to the dominant hemisphere, and face recognition to the non-dominant, both can be processed by either hemisphere (Zaidel, 1989; Damasio *et al*, 1990). More generally, the similarity of the potentials evoked by words and faces provides support for the view that they pass through similar processing stages including feature detection, identification, and contextual integration (Coltheart, 1987; Just and Carpenter, 1987; Bruce, 1988).

The P3b follows the N4 in paradigms that require the definitive identification of the stimulus, and tends to be modulated by the same conditions that modulate the N4, but in the opposite direction (Halgren, 1990a). Indirect evidence suggests that the P3b represents the second phase of the same cognitive contextual integration process as the N4 (Pritchard, 1981). The first (N4) phase would provide relative excitation to facilitate the spread of information from its sensory and memory entry-points into the cognitive network, and the second (P3b) phase would provide both immediate recurrent inhibition to prevent this spread from recruiting spurious elements, and delayed recurrent inhibition to breakup recurrent excitatory loops and thus permit the evolution of new networks (Read *et al*, 1993).

The participation of the ventrolateral prefrontal cortex in the generation of the (N3)–N4–P3b sequence suggests that it also participates in the integration of complex meaningful stimuli with their cognitive context. This inference is consistent with several recent findings. Bachevalier and Mishkin (1986) found that ventromedial but not dorsolateral frontal lobe lesions impair visual object recognition in primates. Similarly, units responding specifically to faces have been found in this area, also in macaques (Pigarev *et al*, 1979; Skelly *et al*, 1992). Finally, the terminal areas of the ventral processing stream in the inferotemporal superior temporal sulcus, perirhinal and entorhinal cortices, project directly to the orbitofrontal cortex, as well as indirectly *via* the temporal pole, amygdala and hippocampal formation (Seltzer and Pandya, 1989; Amaral *et al*, 1992; Morecraft *et al*, 1992).

In metabolic studies also, the principal areas activated by face processing are in orbitofrontal cortex, in addition to occipital and temporal areas. For example, faces evoke metabolic activation of the VLFC (coordinates –3, 25, –17), in a task where the persons must be identified according to their profession (Sergent *et al*, 1992). The same site (coordinates –2, 21, –19) was activated in categorization of objects as animate or inanimate. The center of the activation, however, was far posterior and medial, compared to the area where the N4–P3b were generated in the present study. Even through the N4–P3b generating area extended far medial (to about ± 22 for the N4 and to about ± 10 for the P3b), and posterior (to +14), the N4–P3b were maximal at about ± 39, 43, –5, *ie* about 50 mm distant from the center of metabolic activation. Thus, it appears that PET was not able to detect the neural activation reflected in the large electrophysiological components generated in the ventrolateral prefrontal cortex reported here. That is, either: 1) the synchronous activation of synaptic populations generating the ventrolateral prefrontal EPs did not require sufficient metabolic activity to increase local blood flow above the detection threshold; or 2) the comparison tasks evoked approximately equal N4/P3b's in the VLFC. Judging from its localization, if the PET activation to faces was reflected in any EP component, it would be the N2–P3a-SW generated in the g rectus. Alternatively, individual classification tasks may evoke a novel EP component that was not evoked by the recognition memory tasks used here.

Response choice

A highly regular response observed in the precentral or premotor cortex was a late slow negativity to target faces and words. The waveform of this response was quite broad, beginning as early as 300 ms post-stimulus onset, and achieving maximal amplitude from 600 to 900 ms. This is at about the same time as (or just after) the average key-press latency (634 ms). Responses with similar latency and waveform but more variable task correlates were also observed medially, in the supplementary motor cortex and the central cingulate g. Local generation of these potentials is supported by their large amplitude (up to 150 μV), frequent focal responses (*ie* confined to one or a few contacts on a given electrode), and, in one patient, a polarity-inversion.

The anatomical localization, broad waveform, task correlates, as well as long latency of this

potential all suggest that it is related to the readiness potential (RP, also known as Bereitschaftspotential) that is recorded over the central scalp before voluntary movements (Vaughan, 1975; Halgren, 1990b). These potentials are usually observed in relation to regular uncued key-presses, where the RP is a widespread negativity beginning about 1–3 s before the movement (Kornhuber and Deecke, 1965; Shibasaki *et al*, 1980). The RP is also observed prior to movements that are triggered by a sensory stimulus, although they are smaller than to those that are self-initiated (Kutas and Donchin, 1980). Indeed, scalp recordings over Rolandic cortex in the same face and word recognition tasks as were presented here (Marinkovic and Halgren, in preparation) found a 'lateralized readiness potential' (*cf* Coles, 1989), with the same time-course as that observed for the depth-recorded potentials reported in the current study.

If the slow perimovement negativity observed in the present study is indeed an RP, then its probable widespread generation in precentral, premotor, cingulate, and supplementary motor cortices is in apparent conflict with the observations of Neshige *et al* (1988) suggesting generation confined to precentral cortex. However, RPs have been recorded in other studies outside of precentral cortex (Groll-Knapp *et al*, 1980; Ikeda *et al*, 1992), and unit-firing preceding movements have been reported in the human hippocampus (Halgren *et al*, 1978; Halgren, 1991; Heit *et al*, 1990), and n reticularis thalami (Raeva, 1986). Similarly, topography of the magnetic field associated with the RP after removal of one SMA suggests RP generation in the remaining SMA (Lang *et al*, 1991). Finally, lesions in humans often greatly reduce the RP without producing the pyramidal signs or clear weakness that would be expected were the precentral cortex involved (Shibasaki, 1975).

Similarly, in primates, possible generators of the RP have been found in precentral, postcentral, parietal and supplementary motor cortices, thalamus, basal ganglia and hippocampus (Arezzo *et al*, 1977, 1987; Johnson, 1980; Hashimoto *et al*, 1981; Sasaki and Gemba, 1991), with the extent of activation varying greatly among authors. The clear evidence for cell firing in premotor (PM) and supplementary motor (SMC) cortices during the RP (Pieper *et al*, 1980; Tanji and Kurata, 1982; Weinrich *et al*, 1984) suggests that the failure of some studies to find significant field-potentials in these areas may be due to task factors. Specifically, it seems possible that in simple repetitive key-pressing tasks, performance might become so overlearned and automatized that PM and SMC are no longer engaged. A role of the SMC in the preparation for and planning of voluntary movements (Wise, 1984) is supported by the akinetic mutism that may result from SMC lesions (Laplane *et al*, 1977), and by the increased SMC blood flow during the execution or even the planning of voluntary movements (Roland, 1985). The scalp topography of premovement potentials also suggests that SMC activity precedes that in the precentral gyrus (Deecke *et al*, 1985). The premotor cortex on the lateral surface of the frontal lobe (area 6) may also be activated during the preparation to move, when it plays a role that is unknown, but apparently distinct from that of the SMC (Wise, 1984; Goldberg, 1985).

Several authors have suggested that the RP may reflect the influence of contextual factors on movement (Eccles, 1982; Goldberg, 1985). This would imply that, in fact, the neural substrate of the RP may not be identical across different tasks, but that its extent decreases in highly automatic tasks such as the typical repetitive key-pressing task. In our task, an apparently widespread area is activated prior to a response, despite the fact that the motor action itself is focal and stereotyped. This suggests that the extent of the RP generator can be increased by the degree of cognitive control over movement. Conversely, the widespread and early involvement of premotor areas in generation of the RP may be taken as evidence for a widespread and gradual definition of the behavioral response, beginning long before the previous stage (of contextual integration) is complete. Lesions of these areas would be expected to disrupt actions that require more diverse information to be defined (*ie* are less automatized), or that are generated in response to internally-defined imperatives (*ie* are less environmentally-reactive).

Integrative functions

The results reported here suggest frontal lobe contributions to cerebral processing stages of perception, attention, integration and decision. The nature of these contributions can be inferred from a more global consideration of the unit-firing correlates of frontal neurons, and the neuropsychological deficits observed after frontal lesions.

Frontal lobe neurons in primates have been noted to fire in a sustained and specific manner during the maintenance of information in primary memory (Goldman-Rakic, 1988; Fuster, 1989). This firing may thus be considered to hold the current cognitive context in an active neuronal state. Apparently, different aspects of this context are held in different prefrontal fields, with sensory and spatial information in area 46, response mappings in premotor cortices, socio-emotional information in orbital areas, and visceral status in antero-inferior cingulate and g rectus. In contrast to this sustained activity, the cognitive EPs reported here are phasic events, that would be expected to interact with the sustained activity. Specifically, the sustained firing would be expected to contribute to the neural network being formed during the current EP component. That is, the information being integrated in an EP component might be expected to include information encoded in all of those areas where that EP component is generated. Each EP component involves multiple structures in posterior as well as anterior cortices. Thus, information from remote semantic memory (held in posterior cortical connections) as well as from recent declarative memory (held in medial temporal connections) could be integrated with contextual information (held in frontal cortex firing) during successive components. In short, it is hypothesized that the cognitive EP components envelope successive stages of event and action encoding in the firing of specific distributed networks of cortical and limbic neurons.

Socio-emotional context

Often, the most striking effects of frontal lobe lesions are on the personality. Furthermore, the major generators of the cognitive evoked potential components are mainly in the limbic and perilimbic portions of the frontal lobe. These EP components may thus reflect the dynamics of the frontal lobe contribution to emotional aspects of behavior (Halgren and Marinkovic, 1993). Specifically, the general mechanism described above may help provide a mechanism for the impulsivity, irresponsibility, social innappropriateness, and other personality changes that can follow frontal lesions. Lacking the socio-emotional input to the N2–P3a–SW network, attention might be oriented toward irrelevant or inappropriate items. Lacking the socio-emotional input to the encoding of events during the N4–P3b, their emotional dimension may be unappreciated. Finally, lacking a socio-emotional input during the RP, response choices could be impulsive and unrelated to the social situation.

The same general framework can be used to explicate the inconsistent results of frontal lesions on human emotional behavior, both within humans, and in comparison to lower species. For example, lesions of multiple limbic structures including the orbital and cingulate cortices as well as the amygdala region are necessary to produce the Kluver-Bucy syndrome in humans (Halgren, 1992), even though in monkeys bilateral amygdala lesions are sufficient (Guard *et al*, 1982). Similarly, bilateral amygdala lesions have profound effects on electrothermal responses to conditioned stimuli in monkeys (Bagshaw *et al*, 1972), but very little effect in humans during seemingly homologous situations (Tranel and Damasio, 1989). Apparently, the contribution of the frontal lobe to socio-emotional encoding during the cognitive EPs is sufficient in most people to compensate for the loss of posterior contributions, especially from the amygdala. One may speculate that the greater role of long-range contextual considerations and of self-monitoring in humans corresponds to a greater role for the frontal lobe in neural encoding.

Memory

The most specific and profound deficits in recent declarative memory nearly always involve bilateral hippocampal formation lesions (Squire and Zola-Morgan, 1991). However, subtle but significant disruptions of memory function can be observed after lesions to the frontal lobe (Halgren, 1994). Furthermore, parts of the frontal lobe commonly show functional deficits in pure amnesics, consisting of hypometabolism in the cingulate g and posterior orbital cortex (Fazio *et al*, 1992; Heiss *et al*, 1992). In contrast, frontal lesions do not necessarily result in deficits on standard tests of declarative memory (Milner *et al*, 1985; Stuss and Benson, 1986). The memory deficits following frontal lesions can be interpreted as reflecting a lack of contextual information, and/or of defective modulatory-strategic processes.

For example, subjects with partial fact amnesia may have varying degrees of amnesia for the sources of the facts that they do remember, with greater source amnesia associated with greater apparent frontal lobe damage (Shimamura and Squire, 1987; Janowsky *et al*, 1989). Similarly, a complete absence of contextual information may be reflected in confabulation (fallacious explana-

tions and misplaced experiences: Talland, 1965) which is correlated with the amount of suspected frontal lobe damage (Kapur and Coughlan, 1980; Squire, 1982). Whereas MTL lesions impair the recognition of words and paintings as having been presented previously in the same testing context, frontal lobe lesions impair the discrimination as to which of two previously presented stimuli occurred more recently (Milner *et al*, 1985; Squire, 1982). This may be due to the fact that recency judgements depend upon distinctive contextual markers associated with autobiographical time. Finally, amnesics who fail to exhibit a 'release from proactive interference' (suggesting a weak contextual influence on episodic memory) have correlated deficits indicating frontal dysfunction (Squire, 1982; Mayes and Meudell, 1983). Thus, source amnesia, confabulation, defective recency and memory veracity judgements, and a failure to release from proactive interference all appear to reflect inaccurate contextual information in the declarative memory trace due to frontal lobe damage.

In general, recall of specific autobiographical events requires a conscious effort to elaborate retrieval cues, and to suppress competing sensory or cognitive input from controlling the contents of awareness. This intentional probing of memory to reconstruct previous events and their contexts may also depend upon the frontal lobe, like other instances of intentionality in cognition (Stuss and Benson, 1986; Fuster, 1989). Similarly, at memory input patients with frontal lesions show impaired spontaneous encoding of material to be remembered, whereas other amnesics are normal in this regard (Butters and Cermak, 1980; William and Volpe, 1988).

Thus, the current results suggest a fractionation of the frontal lobe contribution to declarative memory, into: 1) a contribution of contextual information at the initial encoding of an event as well as during its recall in response to a cue event; and 2) a strategic direction of attention and more generally of cognitive resources towards promising external and internal cues. The contribution of contextual information appears to occur during the N4/P3b, which unites different frontal lobe structures (including area 46, anterior cingulate g, and especially the ventrolateral prefrontal cortex), with hippocampal formation (and other posterior structures) during event encoding. An influence of contextual information during retrieval could be embodied in the readiness potential. Finally, the strategic direction of attention appears to occur during the N2/P3s/SW.

Conclusion

This study provides evidence for the active involvement of the frontal lobe in all phases of the brain reaction to faces and words, from orienting and stimulus analysis, through cognitive integration and closure, to response selection. Each phase is represented by different EP components, and each is associated with different parts of the frontal lobe: 1) the orienting N2–P3a–SW is focused in the medial frontal lobe (aCg and gR); 2) the stimulus evaluation and word-specific potentials are localized to area 46; 3) the cognitive integration and encoding N4–P3b is most prominent in ventrolateral prefrontal cortex; and 4) the premovement RP is generated in premotor cortices. The current results thus define the phases during which different frontal regions presumably contribute to cognition.

In many cases, the electrical activity of these four frontal areas resembles that recorded in specific areas in the posterior cortex much more than that in any other frontal area. For example, the responses of the aCg and gR resemble most closely those of the pCg and sMg. Similarly, the VLFC responses resemble those of the amygdala and pHCg much more closely than those in any other frontal region. Thus, the present results confirm and extend proposals based on neuroanatomy and neuropsychology that place different frontal regions in specific neural networks with various posterior cortical and limbic areas (Goldman-Rakic, 1988; Mesulam, 1990; Barbas, 1992). Nonetheless, other evidence considered above suggests that across these different physiological phases, anatomical systems, and cognitive faculties, that the frontal lobe contribution could be constant, in the sense that it always consists of adding the current cognitive context to ongoing brain activity.

Acknowledgments

Supported by the USPHS (NS18741), the US Dept of Veterans Affairs and Office of Naval Research, the French MRT and INSERM, and NATO. For electrode implantation we thank Drs B Devaux, A Musolino and JP Chodkiewicz at Hôpital Sainte-Anne in Paris, and Drs A Birabin, JM Scarabin and J Faivre at Hôpital Pontchaillou in Rennes. We thank M Marinkovic for figure preparation, Dr JM Badier, R Olivier, T Gigg and D Kennelly for technical assistance, Drs M Smith and F Breton for participation in pilot studies, Pr AV Del-

gado-Escueta and M LaMarche for scientific support, Drs JP Vignal, S Trottier, D Broglin and E Landré for clinical collaboration, and our patients for their active cooperation.

References

Alain C, Richer F, Achim A, Saint-Hilaire JM (1989) Human intracerebral potentials associated with target, novel and omitted auditory stimuli. *Brain Topogr* 1, 237–245

Altaffulah I, Halgren E (1988) Focal medial temporal lobe spike-wave complexes evoked by a memory task. *Epilepsia* 29, 8–13.

Amaral DG, Price JL, Pitkänen A, Carmichael ST (1992) Anatomical organization of the primate amygdaloid complex. *In: The Amygdala. Neurobiological aspects of emotion, memory, and mental dysfunction* (Aggleton JP, ed) Wiley-Liss, New York, 1–66

Arezzo JC, Vaughan HG Jr, Koss B (1977) Relationship of neuronal activity to gross movement-related potentials in monkey pre- and postcentral cortex. *Brain Res* 132, 362–369

Arezzo JC, Vaughan HG, Kraut MA, Steinshneider M, Legatt AD (1986) Intracranial generators of event-related potentials in the monkey. *In: Evoked Potentials* (Cracco R, Bodis-Wollner I, eds) Liss, New York, 141–154

Arezzo JC, Tenke CE, Vaughan HG Jr (1987) Movement-related potentials within the hippocampal formation of the monkey. *Brain Res* 401, 79–86

Bachelier J, Mishkin M (1986) Visual recognition impairment follows ventromedial but not dorsolateral prefrontal lesions in monkeys. *Behav Brain Res* 20, 249–261

Bagshaw MH, Mackworth NH, Pribram KH (1972) The effect of resections of the inferotemporal cortex or the amygdala on visual orienting and habituation. *Neuropsychologia* 10, 153–162

Barbas H (1992) Architecture and cortical connections of the prefrontal cortex in the rhesus monkey. *In: Advances in Neurology, Vol 57: Frontal Lobe Seizures and Epilepsies* Chauvel P, Delgado-Escueta AV, Halgren E, Bancaud J, eds) Raven, New York, 91–115

Barbas H, Mesulam MM (1985) Cortical afferent input to the principalis region of the rhesus monkey. *Neuroscience* 15, 619–637

Barbas H, Pandya DN (1989) Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *J Comp Neurol* 286, 353–375

Barbas H, De Olmos J (1990) Projections from the amygdala to basoventral and mediodorsal prefrontal regions in the rhesus monkey. *J Comp Neurol* 300, 549–571

Barrett SE, Rugg MD, Perrett DI (1988) Event-related potentials and the matching of familiar and unfamiliar faces. *Neuropsychologia* 26, 105–117

Barrett SE, Rugg MD (1989) Event-related potentials and the semantic matching of faces. *Neuropsychologia* 27, 913–922

Benson DF (1979) *Aphasia, Alexia and Agraphia.* Churchill Livingstone, New York

Botzel K, Grüsser OJ (1989) Electric brain potentials evoked by pictures of faces ans non-faces: a search for 'face-specific': EEG-potentials. *Exp Brain Res* 77, 349–360

Brodmann K (1909) *Vergleihende Lokalisation lehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues.* Barth JA, Leipzig

Bruce V (1988) *Recognising Faces.* Erlbaum, Hillsdale, NJ

Buser P, Bancaud J (1983) Unilateral connections between amygdala and hippocampus in man. A study of epileptic patients with depth electrodes. *Electroencephalogr Clin Neurophysiol* 55, 1–12

Buser P, Bancaud J, Chauvel P (1992) Callosal transfer between mesial frontal areas in frontal lobe epilepsies. *In: Advances in Neurology, Vol 57. Frontal lobe seizures and epilepsies* (Chauvel P, Delgado-Escueta AV, Halgren E, Bancaud J, eds) Raven, New York, 589–604

Butter N, Cermak LS (1980) *Alcoholic Korsakoff's syndrome: An information processing approach to amnesia.* Academic Press, New York

Caramazza A (1988) Some aspects of language processing revealed through the analysis of acquired aphasia: the lexical systems. *Rev Neurobiol* 11, 395–357

Cavada C, Goldman-Rakic PS (1989) Posterior parietal cortex in rhesus monkey: II. Evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. *J Comp Neurol* 287, 422–445

Clarke JM, Chauvel P, Scarabin JM, Halgren E (1993) Auditory and visual representations in human prefrontal cortex. *Soc Neurosci Abst* 19 (abstract)

Coles MGH (1989) Modern mind-brain reading: Psychophysiology, physiology and cognition. *Psychophysiology* 26, 251–269

Coltheart M (1987) Functional architecture of the language-processing system. *In: The Cognitive Neuropsychology of Language* (Coltheart M, Sartori G, Job R, eds), Erlbaum, Hillsdale NJ, 1–25

Curran T, Tucker DM, Kutas M, Posner MI (1993) Topography of the N400: brain electrical activity reflecting semantic expectancy. *Electroencephalogr Clin Neurophysiol* 88, 188–209

Damasio A (1988) Synchronous activation in multiple cortical regions: a mechanism for recall. *Semin Neurosci* 2, 287–296

Damasio AR, Damasio H, Tranel D (1990) Face agnosia and the neural substrates of memory. *Annu Rev Neurosci* 13, 89–109

Deecke L, Kornhuber HH, Lang W, Lang M, Schreiber H (1985) Timing function of the frontal cortex in sequential motor and learning tasks. *Hum Neurobiol* 4, 143–154

Donchin E, Heffley E, Hillyard SA, Loveless N, Maltzman I, Ohman A, Rosler F, Ruchkin D, Siddle D (1984) Cognition and event-related potentials II. The orienting reflex and P300. *In: Brain and Information: Event-Related Potentials* (Karrer R, Cohen J, Tueting P, eds) New York Academy of Sciences, New York, 39–57

Eccles JC (1982) The initiation of voluntary movements by supplementary motor area. *Arch Psychiatr Nervenkr* 231, 423–441

Fazio F, Perani D, Gilardi MC, Colombo F, Cappa SF, Vallar G, Bettinardi V, Paulesu E, Alberoni M, Bressi S, Franceschi M, Lenzi GL (1992) Metabolic impairment in human amnesia: A PET study of memory networks. *J Cereb Blood Flow Met* 12, 353–358

Felleman DJ, VanEssen DC (1991) Distributed hierarchical processing in the primate cerebral cortex. *Cereb Ctx* 1, 1–47

Field TM, Woodson R, Greenberg R, Cohen D (1982) Discrimination and imitation of facial expressions by neonates. *Science* 218, 179–181

Fried I, Ojemann GA, Fetz EE (1981) Language-related potentials specific to human language cortex. *Science* 212, 353–356

Fuster JM (1989) *The Prefrontal Cortex: Anatomy, Physiology and Neuropsychology of the Frontal Lobe.* Raven, New York

Geschwind N (1965) Disconnexion syndromes in animal and man. *Brain* 88, 237–294

Goldberg G (1985) Supplementary motor artea structure and function: Review and hypotheses. *Behav Brain Res* 8, 567–616

Goldman-Rakic PS (1988) Topography of cognition: Parallel distributed networks in primate association cortex. *Annu Rev Neurosci* 11, 137–156

Groll-Knapp E, Ganglberger JA, Haider M, Schmid H (1980) Stereoelectroencephalographic studies on event-related slow potentials in the human brain. *In: Electroencephalography and Clinical Neurophysiology* (Lechner H, Aranibar A, eds) Excepta Medica, Amsterdam, 746–760

Guard O, Couailler JF, Graule A, Dumas R (1982) Le syndrome de Kluver et Bucy chez l'homme: Presentation d'un cas et revue de la littérature. *In: Comptes Rendus du Congrès de Psychiatrie et de Neurologie de langue Française* (Sizaret P, ed) Masson, Paris, 276–293

Halgren E (1990a) Insights from evoked potentials into the neuropsychological mechanisms of reading. *In: Neurobiology of Cognition* (Scheibel A, Weschsler A, eds) Guilford, New York, 103–150

Halgren E (1990b) Evoked potentials. *In: Neuromethods, Vol 15: Neurophysiological Techniques–Applications to Neural Systems* (Boulton AA, Baker G, Vanderwolf C, eds) Humana, Clifton, NJ, 147–275

Halgren E (1991) Firing of human hippocampal units in relation to voluntary movements. *Hippocamp* 1, 153–161

Halgren E (1992) Emotional neurophysiology of the amygdala within the context of human cognition. *In: The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction* (Aggleton JP, ed) Wiley-Liss, New York, 191–228

Halgren E (1994) Physiological integration of the declarative memory system. *In: The Memory System of the Brain* (Delacour J, ed) World Scientific, New York, 69–155

Halgren E, Smith ME (1987) Cognitive evoked potentials as modulatory processes in human memory formation and retrieval. *Hum Neurobiol* 6, 129–139

Halgren E, Marinkovic K (1993) Neurophysiological networks integrating human emotions. *In: The Cognitive Neurosciences* (Gazzaniga M, ed) MIT Press, Cambridge, Mass

Halgren E, Babb TL, Crandall PH (1978) Activity of human hippocampal formation and amygdala neurons during memory testing. *Electroencephalogr Clin Neurophysiol* 45, 585–601

Halgren E, Squires NK, Wilson CL, Rohrbaugh JW, Babb TL (1980) Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. *Science* 210, 803–805

Halgren E, Wilson CL, Squires NK, Engel J, Walter RD, Crandall PH (1983) Dynamics of the human hippocampal contribution to memory. *In: Neurobiology of the Hippocampus* (Seifert W, ed) Academic, London, 529–572

Halgren E, Stapleton JM, Smith ME, Altafullah I (1986) Generators of the human scalp P3s. *In: Evoked Potentials* (Cracco RQ, Bodis-Wollner, I, eds) Liss, New York, 269–289

Halgren E, Baudena P, Heit G, Chauvel P, Musolino A, Devaux B, Clarke J, Scarabin JM, Vignal JP, Birabin A (1992a) Endogenous potentials in the human superior temporal sulcus evoked by rare and repeated stimuli. *EPIC* Egar, Hungary, 55

Halgren E, Clarke JM, Hervé N (1992b) Rôle des enregistrements profonds dans la localisation, l'agencement séquentiel et la caractérisation des étapes de traitement de l'information dans le cerveau humain. *Psychol Fr* 37, 149–166

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

Hashimoto S, Gemba H, Sasaki K (1981) Distribution of slow cortical potentials preceeding self-placed hand and hindlimb movements in the premotor and motor areas of monkeys. *Brain Res* 224, 247–259

Heiss W-D, Pawlik G, Holthoff V, Kessler J, Szelies B (1992) PET correlates of normal and impaired memory functions. *Cereb Brain Metab Rev* 4, 1–27

Heit G, Smith ME, Halgren E (1990) Neuronal activity in the human medial temporal lobe during recognition memory. *Brain* 113, 1093–1112

Hillyard SA (1993) Electrical and magnetic brain recordings: contributions to cognitive neuroscience. *Curr Opin Neurobiol* 3, 217–224

Houser CR, Miyashiro JE, Swartz BE, Walsh GO, Rich JR, Delgado-Escueta AV (1990) Altered patterns of dynorphin immunoreactivity suggest mossy fiber reorganization in human hippocampal epilepsy. *J Neurosci* 10, 267–282

Ikeda A, Lüders HO, Burgess RC, Shibasaki H (1992) Movement-related potentials recorded from supplementary motor area and primary motor area. *Brain* 115, 1017–1043

Janowsky JS, Shimamura AP, Squire LR (1989) Memory and metamemory: Comparisons between patients with frontal lobe lesions and amnesic patients. *Psychobiology* 17, 3–11

Jeffreys DA, Musselwhite MJ (1987) A face-responsive visual evoked potential in man. *J Physiol* 1, 36

Johnson R Jr (1980) Event-related potentials accompanying voluntary movement in Rhesus monkeys. *Prog Brain Res* 54, 70–73

Johnson R Jr (1988) Scalp-recorded P300 activity in patients following unilateral temporal lobectomy. *Brain* 111, 1517–1529

Jurgens U (1982) Amygdalar vocalization pathways in the squirrel monkey. *Brain Res* 241, 189–196

Just MA, Carpenter PA (1987) *The Psychology of Reading and Language Comprehension*. Allyn and Bacon, Newton, MA

Kapur N, Coughan AK (1980) Confabulation and frontal lobe dysfunction. *J Neurol Neurosurg Psychiat* 43, 461–463

Karbe H, Szeiles B, Herholz K, Heiss W-D (1990) Impairment of language is related to left parieto-temporal glucose metabolism in aphasic stroke patients. *J Neurol* 237, 19–23

Knight RT (1984) Decreased response to novel stimuli after prefrontal lesion in man. *Electroencephalogr Clin Neurophysiol* 59, 9–20

Knight RT, Scabini D, Woods DL, Clayworth CC (1989) Contributions of temporal-parietal junction to the human auditory P3. *Brain Res* 502, 109–116

Kornhuber HH, Deecke L (1965) Hirnpotentialanderungen bei Willkurbewegungen und passiven Bewegungen des Menschen: Bereitschaftspotential und reafferente Potentiale. *Pflügers Archiv Gesamte Physiol* 284, 1–17

Kutas M, Donchin E (1980) Preparation to respond as manifested by movement-related brain potentials. *Brain Res* 202, 95–115

Kutas M, Van Petten C (1988) Event-related brain potential studies of language. *In: Advances in Psychophysiology* (Ackles PK, Jennings JR, Coles MGH, eds), JAI Press, Greenwich, Connecticut, 139–187

Lang W, Cheyne D, Kristeva R, Lindinger G, Deecke L (1991) Functional localisation of motor processes in the human cortex. *Event-Related Brain Res (EEG Suppl 42)* 97

Laplane D, Talairach J, Meininger V, Bancaud J, Orgogozo JM (1977) Clinical consequences of corticectomies involving the supplementary motor area in man. *J Neurol Sci* 34, 310–314

Liberman AM, Cooper FS, Shankweiler DP, Studdert-Kennedy M (1967) Perception of the speech code. *Psychol Rev* 74, 431–461

Mayes AR, Meudell Pr (1983) Amnesia in humans and other animals. *In: Memory in Animals and Humans* (Mayes A, ed) Van Nostrand Reinhold, Wokingham, Berkshire, 203–252

McCarthy RA, Warrington EK (1988) Evidence for modality-specific meaning systems in the brain. *Nature* 334, 428–430

McCarthy G, Wood CC, Williamson PD, Spencer DD (1989) Task-dependent field potentials in human hippocampal formation. *J Neurosci* 9, 4253–4268

Meadows JC (1974) The anatomical basis of prosopagnosia. *J Neurol Neurosurg Psychiat* 37, 489–501

Meltzoff AN, Moore MK (1977) Imitation of facial and manual gestures by human neonates. *Science* 198, 75–78

Mesulam MM (1990) Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Ann Neurol* 28, 597–613

Milner B, Petrides M, Smith ML (1985) Frontal lobes and the temporal organization of memory. *Hum Neurobiol* 4, 137–142

Mitzforf U (1985) Current source density method and application in cat cerebral cortex: Investigation of evoked-potentials and EEG-phenomena. *Physiol Rev* 65, 37–100

Morecraft RJ, Geula C, Mesulam MM (1992) Cytoarchitecture and neural afferents of orbitofrontal cortex in the brain of the monkey. *J Comp Neurol* 323, 341–358

Morton J, Patterson KE (1980) A new attempt at an interpretation, or, an attempt at a new interpretation. *In: Deep Dyslexia* (Coltheart M, Patterson KE, Marshall JC, eds), Routledge and Keagan Paul, London, 91–118

Musolino A, Tournoux P, Missir O, Talairach J (1990) Methodology of '*in vivo*' anatomical study and stereo-electroencephalographic exploration in brain surgery for epilepsy. *J Neurorad* 17, 67–102

Münte TF, Heinze HJ, Mangun GR (1993) Dissociation of brain activity related to syntactic and semantic aspects of language. *J Cog Neurosci* 5, 335–344

Naatanen R, Gaillard AWK (1983) The orienting reflex and the N2 deflection of the ERP. *In: Tutorials in Event Related Potential Research: Endogeneous Components* (Gaillard AWK, Riter W, eds) Elsevier, Amsterdam, 119–141

Neshige R, Lüders H, Shibasaki H (1988) Recording of movement-related potentials from scalp and cortex in man. *Brain* 111, 719–736

Ojemann G (1990) Organization of language cortex derived from investigations during neurosurgery. *Semin Neurosci* 2, 297–305

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

Paller KA, Kutas M, Mayes AR (1987) Neural correlates of encoding in an incidental learning paradigm. *Electroencephalogr Clin Neurophysiol* 67, 360–371

Paller KA, Kutas M (1992) Brain potentials during memory retrieval provide neurophysiological support for the distinction between conscious and unconscious recollection. *J Cog Neurosci* 4, 375–391

Patton HD (1982) Special properties of nerve trunks and tracts. *In: Physiology and biophysics. Vol 4* (Ruch T, Patton HD, eds) WB Saunders, Philadelphia, 101–127

Penfield W, Roberts L (1959) *Speech and brain mechanisms.* Princeton University Press, New Jersey

Petersen SE, Fox PT, Posner MI, Raichle ME, Mintun MA (1989) Positron emission tomographic studies of the processing of single words. *J Cog Neurosci* 1, 153–170

Petersen SE, Fox PT, Snyder AZ, Raichle ME (1990) Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. *Science* 249, 1041–1044

Pieper CF, Goldring S, Jenny AB, McMahon JP (1980) Comparative study of cerebral evoked potentials associated with voluntary movements in monkey and man. *Electroencephalogr Clin Neurophysiol* 48, 266–292

Pigarev IN, Rizzolatti G, Scandolara C (1979) Neurons responding to visual stimuli in the frontal lobe of macaque monkeys. *Neurosci Lett* 12, 207–212

Poeck K, de Bleser R, von Keyserlingk DG (1984) Computed tomography localization of standard aphasic syndromes. *In: Advances in Neurology, Vol 42: Progress in Aphasiology* (Rose FC, ed) Raven Press, New York, 71–89

Popovici M, Voinescu I, Lugoji G (1987) Aphasic symptoms and CT-determined cerebral lesions. *Rev Roum Med-Neurol Psychiat* 25, 161–179

Pritchard WS (1981) Psychophysiology of P300. *Psychol Bull* 89, 506–540

Puce A, Kalnins RM, Berkovic SF, Donnan GA, Bladin PF (1989) Limbic P3 potentials, seizure localization, and surgical pathology in temporal lobe epilepsy. *Ann Neurol* 26, 377–385

Raeva S (1986) Localization in human thalamus of units triggered during 'verbal commands', voluntary movements and tremor. *Electroencephalogr Clin Neurophysiol* 63, 160–173

Read W, Nenov VI, Halgren E (1993) The role of inhibition in memory-retrieval by hippocampal area CA3. *Neurosci Biobehav Rev*, in press

Regan D (1989) *Human Brain Electrophysiology.* Elsevier, New York

Roland PE (1985) Cortical organization of voluntary behavior in man. *Hum Neurobiol* 4, 155–167

Rösler F, Friederici A, Pütz P, Hahne A (1993) Event-related brain potentials while encountering semantic and syntactic constraint violations. *J Cog Neurosci* 5, 345–362

Rugg MD (1987) Dissociation of semantic priming, word and non-word repetition effects by event-related potentials. *Q Exp Psychol* 39, 123–148

Salamy A (1978) Commissural transmission: maturational changes in humans. *Science* 200, 1409–1410

Saron CD, Davidson RJ (1989) Visual evoked potential measures of interhemispheric transfer time in hmans. *Behav Neurosci* 103, 1115–1138

Sasaki K, Gemba H (1991) Cortical potentials associated with voluntary movements in monkeys. *Event-Related Brain Res (EEG suppl 42)* 80–96

Seeck M, Grüsser O-J (1992) Category-related components in visual evoked potentials: photographs of faces, persons, flowers and tools as stimuli. *Exp Brain Res* 92, 338–349

Seltzer B, Pandya DN (1989) Frontal lobe connections of the superior temporal sulcus in the rhesus monkey. *J Comp Neurol* 281, 97–113

Sergent J, Poncet M (1990) From covert to overt recognition of faces in a prosopagnosic patient. *Brain* 113, 989–1004

Sergent J, Shinsuke O, Macdonald B (1992) Functional neuroanatomy of face and object processing: A positron emission tomography study. *Brain* 115, 15–36

Shibasaki H (1975) Movement-associated cortical potentials in unilateral cerebral lesions. *J Neurol* 209, 189–198

Shibasaki H, Barrett G, Halliday E, Halliday AM (1980) Components of the movement-related cortical potential and their scalp topography. *Electroencephalogr Clin Neurophysiol* 49, 213–226

Shimamura AP, Squire LR (1987) A neurophysiological study of fact memory and source amnesia. *J Exp Psychol: Learn Mem Cog* 13, 464–473

Skelly JP, Wilson FAW, Goldman-Rakic PS (1992) Neurons in the prefrontal cortex of the macaque selective for faces. *Soc Neurosci Abst* 18, 705 (abstract)

Smith ME, Halgren E (1987) Event-related potentials elicited by familiar and unfamiliar faces. *Electroencephalogr Clin Neurophysiol (Suplt)* 40, 422–426

Smith ME, Halgren E (1989) Dissociation of recognition memory components following temporal lobe lesions. *J Exp Psychol (Learn Mem Cogn)* 15, 50–60

Smith ME, Stapleton JM, Halgren E (1986) Human medial temporal lobe potentials evoked in memory and language tasks. *Electroencephalogr Clin Neurophysiol* 63, 145–159

Smith ME, Halgren E, Sokolic M, Baudena P, Mussolino A, Liegerois-Chauvel C, Chauvel P (1990) The intracranial topography of the P3 event-related potential elicited during auditory oddball. *Electroencephalogr Clin Neurophysiol* 76, 235–248

Smith ME (1993) Neurophysiological manifestations of recollective experience during recognition memory judgments. *J Cog Neurosci* 5, 1–13

Spitz MC, Emerson RG, Pedley TA (1986) Dissociation of frontal N100 from occipital P100 in pattern reversal visual evoked potentials. *Electroencephalogr Clin Neurophysiol* 65, 161–168

Squire LR (1982) Comparisons between forms of amnesia: some deficits are unique to Korsakoff's syndrome. *J Exp Psychol: Learn Mem Cog* 8, 560–571

Squire LR, Zola-Morgan S (1991) The medial temporal lobe memory system. *Science* 253, 1380–1385

Squires NK, Squires KC, Hillyard SA (1975) Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. *Electroencephalogr Clin Neurophysiol* 83, 387–401

Squires NK, Halgren E, Wilson CL, Crandall PH (1983) Human endogenous limbic potentials: Cross-modality and depth/surface comparisons in epileptic subjects. *In: Tutorials in ERP Research: Endogenous Components* (Gaillard AWK, Ritter W, eds) North Holland, Amsterdam, 217–232

Srebo R (1985) Localization of cortical activity associated with visual recognition in humans. *J Physiol* 360, 247–259

Stapleton JM, Halgren E (1987) Endogenous potentials evoked in simple cognitive tasks: Depth components and task correlates. *Electroencephalogr Clin Neurophysiol* 67, 44–52

Stapleton JM, Halgren E, Moreno KA (1987) Endogenous potentials after anterior temporal lobectomy. *Neuropsychologia* 25, 549–557

Stuss DT, Benson DF (1986) *The Frontal Lobes*. Raven Press, New York

Szikla G, Bouvier G, Hori T, Petron V (1977) *Angiography of the Human Brain Cortex*. Springer-Verlag, New York

Talairach J, Szikla G, Tournoux P, Prossalentis A, Bordas-Ferrer M, Covello L, Jaco M, Mempel E (1967) *Atlas d'Anatomie Stereotaxique du Telencephale*. Masson et Cie. Paris

Talairach J, Bancaud J, Szikla G, Bonis A, Geir S, Vedrenne C (1974) *Approche Nouvelle de la Neurochirurgie de l'Epilepsie. Methodologie Stéréotaxique et Résultats Thérapeutiques*. Masson, Paris

Talairach J, Tournoux P (1988) *Co-Planar Stereotaxic Atlas of the Human Brain*. Thieme Medical Publishers. New York

Talland GA (1965) *Deranged Memory*. Academic, New York

Tanji J, Kurata K (1982) Comparison of movement-related activity in two cortical areas of primates. *J Neurophysiol* 48, 633–653

Tranel D, Damasio H (1989) Intact electrodermal skin conductance responses after bilateral amygdala damage. *Neuropsychologia* 27, 381–390

Van Petten C, Kutas M, Kluender R, Mitchiner M, McIsaac H (1991) Fractionating the word repetition effect with event-related potentials. *J Cog Neurosci* 3, 131–150

Vaughan HG Jr (1975) The motor potentials. *In: Handbook of Electroencephalography and Clinical Neurophysiology, Vol 81*. Elsevier, Amsterdam, 86–92

Vogt BA, Finch DM, Olson CR (1992) Functional heterogeneity in cingulate cortex: The anterior executive and posterior evaluative regions. *Cereb Ctx* 2, 435–443

Weinrich M, Wise SP, Mauritz KH (1984) A neurophysiological study of the premotor cortex in the rhesus monkey. *Brain* 107, 385–414

William H, Volpe BT (1988) Memory strategies with brain damage. *Brain Cogn* 8, 379–408

Wise SP (1984) The nonprimary motor cortex and its role in the cerebral control of movement *In: The non-primary motor cortex and its role in the cerebral control of movement* (Edelman GM, Gall WE, Cowan WM, eds) Wiley, NY, 525–555

Wise R, Chollet F, Hadar U, Friston K, Hoffner E, Frackowiak R (1991) Distribution of cortical neural networks involved in world comprehension and word retrieval. *Brain* 114, 1803–1817

Wood CC, McCarthy G (1985) A possible frontal lobe contribution to scalp P300. *Soc Neurosci Abst* 11, 879–870

Wood CC, McCarthy G, Allison T, Goff WR, Williamson PD, Spencer DD (1982) Endogenous event-related potentials following temporal lobe excisions in humans. *Soc Neurosci Abst* 8, 976–970

Wood CC, McCarthy G, Kim JH, Spencer DD, Williamson PD (1988) Abnormalities in temporal lobe event-related potentials predict hippocampal cell loss in temporal lobe epilepsy. *Soc Neurosci Abst* 14, 5 (Abstract)

Zaidel E (1989) Hemispheric independence and interaction in word recognition. *In: Brain and Reading* (von Euler C, Lundberg I, Lennerstrand G, eds), MacMillan, Hampshire, 77–97

Zatorre RJ, Evans AC, Meyer E, Gjedde A (1992) Lateralization of phonetic and pitch discrimination in speech processing. *Science* 256, 846–849